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Original Article

Appraisal of Factors Associated with Uncontrolled Seizures and Medication Adherence

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ABSTRACT

Aim: The main aim is to assess the factors concerning medication non-adherence and uncontrolled seizures. **Materials and Methods:** This is a hospital-based prospective observational study conducted in the outpatient department over 6 months, with patients who met the inclusion criteria. Patient's medication beliefs were assessed using the Beliefs about Medicines Questionnaire [BMQ]. The level of adherence was calculated using Morisky's Medication Adherence Scale [MMAS-8] to identify factors associated with uncontrolled seizures and non-adherence. **Results:** Two hundred and ten (210) patients were enrolled. We observed Generalised Tonic-Clonic Seizures (53.3%), Tonic seizures (19.5%), Focal seizures (13.3%), Tonic-clonic seizures (9%, and Absence seizures were also seen in (4.8%) of patients. Only (3.8%) of patients have controlled seizures due to poor medication adherence, compared to (37.6%) of patients who have better medication adherence (OR-9.104, *p*-0.0001). Patients who had negative beliefs about their treatment were more likely to have uncontrolled seizures (30.9%). (OR- 2.4904, *p*-0.0019). 49.5% of patients had uncontrolled seizures as a result of anti-epileptic drug's side effects, as compared to just 9% of patients who had no side effects (OR-2.463, *p*-0.008). **Conclusion:** The current study's findings revealed that unemployment, rural location, social habits, co morbidities, poor medication adherence, negative medication beliefs, and the occurrence of adverse drug reactions have a negative impact on epilepsy patients' medication adherence and treatment outcomes. Various studies support that the role of clinical pharmacist activities have a good effect on reducing seizure attacks in epileptic patients. This suggests that the clinical pharmacist's active participation in epilepsy control, through educating patients about medication adherence, avoiding abrupt antiepileptic medication withdrawal, and reporting adverse drug reactions, is effective and safe when done in collaboration with other healthcare professionals as part of their treatment regimen.

Keywords: Adverse Drug Reactions, Clinical Pharmacist, Epilepsy, Health Care Professionals, Medication Adherence, Medication Beliefs, Treatment Outcome.

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INTRODUCTION

Seizures have a major and frustrating impact on patients' lives, accounting for a large amount of the world's illness burden, impacting roughly 50 million people globally. At any given time, the proportion of the general population with active epilepsy is believed to be between 4 and 10 people per 1000. Globally, an estimated 5 million people are diagnosed with epilepsy each year. In high-income countries, there are estimated to be 49 per 100,000 people; in low and middle-income countries, the figure can be as high as 139 per 100,000 (WHO, 2022). At least 8% of the general population will experience a seizure at some point in their lives. Every year, 120 out of every 100,000 people in the United States seek medical help after experiencing a new seizure. Epilepsy has a rate of 44 per 100,000 person-years when adjusted for age. It is, nevertheless, common to experience a seizure without having epilepsy. The risk of recurrence of the initial unprovoked seizure varies between 23 and 80% after 5 years (Dipro *et al.*, 2017). Epilepsy is believed to affect around 10 million people in India. It affects about 1% of the population in our demographic, and seizures are only experienced by some people when they have a fever, but these febrile seizures are not epilepsy. Medication adherence and treatment results for individuals with epilepsy are negatively impacted by unemployment, rural location, social habits, co morbidities, poor medication adherence, unfavourable medicine attitudes, and the prevalence of adverse drug responses. Numerous studies attest to the beneficial impact of clinical pharmacists' actions in lowering seizure episodes in individuals with epilepsy. This implies that when a clinical pharmacist works with other medical professionals as part of a patient's treatment plan, their active involvement in epilepsy control-which includes teaching patients about medication adherence, preventing

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sudden withdrawal of antiepileptic medication, and reporting adverse drug reactions-is both safe and effective (Nandanavana *et al.*, 2014; Dipiro *et al.*, 2017).

MATERIALS AND METHODS

This is a hospital-based prospective observational study conducted in the outpatient department of Chelmada Anand Rao Institute of Medical Sciences, Karimnagar. Inclusion Criteria: Patients aged greater than or equal to 18 years with a seizure diagnosis who have had at least one year of regular follow-up on the antiepileptic drug. Exclusion Criteria: patients who are less than 18 years old with incomplete medical records. Patients who refused to be interviewed or who were too sick to finish the interview, pregnant and lactating mothers were excluded from the study.

Study Method

Patients who met research criteria were discovered through regular evaluation of patient records during the study period and documented in a pre-designed data collection form after receiving clearance from the IRB. Patients and their representatives were contacted for the study done in the neurology outpatient department. Patient interviews and case records were filled out by physicians, nurses, pharmacists, and other healthcare professionals to obtain patient data. All information will be kept private. The information gathered was then placed into a Microsoft Excel database and analysed further. During the data collection period, all approved seizure patients who visited the hospital for their routine follow-up were included in this study. Patients were interviewed using a standard questionnaire to get information on socio-demographics, medication adherence, medication beliefs, and medication necessity. During the follow-up phase, the patients' information was evaluated. The Beliefs about Medicines Questionnaire (BMQ) and Morisky' s Medication Adherence Scale were used to examine beliefs about Medicines and Medication Adherence (MMAS-8). We interviewed the patients about their pharmaceutical attitudes using the Beliefs about Medicine Questionnaire (BMQ). It's a self-administered questionnaire with 25-item measures that assess patients' opinions and worries regarding the need for prescription medications to control their disease. If the average sum of the five-item medication score (ranging from 5-25) is above the midpoint, the patient is deemed to have a strong medication necessity belief; if the score is below the midpoint, they are thought to have a low medication necessity belief. Similarly, if the average score (which ranges from 5-25) is above the midpoint, the patients are said to have a high medication concern belief; if the score is below the midpoint, they are said to have a low medication concern belief. The overall patient belief about the drug is calculated by subtracting the average 5-item medication concern score from the average 5-item medication necessity score. If the outcome was positive, the patient was thought to have a positive medicine belief; if the outcome was negative, the patient was thought to have a negative medication belief. Morisky's Medication Adherence Scale (MMAS-8) was used to assess medication adherence. It is also a self-reported standard questionnaire that involves eight questions, in which the total score ranges from 0-to8 points. It is an eight-item scale with the score given Yes as 0 points and no as 1 point for the first seven questions and a 5-point Like response for the eighth question. The medication adherence was considered as low if the total score is < 6 points, medium adherence for 6 to <8 points, and high adherence for 8 points. The patient is said to be non-adherent if there is low or medium adherence to the medication. We also made a list of the most prevalent side effects related to anti-epileptic drugs.

Statistical Analysis

The significant changes in the odds ratio and *p*-value of factors affecting uncontrolled seizures and medication adherence were calculated by using univariate logistic regression in the Statistical Package for Social Sciences software. The univariate logistic regression test is a regression analysis test, as the formula is based on dividing the odds of the first group by the odds in the second group. The odds ratio is used to explain the comparison of relative odds of the occurrence of the outcome of interest. Odds ratio = a×d /b×c Where a is the number in the exposed group, (positive (bad) outcome), b is the number in the exposed group (negative (good) outcome), and c is the number in the control group (positive (bad) outcome), d is the number in the control group (negative (good) outcome). Significance was set at a one-tailed probability value less than 0.05. The stars are only intended to flag levels of significance for three of the most commonly used levels. If a *p*- value is less than 0.05, it is flagged with one star (*), If a *p*-value is less than 0.01, it is flagged with two stars (**), and If a *p*-value is less than 0.001, it is flagged with three stars (***), and if a *p*-value is less than 0.0001, it is flagged with four stars (****) (Tables 1-8).

RESULTS

Factors Affecting Treatment Outcome in Epilepsy Patients

Factors Affecting Medication Adherence in Epilepsy Patients

Male patients (23.8%) have poor seizure control status than female patients (17.6%). This could be due to social habits or a lack of drug adherence. According to our findings, married patients (48%) had a higher rate of controlled seizures than unmarried individuals (10.4%). Care and compelling patients to take medicine from their families could be the reasons for this. When it comes to educational levels, educated patients are more likely to have controlled seizures (31.9%) than illiterate patients (26.6%). This might be because they are aware of their condition and take their medicine as prescribed. Patients with uncontrolled seizures are more common in rural areas (21.9%) than in urban areas (19.5%). This could be due to a lack of

Table 1: Demographic factors.

Variables	Uncontrolled	Control	Odds Ratio	*p*-Value
Age (in years)				
18-30	31(14.76)	31(14.76)	0.6000	0.1108
31-60	70(33.33)	42(20.0)	1.0606	0.8812
>60	22(10.47)	14(6.66)	0.6364	0.2886
Gender				
Male	50(23.80)	74(35.23)		
			0.895	0.6961
Female	37(17.61)	49(23.33)		
Marital Status				
Married	67(31.90)	101(48.09)		
			0.730	0.363
Single	20(9.52)	22(10.47)		
Education				
Literate	58(27.61)	67(31.90)		
			1.672	0.0771
Illiterate	29(13.80)	56(26.66)		
Employment				
Employed	50(23.80)	72(34.28)		
			0.957	0.877
Unemployed	37(17.61)	51(24.28)		
Residence				
Rural	46(21.90)	64(30.47)		
			1.034	0.9043
Urban	41(19.52)	59(28.09)		

Table 2: Social Habits Affecting Treatment Outcome.

Variables	Uncontrolled	Control	Odds ratio	*p*-Value
Alcohol				
Yes	27(12.85)	16(7.61)		
			1.4211	0.326
No	76(36.19)	64(30.47)		
Smoking				
Yes	11(5.23)	1(0.47)		
			9.0722	0.0367
No	97(46.19)	80(38.09)		
Tobacco Chewing				
Yes	2(0.95)	2(0.95)		
			0.7723	0.7983
No	101(48.09)	78(37.14)		

understanding of their condition, poor medication adherence, or religious or superstitious beliefs. Controlled seizures affect 11.9% of patients, compared to 29.5% of those who have no social habits. Alcohol use has been associated with the development of seizures and a greater risk of seizures in epileptic patients, as per various studies. In our study, alcohol was also revealed to be a marker of uncontrolled seizures. This could be explained by the fact that alcohol intake can cause sleep loss, missed meals,

Table 3: Disease-Related Factors.

Variable	Uncontrolled	Controlled	Odds Ratio	*p*-Value
Types of Seizures				
Generalised Seizures	103 (49.09)	71 (33.80)		
			1.1606	0.6867
Partial Seizures	20 (9.52)	16 (7.61)		
Duration of Epilepsy				
< 5 years	81 (38.57)	71 (33.80)		
			0.4346	0.0131**
≥ 5 years	42 (20.0)	16 (7.61)		

Table 4: Treatment-related factors.

Variable	Uncontrolled	Controlled	Odds Ratio	*p*-Value
Medication Adherence				
Adherent	59 (28.09)	8 (3.80)		
			9.104	0.0001****
Non-Adherent	64 (30.47)	79 (37.61)		
Number of Anti-Epileptic Drugs				
Two	16 (7.61)	0 (0)		
			0.0009	0.0001****
One	107 (50.95)	87 (41.42)		
Adverse Drug Reactions				
Yes	104 (49.52)	60 (28.57)		
			2.463	0.0081
No	19 (9.04)	27 (12.85)		

The table above shows various factors affecting the treatment outcome of epilepsy. Every factor is evaluated by calculating the odds ratios and *p*-value. Factors such as age, gender, marital status, education, employment, residence, and duration of epilepsy are taken into account.

skipped medicine, and increased antiepileptic drug side effects, all of which were linked to seizure-provoking events. As a result, much should be done to promote awareness of epileptic patients' alcohol abstinence. Patients with controlled seizures (33.8%) are more likely to have a duration of epilepsy of fewer than five years than those with a duration of epilepsy of more than five years (OR-0.4346, *p*-0.0131) **.

Medication Adherence

Medication non-adherence was more prevalent among male patients (19%) than females (12%), potentially influenced by occupational stress and social behaviours. At the same time, marital status had a positive impact on adherence, with married individuals demonstrating significantly better compliance (53.3%) than unmarried patients (14.7%), likely due to familial support. Educational status also played a crucial role, as educated patients exhibited higher adherence levels (43.3%) than uneducated individuals (24.7%), reflecting improved disease awareness. Residence was significantly associated with adherence, with rural patients showing poorer compliance (20.4%) compared to urban populations (11.4%) due to limited healthcare access and socioeconomic factors (OR=2.032, *p*=0.0200). Employed patients demonstrated higher rates of poor adherence (12.5%), possibly due to work-related time constraints. Shorter disease duration (<5 years) was associated with better adherence (52.8%) compared to longer duration, indicating positive treatment perceptions (OR=0.4546, *p*=0.0141). Alcohol consumption was linked to reduced adherence (14.2%) relative to non-consumers (47.6%). Poor adherence was strongly correlated with uncontrolled seizures (28.0%) in contrast to controlled cases (3.8%) (OR=9.104, *p*=0.0001). Patients holding negative beliefs about antiepileptic therapy showed lower adherence (28%) and higher seizure instability (30.9%) than those with positive beliefs (40% adherence; 27.6% uncontrolled seizures) (OR=2.4904, *p*=0.0019). Adverse drug reactions were reported by 47.3% of patients and significantly contributed to non-adherence (OR=2.669, *p*=0.0199). Furthermore, seizure control was more commonly observed in patients with epilepsy duration under five years (33.8%) compared to longer duration (OR=0.4346, *p*=0.0131), and higher adherence was significantly associated with improved seizure control (37.6% vs 3.8%) (OR=9.104, *p*=0.0001).

Table 5: Demographic factors.

Variables	Non-Adherent	Adherent	Odds Ratio	*p*-Value
Age (in years)				
18-30	13 (6.19)	49 (23.33)	0.4776	0.0452
31-60	40 (19.04)	72 (34.28)	0.8730	0.7308
>60	14 (6.66)	22 (10.47)	0.4169	0.0587
Gender				
Male	40 (19.04)	84 (40)		
			1.041	0.8951
Female	27 (12.85)	59 (28.09)		
Marital Status				
Married	56 (26.66)	112 (53.33)		
			1.409	0.3758
Single	11(5.23)	31(14.76)		
Education				
Literate	34 (16.19	91 (43.33)		
			0.589	0.0773
Illiterate	33 (15.71)	52 (24.76)		
Employment				
Yes	50 (23.80)	72 (34.28)		
			0.957	0.877
No	37 (17.61)	51 (24.28)		
Residence				
Rural	43 (20.47)	67 (31.90)		
			2.032	0.0200
Urban	24 (11.42)	76(36.19)		

Table 6: Social Habits Affecting Medication Adherence.

Variables	Non-Adherent	Adherent	Odds Ratio	*p*-Value
Alcohol				
Yes	13 (6.19)	30 (14.28)		
			1.0833	0.8337
No	40 (19.04)	100 (47.61)		
Smoking				
Yes	5 (2.38)	1 (0.47)		
			13.4375	0.0191**
No	48 (22.85)	129 (61.42)		

Table 7: Disease-Related Factors.

Variables	Non-Adherent	Adherent	Odds Ratio	*p*-Value
Duration of Epilepsy				
<5years	41 (19.52)	111 (52.85)		
			0.4546	0.0141**
≥5years	26 (12.38)	32 (15.23)		

Table 8: Treatment-Related Factors.

Variables	Non-Adherent	Adherent	Odds Ratio	*p*-Value
Treatment Outcome				
Uncontrol	59 (28.09)	64 (30.47)		
			9.104	0.0001****
Control	8 (3.80)	79 (37.61)		
Number of Anti-Epileptic Drugs				
Two	5 (2.38)	11 (5.23)		
			0.9677	0.9534
One	62(29.52)	132 (62.85)		
Adverse Drug Reactions				
Yes	59 (28.09)	105 (50)		
			2.669	0.0199**
No	8 (3.80)	38 (18.09)		

DISCUSSION

The study was conducted in a tertiary care hospital in Karimnagar. A total of 210 patients met the study's inclusion criteria. In the Yirga Legesse Niriayo study, 60.4% were between the ages of 18 and 30, 36.6% were between the ages of 31 and 60, and only 3% of patients were over the age of 60 (Yirga *et al.,* 2018). This is in contrast to our results, which show that 29.5 % are between the ages of 18 and 30, 53.3% are between the ages of 31 and 60, and 17.5% are over the age of 60. The study had a male participation rate of 59 % and a female participation rate of 40.9%. Males outnumbered females by a significant margin. It mimics the study of Yirga Legesse Niriayo *et al.*, 2018. In our study, 20% of the patients were single, while the other 80% were married. This is in contrast to the Yirga Legesse Niriayo *et al.*, study, which includes 60% of the patients who were single and 25.9%of the patients who were married. Patients are employed in 58.1% of cases, while the remaining 41.9% are unemployed. The tertiary care teaching hospital for our study is located in a rural area, 52.4% of the patients are from rural areas, and 47.6 % are from urban areas. In terms of social drug use, our study found that 20% of people used alcohol, 3.8% used cigarettes, 2.4 % used Tobacco Chewing. This is in contrast to the study of Yirga Legesse Niriayo *et al.,* 2018, which comprise 6.3% of people who used alcohol, 4.4% used cigarettes, and 4.1% used Tobacco Chewing. On set of seizures at age so less than or equal to 15 years (6.1%), 16 to 30 years (34.2%), 31 to 45 years (24.2%), and greater than 45 years (24.2%). 35.2%, the occurrence of the first seizure is higher in the age groups of 16 to 30 years and greater than equals to 45 years, as this age group may have more social drug usage, and educational and work stress. 72.3 % of patients in our study had a duration of epilepsy of fewer than 5 years, while 27.6% had a duration of epilepsy of more than or equal to 5 years. This conflicts with a 2018 study by Yirga Legesse Niriayo *et al.*, that comprise 40.4% of patients had a duration of epilepsy of fewer than 5years, whereas 59.6% of patients had a duration of epilepsy of more than or equal to 5 years. The majority of the patients had hypertension (22.4%) and diabetes (4.3%), whereas a smaller proportion of patients had thyroid (0.95%). This might be due to personal [i.e., diet, social habits, stress] and socioeconomic factors could be to blame. Different types of seizures were observed in the patients; the majority of the patients had generalised tonic-clonic seizures (53.3%), while a smaller proportion of patients had absence seizures (4.8%). The prevalence of adverse medication reactions (78.1%) caused by anti-epileptic medicines was recorded throughout this study period. It could be due to long-term antiepileptic drug use. It mimics the Yirga Legesse Niriayo *et al.*, 2018 report.58.5%of patients have uncontrolled seizures, and only 41.4%are with controlled seizures. The majority of the patients were under monotherapy (92.4%), and 7.6% of patients were under combination therapy. Levetiracetam was the most prescribed drug in monotherapy. A total of 164 ADRs were noted, with CNS adverse effects noted as high. Levetiracetam, carbamazepine, and phenytoin produced headaches, aggression, sedation, and memory loss effects mostly. It mimics the study of Keerthy Jayalekshmi *et al.*, 2016 report. Male patients (23.8%) have poor seizure control status than female patients (17.6%). This could be due to social habits or a lack of drug adherence. According to our findings, married patients (48%) had a higher rate of controlled seizures than unmarried individuals (10.4%). Care and compelling patients to take medicine from their families could be the reasons for this. When it comes to educational levels, educated patients are more likely to have controlled seizures (31.9%) than illiterate patients (26.6%). This might be because they are aware of their condition and take their medicine as prescribed. It mimics the study of Yirga Legesse Niriayo *et al.*, 2018, which comprises 41.9% of educated patients who had controlled seizures. Patients with uncontrolled seizures are more common in rural areas (21.9%) than in urban areas (19.5%). This could be due to a lack of understanding of their condition,

poor medication adherence, or religious or superstitious beliefs. Controlled seizures affect 11.9% of patients, compared to 29.5% of those who have no social habits. Alcohol use has been associated with the development of seizures and a greater risk of seizures in epileptic patients, as per various studies. In our study, alcohol was also revealed to be a marker of uncontrolled seizures. This could be explained by the fact that alcohol intake can cause sleep loss, missed meals, skipped medicine, and increased antiepileptic drug side effects, all of which were linked to seizure-provoking events. As a result, much should be done to promote awareness of epileptic patients' alcohol abstinence. Patients with controlled seizures (33.8%) are more likely to have a duration of epilepsy of fewer than five years than those with a duration of epilepsy of more than five years (OR-0.4346, *p*- 0.0131) **. This is in contrast to the study of Yirga Legesse Niriayo *et al*., 2018, which comprises 17.8% of patients who had a duration of epilepsy of fewer than five years and 28.9% of patients with a duration of epilepsy of more than five years. Only 3.8% have controlled seizures due to poor medication adherence, compared to 37.6% of patients who have better medication adherence (OR-9.104, *p*-0.0001) ****. It mimics the study of Yirga Legesse Niriayo *et al*., 2018, which comprises 36%ofpatients who have controlled seizures with better medication adherence. Patients who had negative beliefs about their treatment were more likely to have uncontrolled seizures (30.9%) than patients who had positive beliefs about the medicine (27.6%) (OR-2.4904, *p*-0.0019) ***. It mimics the study of Yirga Legesse Niriayo *et al*., 2018, which comprises 21.9% of patients with uncontrolled seizures who had negative beliefs. Patients on monotherapy (50.9%) are less likely than those on polytherapy (7.6%) to have uncontrolled seizures (OR-0.0009, *p*-0.0001) ****. This could be due to monotherapy being efficient in curing the disease and the cost-effectiveness of antiepileptic drugs. 49.5% of patients have uncontrolled seizures as a result of antiepileptic drug side effects, compared to just 9% of patients who have no side effects (OR-2.463, *p*-0.0081).

CONCLUSION

Identifying predictors of seizure control is crucial for optimising epilepsy management and improving patient outcomes. In this study, the mean age of participants was similar between males and females (41.5 and 41.8 years), with a male predominance observed. The majority of patients were married (80%), while 20% were single. Generalised tonic-clonic seizures were the most common seizure type (53.3%), whereas absence seizures were the least prevalent (4.8%). Uncontrolled seizures were more frequent (58.5%) compared to controlled seizures (41.4%). Most patients received monotherapy (92.4%), with levetiracetam being the most commonly prescribed antiepileptic drug. A total of 164 adverse drug reactions were documented, primarily involving central nervous system effects such as headache, aggression, sedation, and memory impairment, particularly associated with levetiracetam, carbamazepine, and phenytoin. Treatment outcomes and medication adherence were significantly influenced by factors including marital status, employment, rural residence, social habits, comorbidities, medication adherence levels, medication beliefs, number of antiepileptic drugs, and the occurrence of adverse drug reactions. Specifically, unemployment, rural living, social habits, comorbid conditions, poor adherence, negative beliefs regarding medications, and adverse drug reactions were linked to poorer seizure control. Supporting evidence highlights the beneficial role of clinical pharmacists in reducing seizure frequency through patient education, adherence promotion, prevention of abrupt antiepileptic drug withdrawal, and adverse reaction monitoring in collaboration with healthcare professionals. These findings emphasise the importance of a multidisciplinary approach in epilepsy management and suggest the need for further well-designed studies to establish causal relationships between predictive factors and seizure control outcomes.

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ABBREVIATIONS

BMQ: Beliefs about Medicines Questionnaire; **MMAS-8:** Morisky's Medication Adherence Scale; **ADR:** Adverse Drug Reaction; **CNS:** Central Nervous System; **OR:** Odds Ratio; **WHO:** World Health Organization; **IRB:** Institutional Review Board; **Pharm D:** Doctor of Pharmacy.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

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