

# Comparative Analysis of Seizure Characteristics in Adherent vs. Non-Adherent Antiepileptic Drug Users

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**ABSTRACT:** *Background:* Epilepsy is a common neurological disorder in children, characterized by recurrent seizures that can significantly impact their quality of life. This study aimed to compare seizure characteristics in adherent vs. non-adherent antiepileptic drug users. *Methods:* This cross-sectional study was conducted at the Department of Pediatric Neurology and Development; National Institute of Neurosciences and Hospital (NINS&H), Dhaka, from January 2022 to December 2022. A total of 250 children were selected study subjects by systematic random sampling without a sampling frame technique. Children with epilepsy were categorized into two groups, AEDs adherent (n1) and non-adherent group (n2). Data analysis was carried out using Statistical Package for Social Sciences (SPSS- 23). Statistical significance and confidence interval were set at  $p < 0.05$  and 95% level respectively. *Result:* The analysis showed no significant differences between adherent and non-adherent AED users in seizure onset age (both ~67%) or seizure type (focal onset most common). However, non-adherent children more often had seizures lasting less than 1 minute (91.5% vs. 75.9%,  $p = 0.002$ ), while longer seizures (>5 minutes) were more frequent in the adherent group (8.3% vs. 4.2%,  $p = 0.002$ ). *Conclusion:* The study found no significant differences in age of onset, seizure type, or epilepsy diagnosis between adherent and non-adherent children. However, non-adherent children had shorter seizures, while adherent children experienced longer ones. Despite similar seizure characteristics, AED adherence remains crucial for better seizure management and preventing complications.

**Keywords:** Epilepsy, Seizure, Antiepileptic Drug, Focal Seizure.

## Article at a glance:

**Study Purpose:** The purpose of this study is to compare seizure characteristics — such as frequency, severity, duration, type, and associated complications — between patients who are adherent to antiepileptic drug therapy and those who are non-adherent.

**Key findings:** Non-adherent patients typically experience more frequent seizures than adherent patients.

**Newer findings:** Recent research highlights that forgetfulness, fear of side effects, and mental health issues (like depression) are strong predictors of non-adherence, even more so than socioeconomic factors.

**Abbreviations:** AED: Antiepileptic Drug.

## INTRODUCTION

Epilepsy is a neurological disorder marked by abnormal brain activity, leading to seizures, unusual behavior, altered sensations, and sometimes loss of awareness. It has wide-ranging neurological, cognitive, psychological, and social impacts and contributes significantly to the global disease burden.<sup>1</sup> In 2014, the International League Against Epilepsy (ILAE) redefined epilepsy as a brain disease characterized by any of the following: (i) at least two unprovoked (or reflex) seizures occurring more than 24 hours apart, (ii) a single unprovoked (or reflex)

seizure with a recurrence risk of at least 60% over the next 10 years, similar to the general risk after two unprovoked seizures, or (iii) a confirmed diagnosis of an epilepsy syndrome.<sup>2</sup> In Bangladesh, a nationwide survey reported an epilepsy prevalence of 8.4 per 1,000 people, with a similar rate of 8.2 per 1,000 among children under 18 years. Among those affected, 65.1% have active epilepsy, and 72.5% exhibit low adherence to treatment, contributing to a significant treatment gap.<sup>3</sup> Despite advances in understanding its neurological complexities, epilepsy treatment remains primarily symptomatic. Management should

be individualized, with treatment selection focused on controlling seizures while also preventing associated complications.<sup>4</sup> The goal of antiepileptic drug (AED) therapy is to achieve seizure freedom. However, this goal is often unmet due to poor adherence or an inadequate drug regimen. Effective epilepsy treatment focuses on maintaining a balance between seizure prevention and minimizing side effects to a tolerable level for the patient.<sup>5</sup> Several factors contribute to poor seizure control or uncontrolled epilepsy, including lack of awareness about the disease, unavailability of medications, irregular intake of antiepileptic drugs, premature discontinuation after transient seizure control, low education levels, unemployment, rural residence, early onset of seizures, and higher initial seizure frequency.<sup>6</sup> Poor adherence to prescribed medication is the primary reason for unsuccessful epilepsy treatment.<sup>7</sup> In children with epilepsy, non-adherence remains a significant challenge in achieving the crucial therapeutic goal of complete seizure control.<sup>8</sup>

Non-adherent patients face increased seizure frequency and severity, resulting in a higher likelihood of emergency room visits, hospital admissions, greater risk of injuries and fractures, and significantly elevated inpatient, outpatient, and overall healthcare costs.<sup>9</sup> Non-adherence is defined as the tendency to forget, avoid, discontinue medication, or modify the prescribed dosage without healthcare provider guidance.<sup>10</sup> Non-adherence can vary from occasionally missing a dose to consistently failing to follow prescribed medication regimens. In chronically ill children, it can lead to increased morbidity and mortality, reduced cost-effectiveness due to wasted medications, more frequent clinic visits, emergency room admissions, hospitalizations, and potential bias in clinical trials assessing new therapies.<sup>11, 12</sup> Non-adherence to medication is common among children with epilepsy, compromising the key therapeutic goal of seizure control. Contributing factors may include low socioeconomic status, financial constraints, forgetfulness, multiple drug therapy, prolonged treatment duration, lack of improvement, and medication side effects, inadequate counseling to patient or parents during initiation of treatment, and sometimes decisions based on personal judgments about the effectiveness of the proposed treatment.<sup>13, 14</sup> Adherence to AED medication can be measured using various methods, such as drug level monitoring, pill count, pharmacy refills, and patient self-report. Each

of these methods has its own advantages and limitations in terms of accuracy, feasibility, and reliability.<sup>15</sup> In this study, the Morisky Medication Adherence Scale (MMAS-8), an eight-item self-report measure of medication-taking behavior developed by Uchmanowicz *et al.*, was used to assess adherence.<sup>16</sup> The MMAS-8 is widely used due to evidence from several studies demonstrating its strong psychometric properties, making it a reliable tool for assessing medication adherence, high sensitivity (74.1%) and specificity (38.3%).<sup>17, 18</sup> This study aimed to compare seizure characteristics in adherent vs. non-adherent antiepileptic drug users.

## METHODS

This cross-sectional study was conducted at the Department of Pediatric Neurology and Development; National Institute of Neurosciences and Hospital (NINS&H), Dhaka, from January 2022 to December 2022. Diagnosed cases of Epilepsy (based on ILAE) who visited OPD or were admitted to the inpatient department of Paediatric Neurology, National Institute of Neurosciences and Hospital, Sher-E-Bangla Nagar were considered as the study population. A total of 250 children were selected study subjects by systematic random sampling without a sampling frame technique. Screening was done by thorough history and clinical assessment. Data was collected by face-to-face interview through a preformed semi-structured questionnaire containing information about the age of onset & type of epilepsy, clinical diagnosis, name & dosage of AEDs & status of seizure. Medication non-adherence was assessed by the Morisky Medication Adherence Scale with eight items (MMAS-8) based on self/caregiver reports. After assessment by MMAS-8, children with epilepsy were categorized into two groups, AEDs adherent (n1) and non-adherent group (n2). Data analysis was carried out using Statistical Package for Social Sciences (SPSS- 23). Continuous variables were expressed as the means  $\pm$  SD, and categorical variables were expressed as percentages, frequencies, and proportions. Means were compared using Student's t-test for two groups. Proportions were compared using the chi-square test. Then Logistic regression analysis was performed to determine the factors influencing the risk of seizures. Statistical significance and confidence interval were set at  $p < 0.05$  and 95% level respectively. Written approval was taken from the concerned authority (ethical committee of NINS&H and BCPS) and the

department with due procedure. Informed written consent was taken from the parents or legal guardians.

#### Inclusion Criteria

Children with epilepsy and  
Who had been on at least one antiepileptic drug for 1 year or more before the study and

Aged >1 year to under 18 years.

#### Exclusion Criteria

Patients with comorbid chronic illnesses require daily medication (eg, asthma, kidney diseases, chronic liver disease, etc.).

## RESULTS

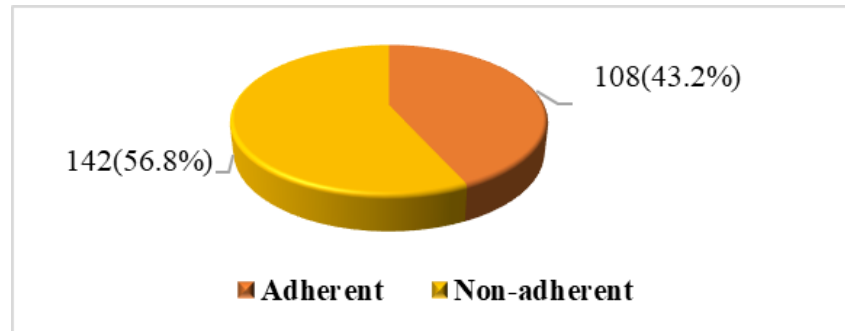


Figure 1: Distribution of Children According to AEDs Non-Adherence

Figure 1 shows that out of 250 participants, 142 (56.8%) had non-adherence, while 108 (43.2%) patients/respondents had adherence to AEDs.

Table 1: Comparison of Sociodemographic Characteristics Between the Studied Groups (n=250)

Variables	Adherent Group n <sub>1</sub> =108(43.2%)	Non-adherent Group n <sub>2</sub> =142(56.8%)	p-value
<b>Age group (years)</b>			
1-5	46(42.6%)	61(43.0%)	-
>5-10	40(37.0%)	52(36.6%)	
>10-15	22(20.4%)	29(20.4%)	
Total	108(100.0%)	142(100.0%)	
Mean±SD	6.65±3.84	6.67±3.74	0.922
<b>Gender</b>			
Male	70(64.8%)	97(68.3%)	-
Female	38(35.2%)	45(31.7%)	
Male: female ratio	1.8:1	2.2:1	0.561
<b>Residence</b>			
Urban	70(64.8%)	89(62.7%)	0.728
Rural	38(35.2%)	53(37.3%)	
<b>Maternal/caregiver education</b>			
No formal education	13(12.0%)	12(8.5%)	0.012*
Primary	65(60.2%)	62(43.7%)	
Secondary/SSC	21(19.4%)	42(29.6%)	
Above secondary	9(8.3%)	26(18.3%)	
<b>Father's occupation</b>			
Service	41(38.0%)	32(22.5%)	0.176
Business	63(50.4%)	84(59.2%)	
Others (farmers, shopkeepers)	24(19.2%)	26(18.3%)	
<b>Monthly family income (Tk.)</b>			
<10000 Tk.	34(31.4%)	68(47.9%)	0.026*

10000 – 30000 Tk.	52(47.9%)	48(33.8%)
>30000 Tk.	22(20.4%)	26(18.3%)

\*= significant

Table 1 shows most children were between 1-5 years, that is 42.6% in the adherent group and 43.0% in the non-adherent group. Comparing between the mean ages of the two groups showed no statistical significance. In both adherent and non-adherent groups majority of children were male, 64.8% and 68.3% respectively, but that difference was not statistically significant. Comparing the distribution of study subjects by residence no statistical difference was observed between the two groups. The highest percentage of respondents belonged to urban areas in both groups. 72.2% of mothers in the adherent group had primary-level education or had no formal

education. Whereas, in the non-adherent group, primary level education or no formal education was found in 52.2% of mothers. This difference was statistically significant. Most of the fathers' profession was business in both groups (50.4% in the adherent group and 59.2% in the non-adherent group) and the difference between the groups was not statistically significant. Regarding family income, statistically significant differences were present between the two groups. The adherent group had higher monthly family income (47.9% had 10,000-30,000 tk and 20.4% had >30,000 tk) than the non-adherent group (<10000 tk. in 47.9% and 10,000-30,000 tk in 33.8% cases).

**Table 2: Comparison of Characteristics of Seizures Between the Studied Groups (n=250)**

Variables	Adherent Group n <sub>1</sub> =108(43.2%)	Non-adherent Group n <sub>2</sub> =142(56.8%)	p-value
<b>Age of onset (years)</b>			
<5	72(66.7%)	95(66.9%)	0.398
5-10	34(31.5%)	40(28.2%)	
>10	2(1.9%)	7(4.9%)	
<b>Type of seizure</b>			
Focal onset	67(62.0%)	91(64.1%)	0.394
Generalized onset	29(26.9%)	42(29.6%)	
Unknown onset	12(11.1%)	9(6.2%)	
<b>Frequency of seizure</b>			
Daily	18(16.7%)	23(16.2%)	0.245
Weekly	5(4.6%)	17(12.0%)	
Fort nightly	14(13.0%)	17(12.0%)	
Monthly or more interval	71(65.7%)	85(59.9%)	
<b>Duration of seizure</b>			
<1min	82(75.9%)	130(91.5%)	0.002*
1-5min	17(15.7%)	6(4.2%)	
>5min	9(8.3%)	6(4.2%)	
<b>Epilepsy type</b>			
Focal epilepsy	55(50.9%)	79(55.6%)	0.271
Generalized epilepsy	29(26.9%)	44(31.0%)	
Combined generalized & focal epilepsy	10(9.3%)	10(7.0%)	
DEEs	14(13.0%)	9(6.3%)	

\*= significant

Table 2 shows, that most of the respondents of both groups had onset of a seizure before 5 years of age (66.7% in the adherent group and 66.9% in the non-adherent group) and the difference between the groups was not statistically significant. In both

adherent and non-adherent groups, the majority of children had focal onset seizure, 62.0% and 64.1% respectively and the difference was not statistically significant. Comparing the frequency of seizures, no statistical difference was observed between the two

groups. The highest percentage of respondents had a seizure at an interval of one month or more in both groups (65.7% in the adherent & 59.9% in the non-adherent group). The majority of participants had a history of seizure episodes persisting for less than 1 minute in both groups (75.9% in the adherent group and 91.5% in the non-adherent group). On the other hand, seizures persisting for more than 5 minutes were more common in the adherent group (8.3%) than

in the non-adherent group (4.2%). These differences were statistically significant. Among the study participants, about half of the patients were diagnosed with focal epilepsy in both groups (50.9% and 55.6% in adherent and non-adherent groups respectively). The next common type was generalized epilepsy. In the adherent group, 13% of participants were diagnosed as DEEs which was more than the other group but was not statistically significant.

**Table 3: Comparison of AED Utilization Between the Studied Groups (n=250)**

	<b>Adherent Group n<sub>1</sub>=108(43.2%)</b>	<b>Non-adherent Group n<sub>2</sub>=142(56.8%)</b>	<b>p-value</b>
<b>Type of AED therapy</b>			
Monotherapy	84(77.8%)	110(77.5%)	0.953
Polytherapy	24(22.2%)	32(22.5%)	
Total	108(100.0%)	142(100.0%)	-
<b>Monthly cost (Tk)</b>			0.385
Cost (Tk.) (mean±SD)	1406.7±2639.1	1183.8±1019.2	
<b>Name of AED</b>			
SVA	25(23.1%)	36(25.4%)	0.350
CBZ/OXC	41(38.0%)	58(40.8%)	
SVA+Others*	14(13.0%)	12(8.5%)	
CBZ+Others*	3(2.8%)	12(8.5%)	
ACTH	7(6.5%)	3(2.1%)	
TPM	7(6.5%)	5(3.5%)	
ETHO	5(4.6%)	7(4.9%)	
LEV	3(2.8%)	5(3.5%)	
Others*	3(2.8%)	4(2.8%)	
Total	108(100.0%)	142(100.0%)	

\*Others- Clobazam, Topiramate, Vigabatrin, Phenobarbitone, Clonazepam, Lamotrigine.

Table 3 shows that most of the respondents in both groups were on AED monotherapy, 77.8% in the adherent group and 77.5% in the non-adherent group. The mean monthly cost of AEDs in the adherent group was 1406.7+/-2639.1 taka and in the non-adherent group was 1183.8+/-1019.2 taka. The mean monthly cost of AEDs was higher in the adherent group than in the non-adherent group but was not statistically significant. The most frequently prescribed AED was Carbamazepine (38.0% in the adherent group and 40.8% in the non-adherent group), followed by Valproic acid (23.1% and 25.4% respectively). The most common AED dual therapy was Valproic acid with other AEDs (13.0% in the adherent and 8.5% in the non-adherent group).

## DISCUSSION

In this study, 56.8% of children with epilepsy (CWE) showed non-adherence to AEDs. The proportion of non-adherence found in this study was high, which can affect/ hamper the goal of achieving seizure control in CWE in our country. This finding is similar to the 61.3% found in another study on adults from Bangladesh by Chowdhury *et al.*, and 44.8% in Nigeria.<sup>4, 13</sup> A higher level of low adherence (72.5%) to AEDs was found by Mohammad *et al.*, in 2020 in a national household survey done on both children and adults in Bangladesh.<sup>3</sup> But studies are showing lower rates of non-adherence to AEDs, 27.7% in Iran and 20.5% in Jordan.<sup>14, 15</sup> The present study showed that the maximum children's age was between 1-5 years in both groups, 42.6% in the adherent group and 43.0% in the non-adherent group. The mean age in the two groups was almost similar (6.65±3.84 and 6.67±3.74



respectively) without any statistical significance. Similar results were found in different studies done in Iran and Jordan where the mean age of the participants was  $7\pm4.6$  years and  $7.3\pm4.0$  years respectively.<sup>14, 19</sup> In both adherent and non-adherent groups, the majority of children were male, 64.8% and 68.3% respectively. Similar findings were found in a study done in Nigeria (male 52.1%, female 47.9%) and in an Iranian study without statistical significance (male: female=1.29).<sup>13, 14</sup> Most of the fathers' professions were business (50.4% in the adherent group and 59.2% in the non-adherent group). Others were service holders, farmers, or shopkeepers. Another study done by Dima SA and Shibeshi MS found that the majority of parents were employees/service holders, followed by merchants and farmers.<sup>20</sup> Another study done in Uganda revealed caregiver (mother/other) having an occupation had an increased likelihood of non-adherence to AEDs.<sup>21</sup> The majority of children had focal onset seizures both in the adherent and non-adherent groups, (62.0% and 64.1% respectively). The next common seizure type was generalized onset and lastly unknown onset. These findings were similar to other previous studies.<sup>6, 22, 23</sup>

But in an Iranian study, the most common types of seizure were generalized tonic-clonic seizures (36.5%) followed by myoclonic seizures (19.9%), and tonic seizures (17%).<sup>14</sup> The same result was found in a Bangladeshi survey including adults and children showing generalized epilepsies was more common.<sup>3</sup> Most of the participants in both adherent and non-adherent groups had a history of seizure frequency of one or less/month. Other participants had a history of variable seizure frequency including daily, weekly, or fortnightly. These findings were almost similar to different previous studies done in Jordan, Scotland, and China.<sup>19, 23, 24</sup> This study showed, that most of the children had seizure duration of <1 minute in each group, 75.9% in the adherent group and 91.5% in the non-adherent group. Seizures persisting for >5 minutes were more common in the adherent group (8.3%) than in the non-adherent group (4.2%). As DEEs were relatively more common in the adherent group, so despite their drug adherence, the duration of seizure was more. These differences were statistically significant. This finding had similarities with previous studies.<sup>6</sup> Among the participants of the present study, about half were diagnosed with focal epilepsy in both groups and the next common type

was generalized epilepsy. These findings were similar to other previous studies.<sup>22, 23, 25</sup> However, some other studies done in Bangladesh, Nigeria, and Iran found generalized epilepsy to be more common followed by partial epilepsy and then unclassified epilepsy.<sup>3, 13, 14</sup> Most of the respondents in both groups of the present study were on AED monotherapy. Findings from a previous study from Nigeria showed, 59.3% got monotherapy and 40.7% got polytherapy. Polytherapy was a bit higher in the non-adherent group.<sup>13</sup> Similar results were also found in another study done in Iran.<sup>14</sup>

However, a study in Jordan revealed polytherapy was more than monotherapy.<sup>19</sup> This study showed the mean monthly cost of AEDs in the adherent group was  $1406.7\pm2639.1$  taka and in the non-adherent group was  $1183.8\pm1019.2$  taka. The mean monthly cost of AEDs was more in an adherent group than non-adherent group. Some patients with a diagnosis of DEEs were more in the adherent group. Many of these patients (DEEs) got treatment with injectable steroids (ACTH) and/or oral Vigabatrin. Both the drugs are costly. This may explain the finding of more monthly expenditure for AEDs in the adherent group. Similar results were found in a previous study done in Pakistan, but another Indian study found relatively less expenditure on AEDs.<sup>26, 27</sup> The most frequently prescribed AED found in this study was Carbamazepine (38.0% in the adherent group and 40.8% in the non-adherent group), followed by Valproic acid (23.1% and 25.4% respectively). The most common AED dual therapy was Valproic acid with another AED followed by Carbamazepine with another AED. In another study done in Iran, the most common drugs prescribed were Phenobarbital (33.7%), followed by Carbamazepine (27.6%) and Valproic acid (18.8%).<sup>14</sup> The results of this study showed that uncontrolled seizure was more common and significantly higher ( $p<0.05$ ) in the non-adherent group than the adherent group which is similar to other previous studies.<sup>4, 25, 28-43</sup> After logistic regression analysis, higher maternal education level (SSC & above) and uncontrolled seizures were found to be significantly associated with children's AEDs non-adherence.

## CONCLUSION

The study found no significant differences between adherent and non-adherent children with epilepsy in terms of age of seizure onset, type of

seizure, or epilepsy diagnosis. However, non-adherent children were more likely to experience shorter seizures, while adherent children had a higher proportion of longer seizures. Despite similar seizure characteristics, adherence to AED therapy remains a key factor in better management and prevention of seizure-related complications.

### Limitations of The Study

The study was conducted in a single hospital with a small sample size. So, the results may not represent the whole community.

### Recommendation

Improving adherence to antiepileptic drug therapy in children with epilepsy requires a multifaceted approach, including enhanced patient and caregiver education, better communication between healthcare providers and families, and addressing socioeconomic barriers such as medication costs. Healthcare professionals should focus on regular monitoring, personalized treatment plans, and strategies to minimize side effects. Additionally, raising awareness in communities and providing accessible resources can help reduce non-adherence and improve overall seizure control and quality of life for pediatric patients with epilepsy.

### Authors' Contributions

TJ, FBR: Concept and design, data acquisition, interpretation and drafting. NS and MMR: Data acquisition, interpretation, drafting, final approval and agree to be accountable for all aspects of the work.

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