A CROSS-SECTIONAL COMPARATIVE STUDY TO EVALUATE MEDICATION ADHERENCE AND QUALITY OF LIFE AMONG EPILEPTIC PATIENTS WHO RECEIVED COMBINATION THERAPY WITH LEVETIRACETAM

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ABSTRACT

Background: Successful epilepsy management hinges on two critical factors: consistent medication adherence and a positive belief system. By combining these elements, patients can unlock the full potential of their treatment plans, leading to better seizure control, enhanced quality of life, and improved long-term health prospects. The purpose of this study was to investigate medication adherence, quality of life and associated factors among ambulatory patients with epilepsy. **Method:** A cross-sectional study was conducted on epileptic who received levetiracetam combination therapy. Medication adherence was assessed using four level medication adherence scale and quality of life was assessed using a QOLIE10p questionnaire. The data were entered into Microsoft Excel Spreadsheet and Statistical analysis was performed by IBM SPSS 22.0.
Result: There were five groups in which levetiracetam was used in combination with other AED were as follows:
- Group A: Levetiracetam + Lacosamide
- Group B: Levetiracetam + Clobazam
- Group C: Levetiracetam + Oxcarbazepine
- Group D: Levetiracetam + Sodium valproate
- Group E: Levetiracetam + Phenytoin

Out of the 90 patients 58 patients where adherent to their medication regimen and 32 patients where nonadherent to their medication. Due to an insufficient sample size, only Group A (LEV-LCM) and Group B (LEV-CLB) were statistically analysed for QOL and there was no significant difference seen. **Conclusion**: Approximately 64.5% of patients were adherent to their medication and 35.5% were non adherent and factors affecting nonadherence was forgetfulness, fear of side effects, symptom improvement, symptom worsening. About 21% of patients complained that seizure is affecting their daily activities, 19% of patients had worry about fits, 19% of patients complained about changes in their energy level, in 15.5% of patient's mental activities, overall quality of life was impaired in 11% of patients in 4% of patient's emotions were affected.

KEYWORDS: Antiepileptic drug, levetiracetam, lacosamide, clobazam.

INTRODUCTION

Epilepsy is a chronic and debilating neurological disorder that can have far-reaching consequences, including cognitive and psychosocial impairment, reduced quality of life, increased risk of physical harm, social isolation, academic underachievement, limited career opportunities, and a shorter life expectancy.[1] It is a global health problem that affects more than 70 million people worldwide and more than 85% of the global burden of epilepsy occurs in developing countries. In resource-constrained settings, the stigma attached to epilepsy exacerbates existing healthcare challenges, resulting in inadequate treatment, suboptimal health outcomes, and a diminished quality of life for individuals living with the condition.[2]

Antiepileptic medications are the cornerstone of epilepsy treatment, offering the potential for seizure control in up to 70% of patients when administered correctly. However, a significant proportion of individuals with

epilepsy in developing regions continue to experience uncontrolled seizures. A key obstacle to effective management is nonadherence to prescribed treatment regimens, which remains the primary reason for therapeutic failure in epilepsy.[3]

Taking medications as prescribed is vital for effective treatment, but most patients don't follow their medication regimens. Various factors influence this adherence, including: personal beliefs about medications, presence of other health conditions, number of medications taken, length of treatment, age, gender, education level. Notably, a patient's beliefs about their medications are the strongest predictor of adherence. When patients don't take their antiepileptic medications as directed, it can lead to reduced seizure control, more frequent hospital visits, higher healthcare expenses, increased quality of life, increased risk of death. Improving medication adherence is crucial for better health outcomes in epilepsy management.[4]

Evaluating how well patients stick to their medication regimens and understanding their beliefs about those medications is crucial for optimizing epilepsy treatment. Identifying the key factors that influence adherence to antiepileptic drugs (AEDs) can help healthcare providers develop targeted strategies to improve treatment outcomes. By doing so, patients can better manage their condition, reduce the risk of complications, and enhance their overall quality of life. The aim of the current study was to identify the medication adherence among epileptic patients who received levetiracetam combination therapy, and the factors affecting medication adherence.[5]

Quality of life (QoL) in patients with epilepsy is a complex issue affected by various factors such as seizure frequency and severity, treatment side effects, lifestyle restrictions, and psychiatric comorbidities. In addition to physical and medical factors, psychosocial aspects such as perceived stigmatization and social exclusion can also play a significant role in a patient's QoL.[6]

To assess and measure QoL in patients with epilepsy, a variety of surveys, scales, and questionnaires are used in both clinical and research settings. These tools help evaluate the impact of seizures, treatments, and other factors on the patient's QoL and guide personalized management plans.[7]

MATERIAL AND METHODS
This study was a cross-sectional comparative study conducted at a tertiary care hospital on 90 epilepsy patients for a period of 6 months.

Both inpatients and outpatients diagnosed with focal epilepsy with or without secondary generalization, patients receiving combination of AEDs with LEV, patients of age 18 years, patients of all gender were included in the study. Pregnant and lactating women, patients with comorbidities leading to seizure were excluded.

Medication adherence was assessed using four level medication adherence scale and quality of life was assessed using a QOLIE10p questionnaire. The data were entered into Microsoft Excel Spreadsheet and Statistical analysis was performed by IBM SPSS 22.0.

After obtaining permission from the IEC, study began with data collection. Case records were retrospectively and prospectively reviewed for demographic data, clinical presentations, investigations, management and adverse reactions.

RESULT AND DISCUSSION
A total of 90 patients met with the inclusion criteria were included in the study

Table 1: Frequency and percentage distribution of samples according to gender.
N=90

SEX	FREQUENCY	PERCENTAGE (%)
MALE	42	47
FEMALE	48	53

Inference: This data shows that out of the 90 samples of epilepsy patients about 48 were females and 42 were males.

Table 2: Frequency and percentage distribution of samples according to age in year.
N=90

Age in years	Frequency	Percentage (%)
18 – 38 YEARS	28	31.2
39 - 58 YEARS	24	26.7
59 – 78 YEARS	32	35.5
79 – 98 YEARS	6	6.6

Inference: About 35.5% of patients where in age group of 59-78 years. Then maximum percentage of patients (31.2 %) where in age group of 18-38 years. About 26.7 % of patients where in age group of 39-58 years. The least percentage of patients about 6.6% where in age group of 79-98 years.

Table 3: Frequency and percentage distribution of samples according to marital status N=90

MARITAL STATUS	FREQUENCY	PERCENTAGE (%)
MARRIED	69	77%
UNMARRIED	21	23%

Inference: The above data shows that about 77% of patients were married and 23% were unmarried.

Table 4: Frequency and percentage distribution of samples according to educational status. N=90

EDUCATIONAL STATUS	FREQUENCY	PERCENTAGE (%)
SCHOOL	36	40%
HIGHER SECONDARY	18	20%
COLLEGE	36	40%

Inference: The above data shows the distribution of samples according to their educational status. The level of education affects the medication adherence and thereby the quality of life of patients. Here about 40% of patients are having at least graduate degree and 40% of patients are either passed matriculation or below. It is important to increase patient education, knowledge about the disease and its treatment to increase adherence.

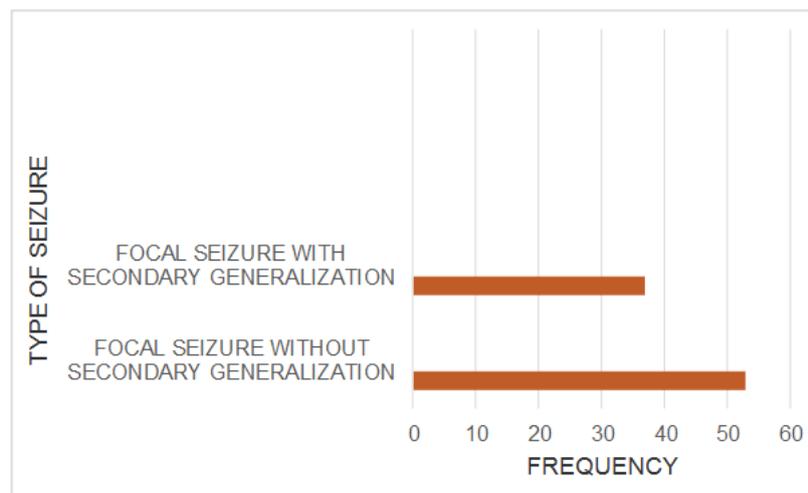**Table 5: Frequency and percentage distribution of samples according to employment status.** N=90

STATUS	FREQUENCY	PERCENTAGE (%)
EMPLOYED	34	37.7%
UNEMPLOYED	56	62.3%

Inference: The above data shows that about 62.3% of patients were unemployed and 37.7% were employed. Employment status can affect the level of medication adherence among the patients. Employed individuals are significantly aware about their condition and the importance of AED regimen in the management of their condition and thereby maintain an optimal quality of life.

Table 6: Frequency and percentage distribution of samples according to type of seizure N=90

TYPE OF SEIZURE	FREQUENCY	PERCENTAGE (%)
FOCAL SEIZURE WITHOUT SECONDARY GENERALIZATION	53	58.9
FOCAL SEIZURE WITH SECONDARY GENERALIZATION	37	41.1

Fig. 1: Frequency distribution of samples according to type of Seizure.

Inference: The above data shows out of the 90 samples 53 cases were focal seizure without secondary generalization and 37 were focal seizure with secondary generalization. In all these cases LEV was used as first line agent. The treatment of epilepsy is mainly based on different factors, out of which type of seizure is a major factor that determines the choice of AEDs.

Table 7: Frequency and percentage distribution of samples according to medication combination.
 N=90

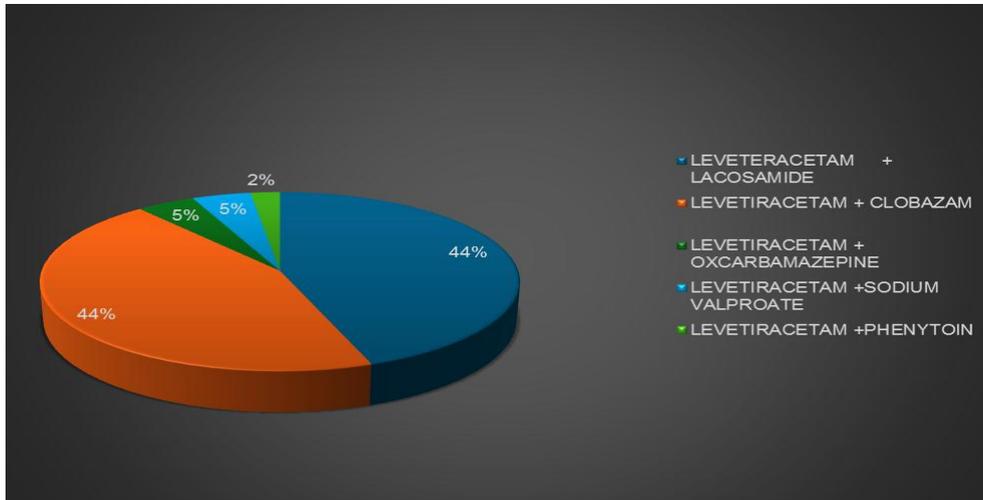| MEDICATION COMBINATION	FREQUENCY	PERCENTAGE (%)
LEV + LCM	40	44
LEV + CLB	40	44
LEV + OXC	4	5
LEV + SODIUM VALPROATE	4	5
LEV +PHT	2	2

Fig 2: Percentage distribution of samples according to medication combination.

Inference: The above data shows various combination of AEDs with LEV in which LEV-LCM and LEV-CLB was prescribed the most. Other combinations are LEV-PHT, LEV-OXC and LEV-sodium valproate.

Table 8: Frequency and distribution of samples according to medication adherence.
N=90

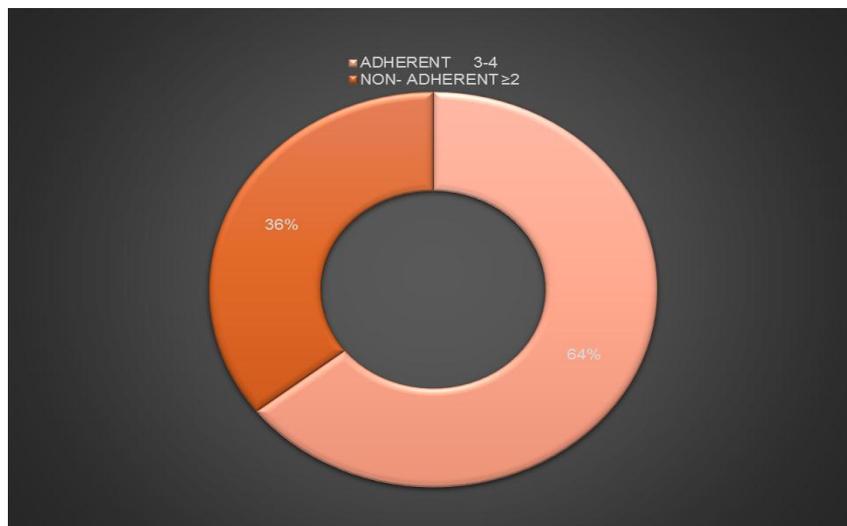| MEDICATION ADHERENCE	FREQUENCY	PERCENTAGE (%)
ADHERENT	58	64.5
NON- ADHERENT	32	35.5

Fig. 2: Percentage distribution of samples according to medication adherenc.

Inference: The above data shows that out of the 90 patients 58 patients where adherent to their medication regimen and 32 patients where nonadherent to their medication.

Adherence to AED treatment were assessed using the four-item Medication Adherence Scale, a standardized, validated questionnaire for measuring self-reported medication adherence.

The four items of the MMAS-4 assess whether:
(a) the patient has ever forgotten to take medication
(b) the patient has ever had problems remembering to take medication
(c) the patient has stopped medication due to alleviating symptoms

(d) the patient has stopped medication due to worsening symptoms

Each item is scored as either 0 (Yes) or 1 (No). The score of each item is then summed to give a range of scores from 0 to 4. A score of 3–4 suggests that the patient is adherent, while a score of ≤2 suggests that the patient is nonadherent.

Table 9: Frequency and percentage distribution of samples according to medication adherence in LCM and CLB group.
n=80

Medication adherence	LCM (n=40)		CLB (n=40)	
	f	%	F	%
Non adherent	12	30.0	15	37.5
Adherent	28	70.0	25	62.5

Fig. 3: Percentage distribution of samples according to medication adherence in group A(LEV+LCM).

Fig. 4: Percentage distribution of samples according to medication adherence in group B(LEV+CLB).

Inference: The number of patients adherent to medication in group A, where LCM was given as an adjuvant include 28 and about 12 patients where non adherent to their regimen. In the group B where CLB was given as an adjuvant the number of patients adherent to their regimen was 25 and about 15 patients where nonadherent to their regimen.

The reasons for nonadherence included forgetfulness, being seizure-free for a period, and fear of adverse drug effects. Nonadherence to AEDs is associated with increased risk of mortality, and a higher incidence of emergency department visits, hospital admissions, injuries, and fractures. Generally, factors affecting adherence to medication can range from sociodemographic factors, such as age, gender, level of education, affordability, number of drugs administered, social support, beliefs about medication, and side effects to medication. It worth mentioning, it is preferable to maintain a patient on a single AED. This increases the probability of compliance, provides a wider therapeutic index, and is more cost-effective than combination drug treatment. Monotherapy in contrast to polytherapy is also associated with fewer idiosyncratic reactions and a lower incidence of teratogenic effects. Combination therapy can be associated with drug interactions between AEDs making it difficult to dose and monitor patients.

Table 10: Association of medication adherence with demographic variables.

Sl. No	Demographic variables	Medication adherence		Total	χ^2 test
		Non adherence	Adherent		
1	Educational Status				χ^2=31.083, df=2, p<0.001***
	Graduate	3	33	36	
	HSS	4	14	18	
	School	25	11	36	
2	Employment Status				χ^2=20.998, df=1, p<0.001***
	Unemployed	30	26	56	
	Employed	2	32	34	
3	Marital Status				χ^2=5.408, df=1, p=0.020*
	Unmarried	3	18	21	
	Married	29	40	69	

NS- Not Significant, ***- Significant at 0.001 level   N=90

Inference: The above table shows the association between educational status and medication adherence which was found to be statistically significant with a p value <0.001. Out of 36 graduates 33 were adherent and among 18 patients who had passed higher secondary education 14 were adherent, out of 36 patients who had passed matriculation or below only 11 patients were adherent.

The association between employment status and medication adherence was also found to be statistically significant with a p value<0.001. Out of 34 employed patients 32 were adherent and out of 56 unemployed patients 26 were adherent.

The association between marital status and medication adherence was found to be statistically significant with a p value<0.02. Out of 69 married patients 40 were adherent and out of 21unmarried patients 18 were adherent.

Table 11: Frequency and percentage distribution of factors affecting medication non adherence.
N=90

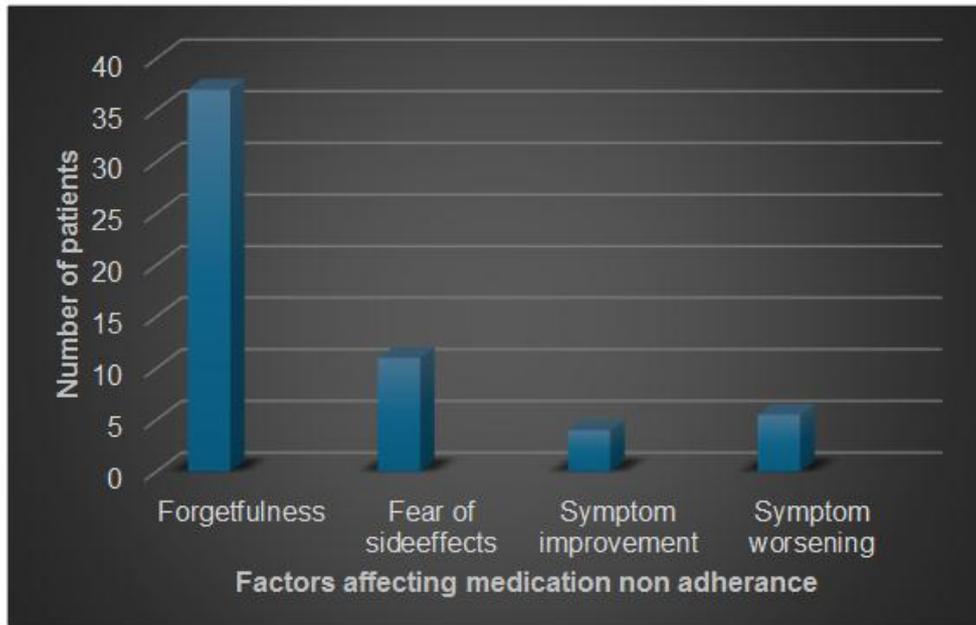| Sl. No	FACTORS	FREQUENCY	PERCENTAGE (%)
1	FORGETFULNESS	33	37
2	FEAR OF SIDE EFFECTS	10	11
3	SYMPTOMS IMPROVEMENT	4	4
4	SYMPTOMS WORSENING	5	5.5

Fig. 5: Factors affecting medication nonadherence.

Inference: The above figure shows the factors affecting medication nonadherence. Forgetfulness, fear of side-effects, symptom improvement and worsening of symptoms were the factors most commonly affecting medication nonadherence. About 37% of patients were having forgetfulness and it caused nonadherence to the prescribed regimen. About 11% of patients were nonadherent due to fear of side effects, 4% patients were nonadherent due to improvement in symptoms and about 5.5% were due to worsening of symptoms.

QUALITY OF LIFE
Table 12: Mean, standard deviation, mean difference, t value and p value of quality of life of patients received LCM and CLB as add on to LEV.

Drug	Min	Max	Mean	Standard deviation	Mean difference	t value (unpaired t test)	p value
LEV+LCM (N=40)	2.18	3.81	2.90	0.41	0.14	1.404	0.164 (NS)
LEV+CLB (N=40)	1.63	3.91	2.76	0.47			

NS- Not Significant n=80
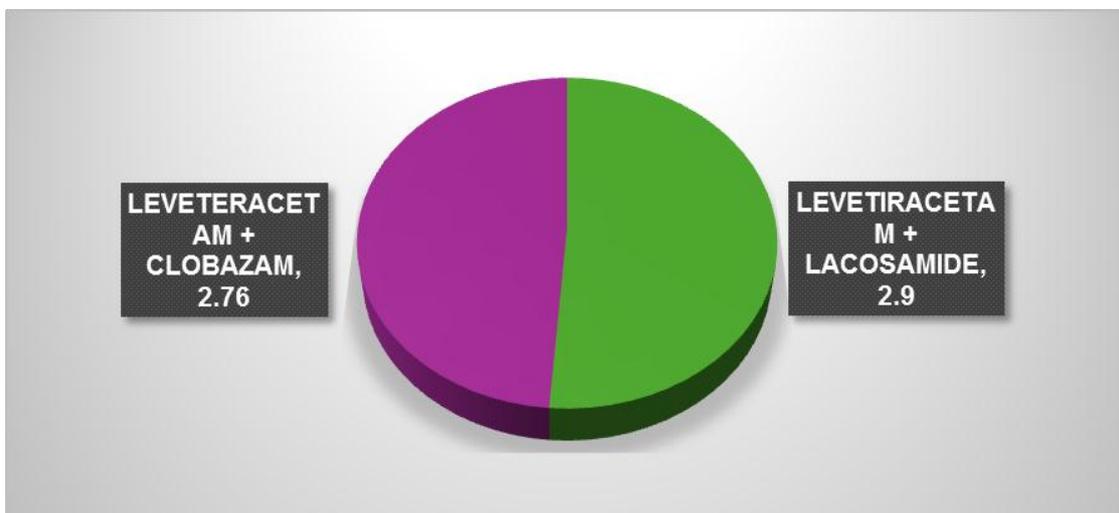
INFERENCE: The quality-of-life score ranges from 1-5.09 A low score indicates better quality of life. The above table shows mean quality of life(±SD) in both groups. And it was 2.90(±0.41) in the group A where LCM was added as an adjuvant. And it was 2.76(±0.47) in group B were CLB was added as an adjuvant. But this difference was not found to be statistically non-significant as the p value was 0.164.

Table 13: Mean and standard deviation of quality-of-life score based on demographic details.
n=80

Sl. No	Demographic variables	Mean	SD
	Educational status		
1	Graduate	2.70	0.40
	HSS	2.88	0.54
	School	2.95	0.41
	Employment status		
2	Unemployed	2.97	0.42
	Employed	2.65	0.41
	Marital status		
3	Unmarried	2.64	0.47
	Married	2.89	0.42

INFERENCE: The above chart shows relationship between quality of life and demographic variables. The quality-of-life score ranges from 1-5.09 A low score indicates better quality of life. The quality-of-life score was found to be 2.70 in patients of high educational status compared to patients who are either passed matriculation or below 2.95. Employed individuals were having high quality of life (qol score=2.65) compared to unemployed patients (qol score=2.97). Comparing marital status with quality of life it was found that unmarried individuals are having high quality of life (qol = 2.64) compared to married individuals(qol=2.89).

Table 14: Frequency and percentage distribution of samples according to various subscales of QOLIE 10p questionnaire.

Sl. No	SUBSCALE	FREQUENCY	PERCENTAGE (%)
1.	Energy(tiredness)	17	19
2.	Emotions(mood)	4	4
3.	Daily activities (Work, driving, social)	19	21
4.	Mental activities (thinking, concentrating, memory)	14	15.5
5.	Medication effects (physical, mental)	8	10
6.	Worry about fits	17	19
7.	Overall quality of life	10	11

INFERENCE: The above table shows the frequency and percentage distribution of samples according to various subscales of QOLIE 10p questionnaire.

It is a epilepsy specific questionnaire which includes 11 questions containing seven domains to be measured: 1) Seizure worry; 2) Overall Quality of life; 3) Emotional well-being; 4) Energy/fatigue; 5) Cognitive functioning; 6) Medication effects; 7) Social functioning.

About 21% of patients complained that seizure is affecting their daily activities, 19% of patients had worry about fits, 19% of patients complained about changes in their energy level, in 15.5% of patients mental activities, overall quality of life was impaired in 11% of patients in 4% of patients emotions were affected.

Table 15: Correlation between medication adherence and QOL.

Drug	Variable	Mean	Standard deviation	r value	Type of correlation	p value
LEV+LCM (n=40)	Quality of life	2.90	0.41	-0.596	Moderate negative	<0.001***
	Medication adherence	3.20	0.99			
LEV+CLB (n=40)	Quality of life	2.77	0.47	-0.281	Low negative	0.079 (NS)
	Medication adherence	3.05	0.90			

***Significant at 0.001 level, NS- Not Significant

INFERENCE: The above table shows correlation between medication adherence and quality of life.

The mean quality of life score in group A where LCM was added as the adjunctive agent was 2.90(±0.41) and the mean medication adherence score was 3.20(±0.99), the r value of the above data was -0.596, which shows moderate negative correlation with a p value <0. 001.The above data suggest that as quality of life score decreases (indicates improved quality of life) the mean medication adherence score increases which is found to be statistically significant.

In the group B where CLB was added as the adjunctive agent the mean quality of life score was found to be 2.77($\pm$0.47) and the mean medication adherence score was 3.05($\pm$0.90), the r value was -0.281 which showed low negative correlation, that indicates a decrease in quality-of-life score, the mean medication adherence score increases showing a low correlation that was statistically nonsignificant with a p value of 0.079.

CONCLUSION
Approximately 64.5% of patients were adherent to their medication regimen, while 35.5% were non-adherent. Factors affecting non-adherence included forgetfulness, fear of side effects, symptom improvement, and symptom worsening. There were no significant difference in the quality of life between patients who received either lacosamide or clobazam as an adjuvant to levetiracetam.

ACKNOWLEDGEMENTS

DECLARATIONS

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