

# Co-morbidity of attention deficit hyper activity disorder and associated factors among children with seizure disorder attending pediatric seizure clinic a cross-sectional study at Gondar University hospital (2016), northwest, Ethiopia

Haregewoin Mulat Sebhat (✉ [mediaug14@gmail.com](mailto:mediaug14@gmail.com))

University of Gondar <https://orcid.org/0000-0001-6478-0075>

Niguse Muluneh

university of Gondar

Tewodros Eyasu

university of Gondar

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## Research article

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# Abstract

## Background

When attention deficit Hyperactivity Disorder (ADHD) presents in epileptic children, it makes the treatment complicated and the prognosis poor. Hence, understanding the magnitude of ADHD and associated factors would be important to have a policy intention towards these people and to design appropriate interventions. Therefore, the current study was conducted to determine co-morbidity of attention deficit hyperactivity disorder (ADHD) and associated factors in children with seizure disorders.

## Methods

A hospital based cross-sectional study was conducted by taking 260 children who had follow ups in the pediatric seizure clinic. The systematic random sampling technique was used to recruit participants. A structured, pretested and interviewer administered questionnaire which included questions on associated factors and standard disruptive behavioural disorder (DBD) rating scale was used to collect data. Data were coded, entered and cleaned by using the Epi-Data version 3.1 and exported to SPSS version 20 for further analysis. The multivariate binary logistic regression was used to check the association between independent and dependent variables. Variables with significant associations were identified on the basis of OR, with a 95%CI and p-value of  $< 0.05$  and considered as statistically significant.

## Result

The prevalence of ADHD among epileptic children was found to be 115(44.2%), with a confidence interval of (38.1-50.5), out of which only 3(2.6%) were detected as having mental health problems by the clinician. The predominant subtype was inattentive type 96(61.1%). Factors significantly associated with ADHD were male sex (AOR = 2.70 CI: 1.46-4.97), family history of seizure disorder (AOR=2.42 CI: 1.26-4.65), family history mental illnesses (AOR=4.14 CI: 1.76-9.68), sudden onset of seizure (AOR=2.37 CI: 1.32-4.27) and uncontrolled seizure (AOR=2.55 CI: 1.41-4.61).

## Conclusion

Attention deficit hyperactivity disorder was common among children with seizure disorders in the study area. Therefore, interventions that would address such factors would help to overcome further complications.

## Background

Attention Deficit Hyperactivity Disorder (ADHD) is one of the most common mental disorders that develop in children and becomes apparent in preschool and early school years. It is characterized by pervasive and impairing symptoms of inattention, hyperactivity, and impulsiveness that occur before 7 years of age(1)

The prevalence of attention deficit hyper activity disorder (ADHD) in the general population ranges between 3% and 5%(2). The prevalence is much higher ranging from 8 to 77% among children with epilepsy than in the general population(3). The prevalence of ADHD among children with epilepsy in high income countries ranges from 23 to 70%(4, 5). Clinical studies show that when ADHD presents in children with seizure disorders, it exerts its effect in the treatment and prognosis of the disorder. It can also have negative impacts on the affected child's behavioral, learning and social development. The studies suggest that 30-40% of children with epilepsy also present with ADHD(6, 7). Despite this high prevalence, ADHD often remains unrecognized and left without treatment.

Studies identified that the magnitude of the problem in children with epilepsy varied across the globe such as, 6.9% in Korea(8), 42.2% in China(9), 27.7% in Israel(10), 29.1% in Brazil(11), 12% in UK(12), 28% in Norway(13), 26.4% in USA(14) and 60.4% in Iran(15).

Another study conducted in central China showed that the magnitude of ADHD among children with epilepsy was 24.7%(16).

A recent study in the Indian tertiary medical center revealed that the co-morbidity of ADHD among epileptic children was 23%(17).

According to a study in Tanzania, the co-morbidity of ADHD among children with epilepsy showed that attention problem were more prevalent in children with epilepsy 53% compared with control groups (19%) (18).

Previous studies revealed that age, sex, type of epilepsy syndrome(6, 16), earlier epilepsy onset, longer period of antiepileptic medication, epileptic children's receiving a combination of antiepileptic drugs(7), and the frequency of seizures (15) were the most common associated factors of ADHD among epileptic children.

Many of the studies were outside Africa, and the magnitude of ADHD among epileptic children in Ethiopia, particularly in the study area was poorly understood. Understanding the magnitude of ADHD and associated factors would be important to formulate policies and design appropriate interventions. Hence, the aim of this study was to assess the prevalence of co-morbidity of ADHD and associated factors among epileptic children who had follow ups at Gondar University hospital pediatric seizure clinic.

## Methods

### Study setting and design

A hospital based cross-sectional design was used to assess attention deficit hyperactivity disorder (ADHD) and associated factors among children with seizure disorders attending the pediatric seizure clinic of the University of Gondar referral hospital. Gondar is located about 723 km from Addis Ababa and

65 km to north of Lake Tana. The University of Gondar referral hospital provides tertiary care to the population of Gondar and its neighboring regions.

All Children attending the pediatric seizure clinic and aged between 6 and 17 years were taken as the source population while children who were available during data collection were considered as the study population. As per the information obtained from the pediatric seizure clinic, about 40 epileptic children with mothers or caregivers used to visit the clinic per week. The single population proportion formula with an assumption of 95% confidence level, a 5% margin of error and 50 % prevalence and a 10% non-response rate were taken to determine the sample size as there were no similar studies in our country. Because the total population was less than 10,000, correction formula was used to get the final sample size of 265.

### **Data collection method and instrument**

Data were collected from parents or caregivers by using the interview technique with the standard DBD rating scale for investigating the presence of ADHD. The scale consists of 45 items representing symptoms of Disruptive Behavior Disorders that are conduct disorder (CD), oppositional defiant disorder (ODD) and ADHD. Of the 45 items, only 18 were used in this study.

Children whose responses to six of the nine questions on hyper activity were “pretty much” or “very much” were considered as positive for the ADHD hyperactive sub type, while children whose responses to the same number of inattentive questions were “pretty much” or “very much” were considered as positive for the ADHD inattentive sub type. A structured questionnaire was developed to identify factors associated with ADHD, and patient charts were revised to get seizure related factors. The internal validity of the instrument was also checked (Cronbach alfa = 0.957) and found to be acceptable.

### **Data quality assurance and analysis**

The collected data were coded, entered and cleaned by using Epi-Data version 3.1 and exported to SPSS version 20. Frequencies and cross tabulations were used to summarize descriptive statistics of the data and tables and graphs were used for presentation. Bivariate logistic regression was first fitted to identify potential confounding factors and variables with p-values less than 0.2 were entered in to the multiple logistic regression model using the backward selection method to identify factors associated with depression. The adjusted odds ratio with a 95% confidence interval was calculated to report the strength and significance of the association.

Data quality was managed by training and appropriate supervision of data collectors by the principal investigator. A pre-test was done on 42 children at Feleg-hiwot hospital pediatric seizure clinic, Bahirdar. Appropriate modifications were made on the instrument after analyzing the pre-test result before the actual data collection.

## **Results**

## **Socio-demographic and family related factors**

A total of 260 children on follow up at Gondar University hospital pediatric seizure clinic participated in the study with a response rate of 98.1%. Out of the total participants, 158(60.8%) were male sex, with a mean age of  $10.5 \pm 2.7$  years (Table 1).

Table1.Socio-demographic and family related characteristics of participants (n=260), university of Gondar referral hospital

	frequency	Percent (%)	
<b>Age</b>	184	70.8	mean age
<b>7-11</b>	76	29.2	10.5± 2.7 years
<b>≥12</b>			
<b>Sex</b>	158	60.8	
<b>Male</b>	102	39.2	
<b>Female</b>			
<b>Religion</b>	214	82.3	
<b>Orthodox</b>	46	17.7	
<b>others</b>			
<b>Ethnicity</b>	244	93.8	
<b>Amhara</b>	16	6.2	
<b>others</b>			
<b>Is the mother alive</b>	239	91.9	
<b>Yes</b>	21	8.1	
<b>No</b>			
<b>Is the father alive</b>	237	91.2	
<b>Yes</b>	23	8.8	
<b>No</b>			
<b>Living arrangement</b>	222	85.4	
<b>-With both parents</b>	38	14.6	
<b>-One parent or others</b>			
<b>Seizure disorder in the family</b>	69	26.5	
<b>Yes</b>	191	73.5	
<b>No</b>			
<b>Mental illness in the family</b>	41	15.8	
<b>Yes</b>	219	84.2	
<b>No</b>			

## Pregnancy, delivery and childhood related factors

One fourth, 69(26.5%), and 41(15.8%) of the children had family history of seizure disorder and psychiatric illness, respectively, while 32 (12.3%) had severe medical illness before the age of seven years (Table 2)

Table 2 Pregnancy, delivery and childhood related characteristics of participants (n=260), University of Gondar referral hospital

	frequency	Percent (%)
<b>Mother's health during pregnancy</b>	251	96.5
Healthy	3	1.5
Acute illness	6	2.3
Chronic illness		
<b>Substance abuse during pregnancy</b>	256	98.5
Yes	4	1.5
No		
<b>Place of delivery</b>	190	73.1
Home	70	26.9
Health institution		
<b>Mode of delivery</b>	219	84.2
SVD	28	10.8
Instrumental delivery	13	5
CS		
<b>Birth complication</b>	26	90
Yes	234	10
no		
<b>Feeding</b>	244	93.8
Exclusive breast feeding	3	1.2
Formula	13	5
Mixed		
<b>Health problem before the age of 7 yrs</b>	228	87.7
Yes	32	12.3
no		

## Seizure related factors

Most, 224(86.2%) of the children were diagnosed with generalized tonic- clonic seizure; among 135(51.9%) participants' seizure started suddenly. More than half 173(66.5%) of the children had seizure at least once per month before they started medication. Seizure was not controlled among more than half 142(54.6%) of the participants (Table 3).

Table 3 Seizure related factors (n=260), University of Gondar referral hospital

	frequency	Percent (%)
<b>Age of set</b>	152	58.5
Before age 7	108	41.5
Age 7 above		
<b>One set</b>	135	51.9
Sudden	125	48.1
gradual		
<b>Seizure type</b>	224	86.2
Grandmal	36	13.8
others		
<b>Last seizure</b>	142	54.6
Within 6 months	118	45.4
Before 6 months		
<b>Number of medication</b>	181	69.6
Single	79	30.4
combination		

## Prevalence of ADHD

As shown in Figure 1, the magnitude of ADHD among epileptic children was 115(44.2) with a confidence interval of (38.1-50.5), out of which only 3(2.6%) were detected as having mental health problems by the clinician. The predominant 96(61.1%), subtype was inattentive followed by the hyperactive subtype 61(38.9%).

Fig.1 Magnitude of attention deficit hyperactivity disorder (ADHD)

## Factors associated with ADHD

Among all the covariate age group, sex, mothers and fathers, living arrangements, family history of seizure, and mental illness, seizure type, onset and status were found to have p-value less than 0.2 in the bi-variable logistic regression and considered for the multiple logistic regression model. The model goodness of fit was tested using the Hosmer and Lemeshow test and the p-value was found to be 0.719 and revealed the model was good.

Factors significantly associated with depression were male sex, (AOR = **2.70 CI: 1.46-4.97**), family history of seizure disorder, (AOR= **2.42 CI:1.26-4.65**), family history of other mental illnesses, (AOR=**4.14(1.76-9.68)**), sudden onsets of seizure (AOR= **2.37(1.32-4.27)**) and uncontrolled seizures, **2.55(1.41-4.61)** (Table 4)

**Table 4. Factors associated with ADHD among children with seizure disorders at University of Gondar referral hospital**

	ADHD		COR(95%CI)	AOR(95%CI)
	Yes	No		
<b>Age</b>	86	98	1.42(0.82-2.45)	1.57(0.82-3.02)
7-11	29	47	1.00	1.00
≥12				
<b>Sex</b>	86	72	3.01(1.76-5.11)	<b>2.70(1.46-4.97)*</b>
Male	29	73	1.00	1.00
female				
<b>Mother alive</b>	100	139	3.41(1.54-4.82)	0.659(0.16-2.17)
Yes	15	6	1.00	1.00
No				
<b>Father alive</b>	98	139	4.02(1.53-10.5)	0.38(0.87-1.65)
Yes	17	6	1.00	1.00
No				
<b>Living arrangement</b>	90	25	2.82(1.37-5.81)	1.14(0.38-3.61)
Both parents	25	13	1.00	1.00
One parent or others				
<b>FamilyHx of seizure</b>	43	26	2.73(1.55-4.82)	<b>2.42(1.26-4.65)*</b>
Yes	72	119	1.00	1.00
No				
<b>Family Hx of mental illness</b>	31	10	4.98(2.32-10.68)	<b>4.14(1.76-9.68)*</b>
Yes	84	135	1.00	1.00
No				
<b>Seizure type</b>	107	117	3.2(1.39-7.33)	1.86(0.73-4.75)
<b>GTC</b>	8	28	1.00	1.00
<b>Others</b>				
<b>Seizure onset</b>	74	61	2.48(1.50-4.11)	<b>2.37(1.32-4.27)*</b>
Sudden	41	84	1.00	1.00
Gradual				
<b>Seizure status</b>	75	67	2.18(1.32-3.61)	<b>2.55(1.41-4.61)*</b>

Uncontrolled	118	78	1.00	1.00
Controlled				

\*=P value < 0.05

## Discussion

The prevalence of ADHD among children with seizure disorder was 44.2% (95%CI: 38.1%, 50.5%) which is in line with the result of a study conducted in China(7). The current estimate is by far higher than the results of the studies conducted in Korea(5), Israel(8), Brazil(9), Norway(11), USA(12), Central china (14) and India(15). The differences were due to variations in sample sizes, study populations and screening tools. The sample sizes in the other studies were lower than that of the current study. The studies conducted in Korea and India used DSM-IV criterion which was a diagnostic manual, and epileptic children were observed to confirm the presence of ADHD symptoms. In addition they excluded children who had intellectual disability, other psychiatric disorders and chronic medical illnesses. In the USA, only children with new onsets of epilepsy diagnosed in the past 12 months were taken.

The magnitude of ADHD in our work was lower than those of previous studies conducted in Iran (13) and Tanzania(16), perhaps due to sample size and assessment tool differences. The study conducted in Iran used highly sensitive child symptom inventory. Another study in Tanzania took a large sample and used a child behavioral checklist.

The current study was identified different factors that had associations with ADHD during the course of seizure disorders. Male sex was one of the associated factors of the magnitude of ADHD, a result in line with that of a study conducted in India(15). This was different from what was reported from Korea (5) and the USA(12).

The other factor that had a significant association with ADHD was family history of seizure disorder. If a child had a family history of seizure disorders, the illness would be very severe, and the severity of the seizure disorder might increase the risk of developing childhood psychiatric disorders, including ADHD. Previous studies we reviewed didn't assess family history of seizure disorder as an associated factor.

In contrast to a study in India(15), family history of psychiatric illness was significantly associated with the magnitude of ADHD among children with seizure disorders. That was evidenced by the role of genetic predisposition for psychiatric disorders. Other studies didn't assess family history of psychiatric disorder as a contributing factor.

The other contributing factor was uncontrolled seizure. Children who had seizure episodes during the last six months, had more than two times increased risk for ADHD compared with children who were seizure free for more than six months, similar to the finding in India(15). It was however different what were reported from in Korea (5) and the USA (12) which showed that children's seizure status had no significant associations with the prevalence of ADHD.

Sudden onset of seizure disorder is among the associated factors of the magnitude of seizure disorders. That was because when the onset is sudden the illness becomes severe. This result was different from what was noted in USA, where seizure onsets were not significant associated factor of the prevalence of ADHD.

Like studies conducted in Korea (5), USA (12) and India (15) age in this work had no significant association with the magnitude of ADHD. Number of antiepileptic drugs, age at onset and prolonged antiepileptic treatments were not associated significantly with ADHD in the current study in distinction from the result of a study conducted in China (7).

In contrast to the studies conducted in Korea (5) and Tanzania (16), type of epilepsy syndrome had no significant association with the magnitude of ADHD in our study. The institution based cross-sectional design of our study has limited its generalizability as well as its capacity of establishing temporal relationships, respectively.

## **Conclusion And Recommendation**

The magnitude of ADHD among children with seizure disorders was relatively higher in this attempt than most study reports worldwide. Despite this high prevalence only a few number of children were diagnosed as having ADHD. Male sex, sudden onsets of seizure, family history of seizure and that of other psychiatric disorders as well as uncontrolled seizures were factors that increased the odds of ADHD. To increasing early detection and management of co-morbid ADHD training should be given about mental health problems for health professional working in pediatric seizure clinic. Treating seizure disorder appropriately and controlling seizure could minimize the risk of having co-morbid ADHD.

## **Declarations**

### **Ethical approval and consent to participate**

Ethical clearance was obtained from the University of Gondar Ethical Review committee (IRB). A written support letter was secured from the hospital chief executive officer and medical director. Verbal and written consent was sought from participants' parents or care givers' before starting data collection. Parents of children confirmed to have ADHD were advised and linked to the psychiatry clinic of the hospital.

### **Availability of data and materials**

The datasets generated used and/or analyzed during the current study are available from the corresponding author on reasonable request.

## **Competing interest**

There is no any competing interest

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## Author's contributions

HM was initializing and designed the study. HM,NY,TE contribute in data collection and analysis. HM wrote the paper. HM,NY,TE edit the paper.

## Abbreviations

AOR= adjusted odd ratio

ADHD= Attention Deficit Hyperactivity Disorder

CD= conduct disorder

COR= crude odd ratio

DBD= disruptive behavioural disorder

ODD= oppositional defiant disorder

OR=odd ratio

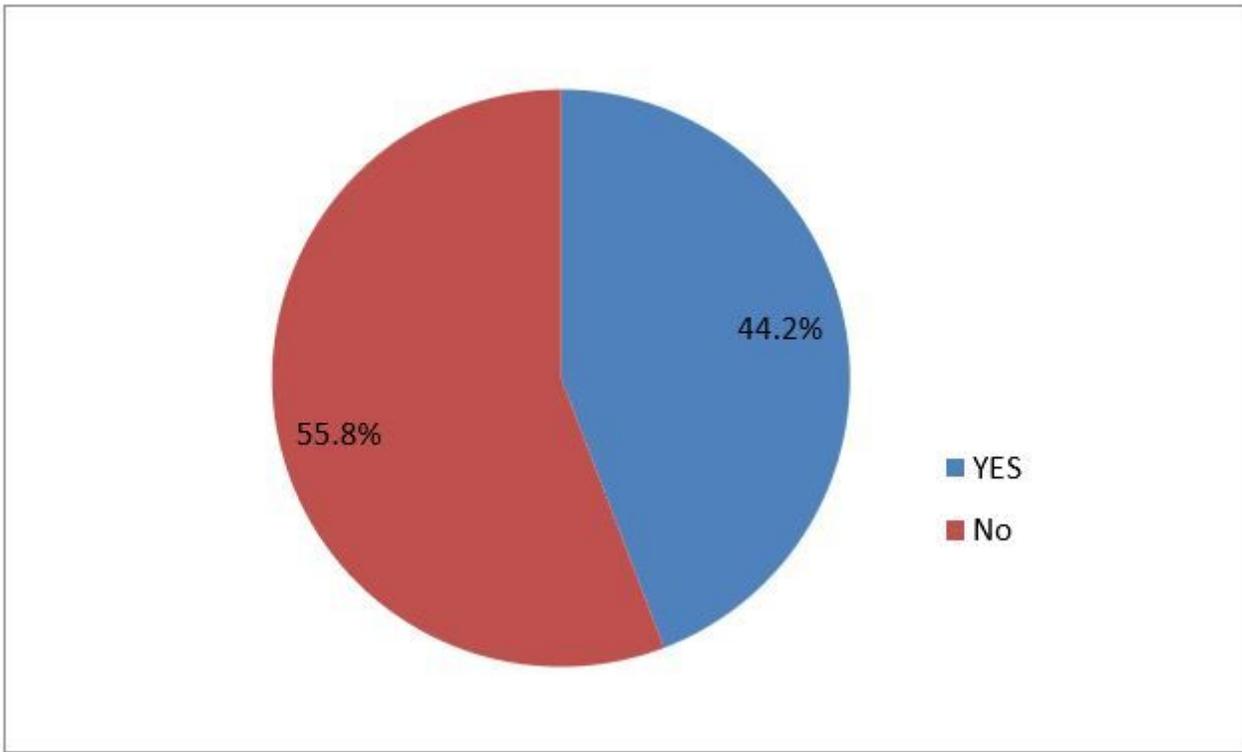
SPSS= statistical package for social sciences

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# Figures



**Figure 1**

magnitude of attention deficit hyperactivity disorder