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A Study of Factors Associated with Adherence to Treatment in Patients with Epilepsy

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Abstract: **Introduction:** Non-adherence to antiseizure medications is one of the main reasons for treatment failure and seizure recurrence. **Objective:** Evaluation of adherence and association with belief about antiseizure drugs in patients with epilepsy were examined. **Materials and methods:** This was a prospective, cross-sectional study of patients with epilepsy in the neurology department for six months. Patient adherence and persistence in long-term treatment continuation were assessed using the Modified Morisky Adherence Scale and Beliefs about Medicines questionnaire scale. **Results:** A total of 100 patients were enrolled out of which 46% of the patients were adherent, 54 % were non adherent to their medications. GTCS was the commonest seizure (58%), followed by partial seizures (41%) and unclassified seizures (1%). Levetiracetam(37%) was the commonest drug prescribed, followed by valproic acid(24%), carbamazepine(19%), oxcarbazepine(14%), phenytoin(5%), phenobarbitone (1%). Male patients were found to be more adherent to drug therapy as compared to females. ($p<0.05$). Participants with higher education were highly (73 %) adherent to antiepileptic drugs, followed by high school (37%) and primary school 33%). The specific necessity score was significantly higher in the adherent group than the nonadherent group. Patients who believed that antiepileptic drugs do more harm than benefit were significantly more in the nonadherent group.**Conclusions:** Patient with high educational status, positive attitude, and belief toward therapy were found to be more adherent to their medication. Assessment of adherence to medication and counseling should be a routine part of management for better health care and quality of life.

Key Words: epilepsy; adherence; modified morisky adherence scale; belief about medication score

I. INTRODUCTION

Epilepsy is a neurological disorder characterized by recurrent episodes of seizures causing neurobiological, cognitive, psychological, and social consequences [1].

The annual incidence of epilepsy in India is about 27.3 per 100,000 per year, with a prevalence of 5.59 to 10 per 1000 [2]. Epilepsy is associated with physical, psychological, and social problems [3]. The risk of sudden unexpected death is higher in patients with epilepsy as compared to the general population [4]. Prolonged seizures may cause physical injury and disruption of neural networks, causing neuronal loss and leading to cognitive impairment [5]. However, management of epilepsy has been shown to be successful with antiepileptic agents. Most interesting is that 60% of treated adults stopped taking the medication without relapse within 2-5 years of treatment [6]. Therefore, with appropriate drug management, improved quality of life in epileptic patients can be achieved.

Epilepsy has been shown to have significant effects on patients' lives. This is reflected in the ability to work and the standard of living in epileptic patients. Approximately half of epilepsy patients feel that the disorder affects their ambitions and social life [7]. Patients also admit to missing school or work due to this disorder. Furthermore, these patients also feel that the disease influences their memory [8]. Children and adolescents with epilepsy also admit that they feel embarrassed about their disorder and feel excluded by their peers [9]. Employment opportunities and the capability to work for patients with epilepsy are essential for self-esteem, self-image, and quality of life [10].

Seizure Control can be attained through adherence to antisezure medications. More than half of epilepsy patients have poor seizure control due to nonadherence to medication

[11]. Effects of nonadherence have also been linked to other problems. Amongst the effects of medication nonadherence is an increased likelihood of an episode of status epilepticus [12]. In addition, nonadherent patients were also more likely to be hospitalized and experience an emergency room admission [13]. In view of the state of the disorder, there is also a high rate of road accidents resulting in fracture, head injury, and sudden unexpected death in patients with noncontrolled seizures [14].

Medication adherence is, therefore, important, especially in chronic disease patients. Unfortunately, adherence in these groups of patients is poor [15], [16]. Medication adherence is affected by various patient factors such as age, duration of disease, and co-morbidities [15], [17].

Nonadherence to antiepileptic medications has been reported to be high. Studies showed a high prevalence of seizure (21-45%) in patients who did not adhere to their antiepileptic medications [18]. Patients who are nonadherent to their medication are frequently hospitalized with prolonged lengths of stay, have repeated emergency department visits, and miss school or work frequently because of the seizure effects or out of fear of seizure occurrence [19]. The direct effect of nonadherence with reducing the quality of life in epilepsy patients, however, is a concern. So far, studies investigating self-reported adherence in epilepsy have not used validated questionnaires. Therefore, this work aimed to identify the level of medication adherence and perceived belief about medication for epilepsy patients. This study also investigated the extent of nonadherence associated with poor seizure control, which was measured using a validated self-report questionnaire. We also investigated the relationship between seizure control and beliefs about medication and illness.

II. MATERIALS AND METHODS

The study was conducted on the patients visiting the outpatient neurology department of the Himalayan Institute of Medical College and Hospital, Jolly Grant Dehradun. This was a prospective, cross-sectional study enrolling 100 patients with epilepsy. Patients were enrolled after applying inclusion and exclusion criteria. Ethical approval was obtained from the Medical Research and Ethics Committee, and informed consent was obtained from all patients before inclusion into the study.

INCLUSION CRITERIA

- Adults treated for epilepsy with at least one drug was included in the study.
- Patients of both genders in the age group of aged 18 years or older.
- Patients who were not known to have cognitive impairment or psychiatric illness, without other severe co-morbidities.
- Patients who consented to participate in the current study.

EXCLUSION CRITERIA

- Inability to understand spoken words due to hearing loss.
- Severe visual impairment hindering reading.

Patient information, demographic data, seizure control (more than 1 episode per month, one episode per month, more than one episode per year, and seizure-free), and complexity of medication (one or more medications) were obtained from patient medical records. Patients were then interviewed to assess patient adherence intention.

Patient adherence and persistence in long-term treatment continuation were assessed using the Modified Morisky Adherence Scale [20], [21], and beliefs about medicines questionnaire BMQ scale [22]. The Validated 8-item Morisky Medication Adherence Scale (MMAS-8), a self-reporting tool, assessed the patient's adherence to antiepileptic drug(AED) therapy. Eight questions evaluated the patient's forgetfulness, the patient's understanding of the need for continued therapy, and whether the patient felt it was inconvenient to adhere to a daily medication treatment plan. For questions 1, 2, 3, 4, 6, and 7, a score of zero was given for a positive response, whereas a score of one was given for a negative response (Yes = 0; No = 1). Conversely, for item 5, a score of zero was given for a negative response, whereas a score of one was given for a positive response (Yes = 1; No= 0). For item 8, a score of one was given for 'Never/Rarely' whereas a score of zero was given for 'Once in a while' / 'Sometimes' / 'Usually' / 'All the time'. The total score of MMAS-8 was 8. A Higher score indicated a higher level of self-reported adherence. Adherence level was categorized as adherent (Score: 8), nonadherent (Score: < 8).

The beliefs about medicines questionnaire comprises 18 statements, and subjects were asked about the extent to which they agree or disagree with the statement on a five-point scale.

The questionnaire was divided into two sections, measuring beliefs about medicines in general and a specified medication (general and specific sections). The general section of the questionnaire consists of the overuse subscale (e.g., "doctors use too many medicines") and the harm subscale (e.g., "medicines do more harm than good"). Subscales assess general perceptions of a) the benefit of medications, b) the harm associated with the intake of drugs, and c) the overuse of prescribed medications by physicians. The perceived necessity of AEDs and concerns about the adverse effects of AEDs assessed specific beliefs about AEDs. Responses ranged from (1) - strongly disagree' to (5) - strongly agree.

Data was analyzed using SPSS version -20 (Statistical Package for Social Sciences). Descriptive statistics was used to describe the patients' demographic and disease characteristics and medication adherence scores. Frequencies and percentages were used for the categorical variables, while means and standard deviations were calculated for the continuous variables. The sample's characteristics and the adherent and nonadherent groups were presented. The normality of the data was determined by using a one-sample Kolmogorov-

Number of patients 100	Frequency and percentage
Male	69%
Female	31%
Mean age	
<35	76%
>35	24 %
Education	
Less than primary	12.1%
High School	64.6%
Higher Education	23.2%
Religion	
Hindu	90%
Muslim	10%
Marital status	
Single	42%
Married	58%
Domicile	
Urban	32 %
Rural	68%
Mean duration of epilepsy	1.22 ± 1.41
Type of seizure	
GTCS/Partial/unclassified	58 % / 41% / 1%

TABLE 1: Socio Demographic Characteristics

Number of patients 100	Frequency and percentage
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TABLE 2: Morisky Score according to Gender and Education

Smirnov test. Comparison between the two groups was done using the Whitney U test for non-normally distributed variables. In contrast, the Kruskal-Wallis test was used to compare more than two groups. The Chi-square test was used for the analysis of categorical variables.

III. RESULTS

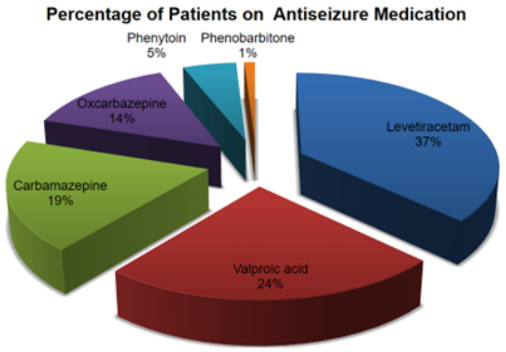
Table 1 shows that 76% of the participants belonged to the age group <35 years, while 24% were over 35 years old. Among the participants, 69% were male, and 31% were female. The majority of the participants (68%) were from rural areas, while 32% were from urban areas.

Regarding seizure types, the majority of participants (58%) had generalized tonic-clonic seizures, 41% had partial seizures, and 1% had unclassified seizures.

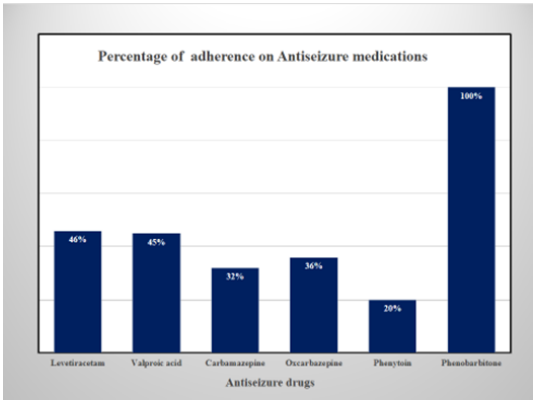
Table 2 presents the results, which indicate that male participants exhibited higher adherence to drug therapy compared to females ($p < 0.05$). Regarding the educational status of the participants, the majority (65%) had completed high school, followed by 23.2% with higher education, and 12.1% with less than primary school education. Notably, participants with higher education demonstrated the highest adherence rate (73%), followed by those with a high school education (37%), and those with less than primary school education (33%).

Table 3 presents the results, which show that the Specific Necessity Score was significantly higher in the adherent group compared to the non-adherent group. On the other hand, the non-adherent group exhibited higher scores for specific concerns, general overuse of drugs, and general harm of drugs. The statistical test used in Table 3 is Mann Whitney test.

Table 4 shows that there is no significant difference in specific necessity scores between genders. However, females exhibit greater specific concerns about medication ($p = 0.05$), general overuse ($p < 0.05$), and general harm compared to males.



Majority of patients were prescribed Levetiracetam (37%) followed by Valproic acid (24%), Carbamazepine (19%), Oxcarbaepine (14%) and Phenytoin (5%).



Variables	Median		p-value
	(Non-Adherent)	(Adherent)	
Average duration of illness	2.00(3.00-1.00)	2.00(2.50-1.50)	0.67
Specific necessity	19.00(20.00-15.75)	21.00(21.00-20.00)	<0.001
Specific concerns	14.00(16.00-12.00)	13.00(15.50-12.00)	0.74
General overuse	12.00(13.00-10.00)	11.00(12.00-9.00)	0.06
General harm	9.00(11.00-8.00)	8.00(9.00-8.00)	0.01

TABLE 3: Comparison between Adherent and Non-Adherent Groups of Patients regarding Beliefs about Medicines Questionnaire Scores (BMQ)

BMQ	Total	Male	Female	P value
Specific Necessity	20(18-21)	20(18-20)	20 (17-21)	0.42
Specific Concern	14(12-16)	13(12-15)	14(13-17)	0.05
General Overuse	11(10-13)	11(9-12)	12(10-14)	0.028
General Harm	8 (8-10)	8(8-10)	9(8-11)	0.062

TABLE 4: A Comparison in the Mean of Beliefs about Medicines Questionnaire Scores (BMQ) in Both Sexes

IV. DISCUSSION

Nonadherence to medication poses challenging issues for all clinicians in the pharmacological management of conditions that need long-term therapy.

High adherence to antiseizure drugs plays a vital role in the successful treatment of epilepsy. Poor adherence to drug therapy is considered one of the major causes of non-responsiveness to chronic drug therapy such as antiepileptic drugs [23].

To suppress epileptic seizures, more than 95% adherence is adequately required. Even missing antiepileptic drug doses once or twice per week may be sufficient for the failure of therapy and is responsible for the reoccurrence of seizures [24].

According to the Modified Morisky Adherence score, we have classified our patients into Nonadherent and Adherent to their medications. Several factors influence patients' adherence to their medications. The primary purpose of this current study was to assess factors influencing medication adherence among epileptic patients and to provide recommendations for improving their healthcare and quality of life.

In this current study, 46% of the patients were adherent, and 54 % were poorly adherent to their medications (Table 2), which needs improvement. Reported patient adherence to drug therapy was different in various studies as 22% [23], 51.9 % [25] and 41% [26]. At the same time, Asadi-Pooya reported 75 % of patients compliance to antiepileptic drugs [27]. These differences in compliance between different studies may be due to different cultures, patient beliefs about illness, effectiveness of medication, education, and clinician approach to the patient with epilepsy. All these factors influence adherence to the therapy and control of seizure [28].

The effect of gender was an important contributing factor affecting medication adherence in this study. Male patients (31.3%) were more adherent to antiepileptic drugs as compared to females (14.1%) $p<0.05$. Our results did not agree with those carried out by [2], [18] (2011), who concluded in his research that there were no demographic differences based on gender between adherent and nonadherent patients. In our study, the younger age (23.4± 12.4) group was found to be more adherent to drug therapy as compared to the higher age (33.26± 16.34) $p<0.05$, (Table 1).

Our study population consists of patients with primary school (12.1%), high school (64.6%), and higher education (23.2%). Medication adherence did not show any significant difference among all the study groups.

The mean duration of epilepsy was 1.22 ±1.41. The age of disease onset and duration did not significantly correlate with the rate of adherence among our patients. In contrast, Kyngas found that the duration of the illness is significantly related to patient adherence [23].

Good motivation with a positive attitude toward disease and treatment with no fear of complications and no fear of seizures explains good adherence [23].

The effect of patient beliefs on medication adherence was studied in this current research. It was found that there was a positive association between adherence score (MMAS-8) and Belief about specific necessity score. Patients with positive necessity concern differential scores were higher in adherent patients to antiepileptic drugs than those with negative scores ($p<0.05$). In addition, patients who believed that antiepileptic drugs benefit more than harmful were significantly more adherent (Tables 3 and 4). Results obtained by Jones et al. [11] also found that epileptic patients, who had a greater belief in the need for medication, were significantly more adherent.

It was evident that there was an increase in adherence in patients with stronger beliefs in the necessity of treatment as they want to remain seizure-free with the help of antiepileptic drugs and also protect them from becoming worse.

Conversely, there was a negative association between adherence score and BMQ-specific concerns, general overuse, and general harm. Patients who believed that antiepileptic drugs do more harm than benefit were significantly higher in the nonadherent group, (Table 3).

Nonadherent patients have Beliefs about the negative impact of medication (specific concerns) like long-term effects, dependency on medication, and doctors' overuse of medication to treat them, and low concern about them. Nonadherent patients also have the Belief that medicines most medicines

are addictive, poisonous, and should be stopped.

Patients also had Beliefs about the general overuse of drugs -doctors use too many medications, and natural remedies are more are safer than medicines. General harm scores were higher in nonadherent compared to adherent patients ($p<0.05$), (Table 3).

In addition, our results suggest that women with epilepsy who are less adherent may also have more significant concerns about AEDs and more doubts about their personal need for AEDs [28].

Belief scores about a specific concern, general overuse, and general harm were significantly higher in females (p-value < 0.05) than males. In the current study, women were more concerned about the adverse effects of antiepileptic drugs.

V. CONCLUSION

Nonadherence to medication is a prevalent issue among epileptic patients receiving antiseizure treatment, and it significantly contributes to treatment failure. Several factors, such as the patient's higher educational attainment and a positive attitude toward therapy, can positively influence medication adherence. Additionally, patients' beliefs about these drugs play a pivotal role in achieving higher adherence levels. There is a growing concern regarding the potential negative impact of antiseizure medication on adherence. In addition to the accurate diagnosis and appropriate pharmacotherapy, the assessment of medication adherence holds a critical role in the management of epilepsy. To enhance the quality of life for individuals living with epilepsy, it is imperative to strengthen adherence to antiseizure medication.

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CONFLICT OF INTERESTS

The authors declare no conflicts of interest.

AUTHORS' CONTRIBUTIONS

All authors contributed equally to this paper. They have all read and approved the final version.

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