Adherence to Anti-Seizure Medications in Children with Epilepsy Attending a Tertiary Care Center in Bangladesh

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Abstract

Background: *Epilepsy is one of the most common neurological morbidities in children worldwide. Anti-Seizure Medication (ASM) is the mainstay of epilepsy treatment. Adherence to Anti-Seizure Medication (ASM) is the key to achieving seizure remission. So this study aimed to assess the adherence to anti-seizure medication among children with epilepsy and to identify the factors that influence adherence.*

Materials and methods: *It was a cross-sectional study involving Infants and children aged six months to twelve years old with seizure disorder irrespective of etiology, taking anti-seizure medications for more than six months and receiving mono or polytherapy were enrolled as the study subject. Self-reporting measures were used to assess adherence. Patients' caregivers were interviewed for the assessment of adherence. Descriptive statistical analysis was used to analyze the data, and univariate analysis with a chi-square test was used to observe the association between the variables and adherence.*

Results: *The mean±SD age of the participants was 34.75 ± 38.39 months. A significant association was found between the age of the respondent and compliance with anti-seizure medication (30.5± 27.25 vs. 39.99±36.67 months p=0.012). Males were more than females 28(70%) Vs. 12(30%). Most of the study subjects were belonging to lower-middle-class families 13(33.3%). The generalized onset of seizure was the frequent type of seizure 28(70%). The majority of the participants 24 (60%) did have a seizure with structural etiology. Most of the study subjects received monotherapy 34(85%). Sodium valproate 19(47.5%) was the most frequently used drug. Seizure remission was found in 28(70%) of the study population. No significant association was found between the treatment outcome and adherence to anti-seizure medication (ASM). Adherence to ASM was found in 55% of this study. Unable to afford cost was found to be the main cause of non-adherence 14(35%). There is a significant association found between the duration of taking ASM and compliance with ASM (7.05 ± 5.3 vs. 17.56± 15.43 months p=0.005).*

Conclusion: *Adherence to Anti-Seizure Medication (ASM) is low in our study. Unable to afford cost was the main factor accountable for non-adherence appropriate interventions are needed to improve ASM compliance and consequently treatment outcome.*

Key words: Adherence; Anti-seizure medication; Epilepsy.

INTRODUCTION

Epilepsy is common neurological morbidity in children worldwide. The incidence of epilepsy is 3%. The majority of people with epilepsy live in developing countries[1]. About 10% of the whole world population living a normal life span can expect to have at least one epileptic seizure.[2] It is estimated that 70 million people in the world

are living with epilepsy[3]. World Health Organization (WHO) recognizes epilepsy as a major public health problem as it constitutes 0.5% of the global burden of disease.[4] Recent reviews on epilepsy in 23 Asian countries including Bangladesh reported the lifetime prevalence of epilepsy from 1.5 to 14.0 per 1000 population.[5-6] Moreover a recent nationwide cross-sectional survey suggested the overall prevalence of Epilepsy in Bangladesh is 8.4 per thousand population.[7] The goal of treatment of epilepsy is to maintain a normal lifestyle, free of seizures and with minimal side effects while on medication. Administration of Anti-Seizure Medication (ASM) remains the mainstay of epilepsy treatment. A seizure can be eliminated effectively in up to 67% of patients with epilepsy with appropriate anti-seizure medication and dosage.[8] Adherence to anti-seizure medication is the key to achieving seizure remission. Medication adherence refers to the extent to which a patient's behavior corresponds with the recommendations of a health professional[8]. Patient involvement in the treatment and cooperation and mutual agreement between the health providers and patient is considered to be better medication adherence[8]. Poor adherence to prescribed medication is considered to be the main cause of unsuccessful drug treatment for epilepsy. Non-adherence is associated with increased morbidity and mortality, reduced quality of life, and increased health care costs.[9] Self-report, pill count, appointment attendance, medication refill history, blood or urine drug levels, and drug diary are commonly used methods for measuring therapeutic adherence.[10] There is no single measurement strategy that has been considered optimal. Measurement of serum levels may be influenced by altered pharmacokinetics resulting from co-medication, poor absorption, and genetic differences in drug metabolic rates of anticonvulsant drugs. Self-reporting method is one of the best methods for assessing adherence in low-resource settings. However, it is reported to overestimate adherence. Although the Self-reporting method is prone to social desirability and recall biases it shows moderate correspondence to other adherence measures and can provide actionable information.[11-13]

Several factors can influence adherence to anti-seizure medication. These are socioeconomic factors, the health care system, the characteristics of the disease, the treatment the patient receives, and patient-related factors.[14] In the previous studies, some of the predictors of adherence were identified these includes, duration of treatment, seizure type and parental depressed mood, seizure frequency, pill burden and drug costs, comorbidities, stigma, parent and child satisfaction with medical care, and medication adverse effects.[15-18]

So this study aimed to evaluate the pattern and extent of adherence to anti-seizure medication among children with epilepsy and to identify the factors that influence adherence. Identification of the factors associated with adherence would allow the development of strategies to improve adherence.

MATERIALS AND METHODS

It was a cross-sectional study conducted in the Department of Child Neurology Unit and Autism and Child Developmental center of Chattagram Maa-Shishu O General Hospital, Bangladesh for six months duration from June 2022 to December 2022. Infants and children aged six months to twelve years old in the attended Outpatient Department (OPD) of this center with seizure disorders irrespective of etiology, taking anti-seizure medications for more than six months, and receiving mono or polytherapy were enrolled as study subjects. Informed consent was taken before participation. Patients with other co-morbidities and unwillingness to participate were excluded from the study.

Data was collected using a specially designed case record form that included items on socio-demographic history, seizure history, duration of epilepsy, and anti-seizure medications prescribed. The participants were classified according to their age, gender, and socioeconomic class. Socioeconomic status is categorized according to the scale used by Rahaman R et al which takes into account monthly family income, types of houses, assets, and types of latrines.[19] Epilepsy was diagnosed based on detailed medical history, neurological evaluation by a qualified child neurologist, and electroencephalography and neuroimaging techniques (i.e. Computed tomography and magnetic resonance imaging) Details on the patient anti-seizure medication, including the generic name of the drug, dose, and duration, were also collected.

Adherence was assessed by interviewing the patient's caregiver whether the participants take ASM regularly, irregularly, or stopped taking ASM. Adherent to anti-seizure medications considered those who were taking the drug regularly subsequently who were taking the drug irregularly or stopped taking drugs were considered non-adherent. Factors associated with adherence and non-adherence were evaluated respectively. Data were expressed as frequency (Percentage). Descriptive statistical analysis was used to analyze the data, and univariate analysis with a chi-square test was used to observe the association between the variables and adherence. p-value < 0.05 was considered statistically significant.
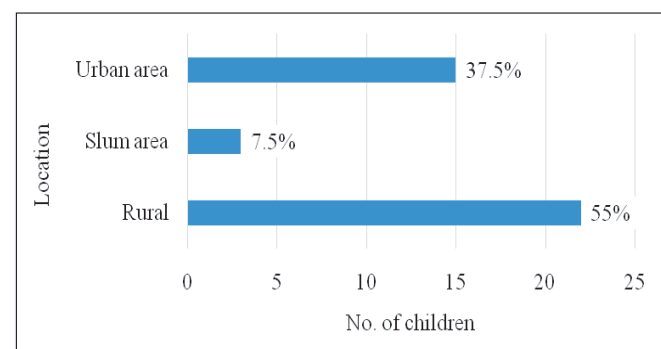
RESULTS

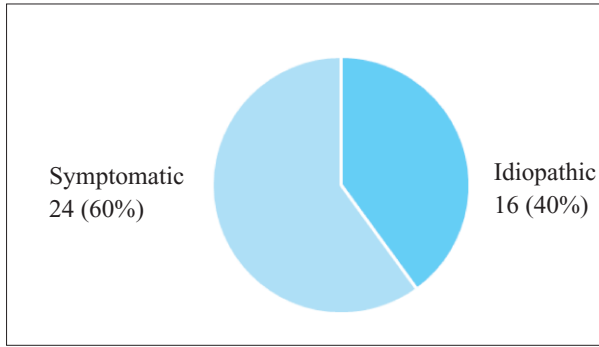**Figure 1** Area of origin of the study population

Figure 2 Category of seizure disorder
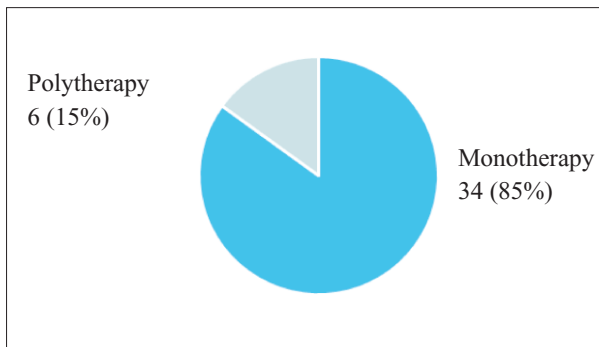

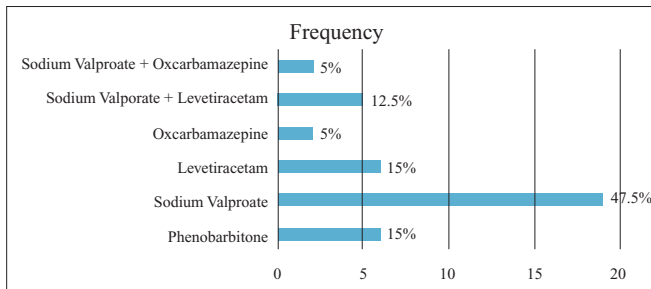**Figure 3** Percentage of the study population receiving mono or polytherapy

Figure 4 Anti-seizure medications received by participants

Table I Treatment outcome and adherence to anti-seizure medications

Treatment outcome	Regular	Irregular	Stopped taking AED	Total	p value
Seizure remission	16 (57.1%)	12(42.9%)	0 (0%)	28	0.25
Refractory seizure	1 (33.3%)	2 (66.7%)	0 (0%)	3	0.67
Recurrent seizure	5 (55.6%)	3 (33.3%)	1 (11.1%)	9	0.16
Total	22 (55%)	17 (42.5%)	1(2.5%)	40	

Table II Percentage of adherence to anti-seizure medication

Variable	Adherence to Drug	
	Frequency	Percentage
adherent	22	55%
non-adherent	18	45%
Total	40	100%

Table III Association between different Variables and compliance to Anti-Seizure Medication (ASM)

Variables	Compliance with ASM medications			χ^2	p Value
	Regularly	Irregularly	Stopped taking AED		
Gender	16(40%)	12(30%)	0(0%)		
Male 28(70%)				2.41(app)	0.299
Female 12(30%)	6(15%)	5(12.5%)	1(2.5%)		
Age (Mean ± SD)	30.5±27.25	39.99±36.67	0(0%)	67.48(app)	0.012*
Monotherapy 34(85%)	20(50%)	13(32.5%)	1(2.5%)	1.75(app)	0.417
Polytherapy 6(15%)	2(5%)	4(10%)	0(0%)		
Reason for AED					
No Comments 5(12.5%)	5(12.5%)	0(0%)	0(0%)		
Negligence 8(20%)	0(0%)	8(20%)	0(0%)		
Drug Unavailable 7(17.5%)	0(0%)	7(17.5%)	0(0%)	45.62(app)	0.000**
Unable to afford cost 14(35%)	0(0%)	12(35%)	2(2.5%)		
Unable to leave the house for lockdown 6(15%)	0(0%)	6(15%)	0(0%)		
Socio-Economic Condition of the respondents					
Lower Class	4(10.3%)	0(0%)	0(0%)	3.87(app)	0.424
Lower Middle Class	13(33.3%)	12(30.8%)	1(2.6%)		
Upper Middle Class	5(12.8%)	4(10.3%)	0(0%)		
Upper Class	1(2.6%)	0(0%)	0(0%)		

Table IV Association between drug and seizure duration with patient compliance

Drug and seizure duration	Patient compliance	No. of study subjects	Mean duration	Std. Deviation	p value
Duration of taking AED (In months)	Adherent	22	7.05	5.349	0.005
	Non-adherent	18	17.56	15.432	
Duration of the seizure (In months)	Adherent	22	8.86	14.230	0.132
	Non-adherent	18	17.61	21.582	

In this study, a total of forty numbers of participants were enrolled. The mean age of the participants was 34.75 ± 38.39 months. A significant association was found between the age of the respondent and the non-adherence group to ASM (30.5± 27.25 vs. 39.99±36.67 months p=0.012). Males were more than females 28(70%) Vs. 12(30%). Most of the study subjects were belonging to lower-middle-class families 13(33.3%). Only 4(10.3%) came up from lower-class families and 5(12.8%) and 1(2.6%) belonged to the upper middle class and upper-class families respectively.

The majority of the study population came from the rural area. Most of the participants 24(60%) did have a seizure with structural (Symptomatic) etiology. The generalized onset of seizure was the frequent type of seizure 28(70%). Most of the

study subjects received monotherapy 34(85%). The major proportion of the participants received sodium valproate 19(47.5%). Others anti-seizure medications were levetiracetam 6(15%), Phenobarbitone 6(15%), oxcarbazepine 2 (5%), sodium valproate along with levetiracetam combination 5(12.5%), sodium valproate plus oxcarbazepine 2 (5%).

Twenty-eight numbers of participants (70%) were found to have seizure remission. Among them, 16(57%) were taking regular ASM and 12(42.9%) were taking ASM irregularly. The refractory seizure was found in three cases only. 2(66.7%) of the participants with refractory seizure received ASM irregularly and 1(33.3%) received ASM regularly.

Nine participants had recurrent seizure attack despite taking ASM and 5(55.6%) among them was taking ASM regularly, and 3(33%) was taking ASM irregularly. No significant association was found between the treatment outcome and adherence to ASM. Adherence to ASM was found in 22(55%) of respondents in this study.

Unable to afford costs was found to be the main cause of non-adherence. It comprises 14(35%). Other factors accountable for non-adherence was Negligence 8(20%), unavailability of the drug 7(17.5%), and unable to leave the house for lockdown 6 (15%). All these factors were highly significantly associated with adherence to ASM (p=0.000)

The mean ± SD duration of taking ASM among the adherent and the non-adherent group was 7.05 ±5.3 months & 17.56 ± 15.4 months subsequently. The mean± SD duration of seizure among the adherent and the non-adherent group was 8.86 ± 14.23 months and 17.61±21.58 months. A significant association was found between the duration of taking ASM and compliance to ASM (7.05 ± 5.3 vs. 17.56± 15.43 months p=0.005)

DISCUSSION

Adherence to Anti-Seizure Medication (ASM) is quite challenging for a resource-poor country. Adherence to ASM is the key to the success in the treatment of epilepsy. Poor adherence is considered to be one of the major causes of non-responsiveness to anti-epileptic drug therapy.

Adherence to ASM has not been studied extensively in the pediatric age group in Bangladesh. Henceforth this study is aimed to assess the extent of adherence to ASM as well as factors influencing ASM adherence among children with a seizure disorder.

In this study, self-reporting measures were used to assess adherence. The patient's caregivers were interviewed. Respondents who were taking ASM on regular basis were considered adhering to ASM. In this study, it was found that 22(55%).In other studies it was found 72.3% and 51.9% respectively.[20,21] These results suggest that the adherence rate in our study is a bit different than other studies. This could be caused by the small sample size and different methods of assessment of adherence.

Twenty-eight numbers of participants (70%) were found to have seizure remission. No significant association was found between the treatment outcome and adherence to ASM. This result is consistent with the findings of Gurumurthy R et al.[20]

In this present study, no significant differences were found between the genders and non-adherent patient groups. But the age was significantly associated with non-adherence to ASM. The younger age group is more adherences to ASM. This finding is in partial agreement with the study conducted by Gurumurthy R et al and Liu et al.[20,21] They did not find any significant difference in the rate of non-adherence among the age groups and genders.

In this study, we did not find any significant association between ASM Adherence and socio-economic status (Based on a scale used by Rahaman R et al which takes into account monthly family income, types of house, assets, and types of latrine).[19] This is similar to the findings of Asadi-Pooya AA et al.[22] Who found no significant association between anti-epileptic drug adherence and socioeconomic status. This is in contrast to the findings of Gurumurthy R et al who found that children with epilepsy of a lower socioeconomic class are at a higher risk of adherence.[20]

Moreover in our study, the duration of epilepsy did not have any significant association with adherence. This finding is in line with the study reported by Gabr and Shams [23]. But it differs from the result of Kyngas's study, they observed duration of epilepsy of more than 3 years was significantly related to adherence to medications.[24]

On the other hand, the study subjects in our study who were taking ASM for a longer period were significantly associated with non-adherence to drugs. Financial conditions, unawareness, and negligence could be the possible explanation for this reason.

In our study types of ASM treatment like monotherapy and polytherapy do not have any significant influence on the extent of adherence. This finding is in agreement with those of Sweileh et al who also did not find any significant difference in ASM adherence between patients on monotherapy and those on polytherapy.[25]

In contrast, the studies by Gabr - Shams, Rundle- Gonzalez and Harimanana et al observed that patient's on monotherapy were significantly more adherent to medications than those on polytherapy.[23,26,27] This may be the result of the complexity of a treatment regimen. Because large numbers of pills need to be taken at different time intervals this increases the likelihood of missed doses.

Furthermore in our study, all reasons accountable for non-adherence were significantly associated with non-adherence to ASM. Unable to afford cost was the main reason for non-adherence 14(35%). This result is in agreement with the studies from kenya and Ethiopia.[28,29] Patients with low income would

have poor adherence as they cannot afford to buy these drugs. However, this finding is not consistent with the study carried out by Liu et al and Paschal et al[21,30]. They reported that the primary reason for non-adherence in their study was forgetfulness (69.9% and 32.5%) respectively.

LIMITATION

The sample size in this study is very small and no validated and reliable tools were used to measure adherence. Adherence in this study was assessed by self-reporting measures by interviewing the patient's caregiver. This could have recall bias and a tendency to overestimate the adherence level.

CONCLUSION

Adherence to ASM in children is low in our setting. Unable to afford cost was the main factor accountable for non-adherence. Appropriate interventions that address modifiable determinants of poor adherence are needed to improve ASM compliance and consequently treatment outcome. The measures could be providing free ASM to children with financial constraints. Relevant information about the illness and its treatment should be provided during each visit to epileptic children and their caregivers.

RECOMMENDATION

We would suggest further multicentre studies be conducted with a larger sample size and using multiple validated tools to measure adherence.

DISCLOSURE

All the authors declared no competing interest.

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