Adherence to Antiepileptic Drugs and Influencing Factors among Persons with Epilepsy Attending an Epilepsy Clinic of a Tertiary Hospital in Bangladesh

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Abstract:

Background:
Epilepsy is one of the most prevalent and debilitating chronic neurological illnesses. Treatment adherence is one of the determinants of seizure control in persons with epilepsy (PWE). The purpose of this study was to assess adherence to antiepileptic drugs (AEDs) and factors associated with non-adherence in a sample of Bangladeshi PWE attended to an Epilepsy Clinic of a tertiary hospital in Bangladesh.

Objective:
The aim of study was to assess the extent of AED adherence and the factors influencing AED adherence among PWE.

Methods:
This analytic cross-sectional study was conducted in the Department of Neurology at Rangpur Medical College Hospital, Rangpur, Bangladesh, from July 2022 to June 2023. The patients were recruited from the epilepsy clinic. Data on adherence to medication and related factors for each patient were gathered using an interviewer administered structured questionnaire. Adherence was defined as not missing a dose and non-adherence is missing a dose or stopping treatment in the last month.

Results:
Of a total of 225 patients studied, 63(28%) patients were non-adherent with regards to AEDs. There were no demographic differences (based on gender, age, residential location, education, marital status, socioeconomic status, and seizure type) between adherent and non-adherent patients. The primary reason for non-adherence was forgetfulness or inability to buy drugs (66.6%), followed by a Lack of understanding of the need for long-term medication (22.2%). PWE who were on single AED were more likely to be adherent to AED than those were on polytherapy number of AEDs and adherence (p=0.037). Patients not-adherent to AEDs had a longer duration of illness [9.5 (4.0-17.0) years] (p<0.001). than the patient's adherent to AEDs [median (Interquartile rage) 5.0 (2-11) years]

Conclusions:
About one-third of PWE needed to be more compliant with their medication. If the treatment of PWE is restricted to monotherapy as far as possible and they are educated about the duration of therapy and possible adverse effects of AEDs, non-adherence may be reduced.

Keywords: Epilepsy, Adherence, Antiepileptic drug, Bangladesh.

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Introduction:

Epilepsy is one of the foremost neurological disorders, affecting nearly 1% of the global population and nearly 80% of PWE live in low- and middle-income countries.[1] Epilepsy is characterized by recurrent unprovoked seizures stemming from various aetiologies.[2] Despite the introduction of over 20 new AEDs in recent decades, the proportion of patients achieving seizure freedom (a 100 % reduction in seizure

frequency) remains unchanged.[3,4]

The leading cause of breakthrough seizures is AED nonadherence and the prevalence of nonadherence to AEDs in PWEs ranges from 26% to 79% depending on the populations studied, definition used for non-adherence, and research methods.[5-8] Those with uncontrolled seizures suffer a reduced quality of life due to increased comorbidities, cognitive decline, and rising healthcare costs.[8,9] They also face higher risks of injuries, premature death from status epilepticus, and sudden unexpected death in epilepsy.[10] Multiple studies have been conducted to better understand which factors can predict poor adherence, depicting that age, education, frequency of dosing, forgetfulness and fear of adverse side effects all contribute to adherence.[5-8,11,12]

Although poor adherence is considered to be one of the significant causes of non-responsiveness to AED therapy, this has yet to be studied extensively in Bangladesh. Hence, we assessed the extent of AED adherence and the factors influencing AED adherence among PWE who attended an epilepsy clinic at a tertiary-level hospital in Bangladesh.

Method:

An analytical cross-sectional study carried out in epilepsy Clinic of Department of Neurology at Rangpur Medical College Hospital, Rangpur from July 2022 to June 2023. This is the only center in this division comprising 8 districts and 17,610,956 inhabitants which provides such type of facilities.[12] Therefore patients are referred here from all over the division.

Ethical clearance was obtained from the Ethical Review Committee of Rangpur Medical College before starting the study. Diagnosed PWEs attending the epilepsy clinic who were on therapy with at least one AED, irrespective of any standard or non-standard treatment and no change in AEDs in the last six months were invited to participate in the study. Patients with pseudo seizures were excluded. Informed consent was obtained from the patients or the attending caregivers. Relevant data were collected by using a structured questionnaire.

A structured questionnaire was used to collect sociodemographic (gender, age, socioeconomic status, education, residential status, marital status), seizure history (type and frequency), current AED treatments, self-reported adherence to medication, and the reasons of non-adherence were collected by interviewing the PWE or their caregivers. Based on a consensus and published literature supporting a recall period of one month, adherence was defined as not missing a dose and non-adherence as missing a dose or stopping treatment in the last month.[13]

Qualitative data were expressed as frequency (percentage) and quantitative data by mean (standard deviation) or median (interquartile range) according to their distribution. We used the Chi-square test (for qualitative data) and Mann-Whitney U test (for duration of epilepsy) to compare adherence between different groups and with other factors; significance was defined as <0.05. Data analysis was done using SPSS version 23.0.

Results:

For this study 225 PWE were recruited. The median age was 18 with a range between 0 and 73 years old. The most frequent age group was 0-19 years with 121(53.8%) patients, followed by 20-39 years with 84(37.3%) PWE. Only 20(8.9%) of the PWE were 40 years and above. In this sample, 53.3% PWEs of the sample were males and 46.7% females. The majority of participants were from rural area (71.1%) and about 46.6% of the adult PWEs were unmarried (Table-I).

Table-I: Sociodemographic characteristics of the persons with epilepsy (n=225)

Characteristics	no. (%)
Age group (Years)	
0-19	121(53.8)
20-39	84(37.3)
40 and above	20(8.9)
Sex	
Male	120(53.3)
Female	105(46.7)
Residence	
Rural	160(71.1)
Urban	65(28.9)
Socioeconomic status	
Lower	52(23.1)
Lower middle	141(62.7)
Middle & Upper middle	32(14.2)
Marital status (n=118)*	
Married	63(53.4)
Unmarried	55(46.6)
Educational level (n=206) †	
No formal education	29(14.1)
Primary	50(24.3)
High school	67(32.5)
Secondary	14(6.8)
Higher secondary & above	46(22.3)

*PWE <18 years were excluded †PWE <6 years were excluded

The median age of the 1st seizure was 10 years (range 4.0-17.0), and the median duration of epilepsy was 6.0(2.5-12) years in the present study. Out of 225 PWE, 76(33.8%) were on multiple AEDs. Generalized seizure was the most common seizure type (60.9%), followed by focal seizure (39.1%). In the present study, 162(72%) patients were categorized as adherent and 63(28%) as not adherent (Figure-1).

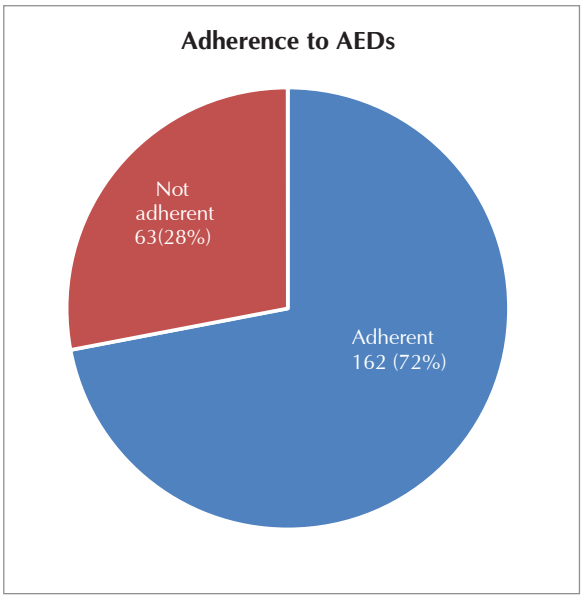

Figure-1: AED adherence pattern among the studied PWEs (n=225)

The prevalence of non-adherence was the highest (79.8%) among epileptic patients aged 20-39 years, followed by ≥40 years age group (40%), and 0-19 years (66.9%). However, there was no significant difference between age and adherence (p=0.130). Of the patients who did not adhere to drugs (28%), the primary reason was forgetfulness (33.3%) or inability to buy drugs (33.3%), followed by patients' lack of knowledge regarding continuation of drugs (22.2%), a bad patient-prescriber relationship (9.5%), and worry about side effects (1.6%). The number of factors associated with non-adherence were similar among different age groups (Table-II).

Table-II: The reasons for non-adherence among different age groups

Characteristics	Age group no. (%)			Total	p-value
	0-19 years	20-39 years	≥40 years		
No. of patients	121(53.8)	84(37.3)	20(8.9)	225(100.0)	
Patient adherence	81(66.9)	67(79.8)	14(70.0)	162(72.0)	0.130
Reasons for non-adherence					
Forgetfulness	13(32.5)	6(35.3)	2(33.3)	21(33.3)	
Unable to buy drugs	14(35.0)	6(35.3)	1(16.7)	21(33.3)	
Lack of knowledge	9(22.5)	4(23.5)	1(16.7)	14(22.2)	
Mistrust physician	4(10.0)	0(0)	2(33.3)	6(9.5)	
Feared of side effects	0(0)	1(5.9)	0(0)	1(1.6)	

However, there was no significant difference in adherence between male and female patients, no significant difference in adherence between patients from rural or urban settlements, and no significant

Table-III: Association of drug adherence with sociodemographic and clinical factors (n=225)

Variables	Drug adherence		p-value
	Adherent (n=162)	Not-adherent (n=63)	
Male	85(52.5)	35(55.6)	0.679
Female	77(47.5)	28(44.4)	
Residence			
Rural	111(68.5)	46(77.8)	0.167
Urban	51(31.5)	14(22.2)	
Socioeconomic status			
Lower	36(22.2)	16(25.4)	
Lower middle	100(61.7)	41(65.1)	0.441
Middle & Upper middle	26(16.0)	6(9.5)	
Marital status (n=118)*			
Married	50(56.8)	13(43.3)	0.201
Unmarried	38(43.2)	17(56.7)	
Educational level (n=206)†			
No formal education	20(13.5)	9(15.5)	
Primary	36(24.3)	14(24.1)	0.960
High school	47(31.8)	20(34.5)	
Secondary	10(6.8)	4(6.9)	
Higher secondary & above	35(23.6)	11(19.0)	
Number of AED			
Monotherapy	113(69.7)	35(55.6)	0.037
Polytherapy	48(30.3)	23(44.4)	
Type of seizure			
Generalized	103(63.6)	34(54.0)	0.404
Focal seizure	59(36.4)	29(46.0)	

AED: Anti-epileptic drugs; *Chi-square test.

difference between seizure type and adherence. However, patients who were on single AED were more likely to be adherent to AED than those were on polytherapy number of AEDs and adherence (p=0.037) (Table-III).
A significant difference of duration of illness was obtained between adherence and not-adherent PWEs (p<0.001). Patients not-adherent to AEDs had a longer duration of illness[9.5(4.0-17.0) years] than the patients' adherent to AEDs [median (Interquartile rage) 5.0(2-11) years] (Figure-2).

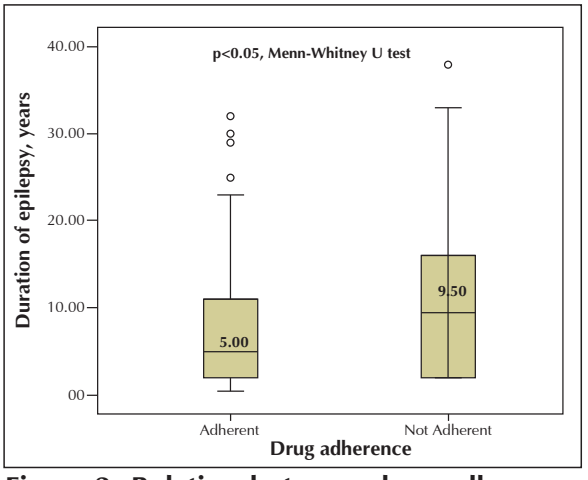

Figure-2: Relation between drug adherence and duration of epilepsy in the studied PWE (n=225)

Discussion:

Adherence to medication is regarded as a major challenge in developing countries as a result of low income, illiteracy and ignorance. Although non-adherence is considered to be one of the major causes of non responsiveness to AED therapy, this has not been studied extensively in Bangladesh. To fill this gap, we assessed the extent of AED adherence, as well as the factors influencing AED adherence among PWEs at a tertiary-level teaching hospital in Rangpur, Bangladesh.
In the present study, adherence rate to AEDs was 72%, which was similar to a recent study conducted in India (70%),[5] but quite higher than a previous study conducted in another tertiary hospital in Bangladesh, where the adherence rate was 38.7%.[6] In 2003, WHO reported that the prevalence of adherence to AEDs in developing countries ranged between 20% and 80%.[14] These variations in rate of adherence between different studies may reflect the differences in patient attitude toward the prescribed drug due to different cultures, beliefs, education, and physician approach to the patient with epilepsy or the degree of medical and parental support. Treatment adherence depends on many factors, and nonadherence has no simple explanation. Forgetfulness is a widely reported factor that causes nonadherence to medication.[6,7] In the present study, forgetfulness and inability to buy drugs (either due to shortage of money or time) were the two main reasons for nonadherence reported by two-thirds of the patients (66.6%). Patients' knowledge about their disease and treatment is not always adequate. They may lack an understanding of the role of therapy, be fearful of dependency on long-term medication, lack knowledge about the disease and consequences of poor compliance, and may assume that the need for medication is intermittent and thus stop taking the drug to see whether medication is still required.[15] In our study, 14(22.2%) stopped drugs as they had no seizures and thought that their disease was cured.
In the present study, the two factors we found to be associated with non-adherence were AED polytherapy and longer disease duration. We found that a significant proportion of patients were already on polytherapy (32.4%) in the non-adherent group and 23.6% in the adherent group. Excessive, often irrational use of polytherapy reflects a lack of standardization of prescribing practices for epilepsy in the country.[6] Overuse of polypharmacy provides no benefit in seizure control while unnecessarily adding AED-related side effects and increasing the cost of treatment.[3,4] While our analysis did not directly implicate treatment cost as a factor

leading to non-adherence, the non-adherence related to polytherapy may partly be due to the treatment expenses. A longer duration of treatment also translates into increased costs. Non-adherence in patients with a longer disease duration may also manifest as patients not being informed about the need for prolonged treatment.[15] Patients who are better informed about epilepsy, including the likely duration of treatment and the potential of AED-related adverse effects and how those can be mitigated, may be more likely to adhere to treatment.

Limitations:

Our study has a few limitations. First, this is a single-Centre study, and the sample size was relatively small, thus limiting the significance of the data. Second, data from hospital-based centres were subject to referral bias. Finally, there was a risk of response bias since the measures relied on self-reporting.

Conclusions:

Medication adherence remains an essential issue in epilepsy treatment. Nonadherence to AED is common in our PWE. If the treatment of patients is restricted to monotherapy as far as possible and patients are given enough information, especially about the duration of therapy and possible adverse effects of AEDs, non-adherence may be reduced.A prospective multi-centre study with a larger sample size may yield more reliable data. However, targeted management programs and communication strategies are necessary to improve adherence to AED for PWE and avoid the clinical consequences of poor adherence.

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