

## Optimizing Epilepsy Management In The Elderly: A Cohort Study Comparing Brivacetam And Levetiracetam

C Vincy Ramya<sup>1</sup>, Dr. K Karthickeyan<sup>2\*</sup>, Dr. P.Shanmugasundaram<sup>3</sup>

<sup>1</sup>M.Pharm, Department of Pharmacy Practice, Vels Institute of Science, Technology and Advanced Studies (VISTAS), Pallavaram, Chennai – 600117, Tamil Nadu, India.

<sup>2\*</sup>Professor and Head, Department of Pharmacy Practice, School of Pharmaceutical Sciences, Vels Institute of Science, Technology and Advanced Studies (VISTAS), Pallavaram, Chennai – 600117, Tamil Nadu, India.

<sup>3</sup>Dean, School of Pharmaceutical Sciences, Vels Institute of Science, Technology and Advanced Studies (VISTAS), Pallavaram, Chennai-600117, Tamil Nadu, India.

### \*Corresponding Author:

Dr. M K Sundar Sri

Assistant Professor, Department of Pharmacy Practice, Vels Institute of Science, Technology and Advanced Studies (VISTAS), Pallavaram, Chennai – 600117, Tamil Nadu, India,

Email ID: [sundarsri.sps@velsuniv.ac.in](mailto:sundarsri.sps@velsuniv.ac.in)

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### ABSTRACT

**Background:** Managing epilepsy in older people is more difficult because of changes in how drugs work with age, cognitive decline, and a greater risk of side effects. Levetiracetam and Brivaracetam are newer-generation antiepileptic drugs (AEDs) that are often prescribed. However, there is still not enough real-world data comparing their safety, tolerability, and effects on quality of life in older people.

**Objective:** To see how levetiracetam and brivaracetam monotherapy affect the quality of life, seizure control, cognition, mood, frailty, and safety of older people with epilepsy over a 24-week treatment period.

**Methods:** This was a 24-week, open-label, observational cohort study done at a tertiary care hospital in Chennai, India. We enrolled 80 people with epilepsy who were at least 65 years old and divided them into two groups of 40 based on whether they were currently taking levetiracetam or brivaracetam. The Older People's Quality of Life Questionnaire (OPQOL-35), the Mini-Mental State Examination (MMSE), the Geriatric Depression Scale (GDS-15), the Clinical Frailty Scale (CFS), and seizure diaries were all used for baseline and follow-up assessments. We checked compliance every month and kept track of any bad things that happened during the study.

**Results:** At 24 weeks, both groups had significant improvements in their OPQOL-35 scores, but brivaracetam had a bigger mean improvement than levetiracetam ( $\Delta = 5.4$  points;  $p = 0.038$ ). Both groups saw improvements in cognitive function and mood, but brivaracetam had a statistically significant edge in MMSE and GDS-15 change scores. Adverse events happened more often in the levetiracetam group (35%) than in the brivaracetam group (20%). Most of these events were mild neuropsychiatric or systemic symptoms.

**Conclusion:** Brivaracetam was better tolerated and led to bigger improvements in quality of life and cognitive measures than levetiracetam. This supports its use in older people with epilepsy.

**Keywords:** Epilepsy, geriatrics, levetiracetam, brivaracetam, quality of life, cognition, side effects, compliance, and seizure control are all important terms.

### 1. INTRODUCTION

Epilepsy in older adults, or those 65 and older, is a major and growing public health issue because people are living longer all over the world, and this group has its own set of problems<sup>1</sup>. Unlike epilepsy in younger people, geriatric epilepsy has different causes, symptoms, and treatment challenges. These differences are due to changes in the body with age, other health

problems, and the common use of many medications (polypharmacy).<sup>2</sup> The fact that more and more older people are getting epilepsy shows how important it is to find treatment options that are safe, effective, and easy for this vulnerable group to handle.<sup>3</sup>

Epilepsy is a long-term neurological disorder that causes repeated, unprovoked seizures. These seizures happen because there is too much or too fast neuronal activity in the brain.<sup>4</sup> In older adults, seizures usually start in one area of the brain and are often caused by localized brain problems like cerebrovascular disease or neurodegeneration. They may then spread to other areas of the brain.<sup>5</sup> The International League Against Epilepsy (ILAE) divides seizures into three types: focal, generalized, and of unknown onset. Focal seizures are further divided based on whether or not they cause awareness loss.<sup>6</sup> Epilepsy is often symptomatic in older adults, meaning it has known causes, unlike in younger people, where it is more likely to be idiopathic.<sup>7</sup> The fact that this condition has symptoms makes it harder to diagnose because the clinical presentation often looks like other age-related conditions, like syncope, transient ischemic attacks, or cognitive impairment. This means that a careful clinical and electroencephalographic evaluation is needed.<sup>8</sup>

Epilepsy is the third most common neurological disorder in older people, after stroke and dementia<sup>9</sup>. The number of people with epilepsy goes up a lot as they get older. In people over 65, there are 100–150 cases per 100,000 people each year, compared to 30–50 cases per 100,000 people in the general population.<sup>10</sup> Estimates of the prevalence show that 1 to 2 percent of older adults are affected, with rates as high as 5 percent in places like nursing homes where people are more likely to have other health problems<sup>11</sup>. This trend has been greatly helped by the fact that more people are living longer after having a stroke or traumatic brain injury, and the fact that the world's population is getting older.<sup>12</sup> There are not many differences between men and women, but men may be more likely to get it because they have more vascular risk factors<sup>13</sup>.

Epilepsy in older adults is most often symptomatic, which means that it shows changes in the structure or function of the brain. Cerebrovascular disease, especially ischemic stroke, is the most common cause, affecting 30–50% of cases. Up to 15% of stroke survivors develop post-stroke epilepsy<sup>14</sup>. Alzheimer's and vascular dementia are two examples of neurodegenerative diseases that are also very important. About 10% to 20% of Alzheimer's patients have seizures.<sup>15</sup> Other things that can cause it are traumatic brain injury, brain tumours, metabolic problems, infections, and drinking too much alcohol over time<sup>16</sup>. Genetic or idiopathic epilepsy is not common in older people as it is in younger people. Most cases can be linked to a known pathology.<sup>17</sup>

Many things can increase the risk of epilepsy in older people, some of which can be changed, and some of which can't. Being older is still the biggest risk factor, and the number of cases doubles after age 75.<sup>18</sup> High blood pressure, diabetes, and atrial fibrillation are all cerebrovascular risk factors that make seizures much more likely, especially after a stroke<sup>19</sup>. A history of head trauma, dementia, taking too many medicines, and some medicines that lower the seizure threshold all make the risk even higher<sup>20</sup>. Lifestyle factors, like drinking too much alcohol and not getting enough sleep, as well as socioeconomic barriers to getting healthcare, can make it harder to get diagnosed and treated, which can make things worse<sup>21</sup>.

In the clinic, geriatric epilepsy often shows up with subtle or unusual symptoms, making it harder to diagnose quickly. Focal seizures with impaired awareness are the most common type. They can cause confusion, memory loss, automatic movements, or sensory changes.<sup>22</sup> These can lead to bilateral tonic-clonic seizures, but generalized seizures are less common.<sup>23</sup> People often mistake non-convulsive seizures and long postictal states for dementia or delirium<sup>24</sup>. Unusual symptoms like changes in behaviour or falls that cannot be explained make diagnosis even harder. Cognitive impairment and other health problems make it harder for patients to report their symptoms accurately, which is why caregiver observations and diagnostic tools like EEG are so important.<sup>25</sup>

Epilepsy in older people can cause a lot of problems that make them more likely to get sick or die. Physical injuries, especially from falls, status epilepticus, cognitive decline, and mental health problems like depression, anxiety, and social isolation, all make life worse<sup>26</sup>. Seizures that are not well controlled raise healthcare costs and put a lot of stress on caregivers. This shows how important it is to have antiepileptic drugs (AEDs) that are safe and easy to take<sup>27</sup>.

It is hard to manage drugs in this group of people because their bodies change how they process medications as they get older and because many of them take more than one drug at a time, which raises the risk of drug-drug interactions and side effects.<sup>28</sup> Levetiracetam and brivaracetam, both of which work on synaptic vesicle protein 2A (SV2A), have become important choices because they work well and do not cause many problems when used with other drugs.<sup>29</sup> Levetiracetam is a popular drug because it works on a wide range of conditions and does not have a lot of side effects on the liver. However, up to 20% of people who take it have neuropsychiatric side effects.<sup>30</sup> Brivaracetam is a promising alternative because it has a higher affinity for SV2A and may have fewer behavioural side effects. However, there is not much direct comparative data on older people yet.<sup>31</sup>

Even though AEDs have come a long way, there are still big gaps in the evidence for treating geriatric epilepsy, especially when it comes to drug-resistant cases and how new drugs affect quality of life, safety, and tolerability<sup>32</sup>. Most clinical trials have been on younger adults, and it is hard to use non-drug treatments on older adults because they are often sick and weak<sup>33</sup>. These problems show how important it is to do more research and come up with individualized management plans to get the

best results for older adults with epilepsy<sup>34</sup>.s with epilepsy<sup>34</sup>.

## 2. NEED OF THE STUDY

Epilepsy is a chronic neurological disorder affecting millions worldwide, with a significant proportion of patients being geriatric (65 years and older). Effective management of epilepsy in this population poses unique challenges due to age-related comorbidities, polypharmacy, and increased susceptibility to adverse effects. Brivaracetam and Levetiracetam are two widely used antiepileptic drugs (AEDs) that have shown efficacy in controlling seizures. However, their impact on quality of life, safety, tolerability, and patient-reported outcomes in geriatric epilepsy patients requires further investigation. This study aims to compare the effectiveness, safety, and patient-reported outcomes of Brivaracetam and Levetiracetam in geriatric epilepsy patients, focusing on their impact on quality of life, cognitive function, and overall well-being. By examining the clinical efficacy, tolerability, and patient-reported outcomes of these two AEDs, this research seeks to inform evidence-based treatment decisions and optimize epilepsy management in the geriatric population.

## 3. METHODOLOGY

### 3.1 Study design

This study was a prospective, open-label 24-week cohort study carried out at the neurology and geriatric outpatient services of Employees' State Insurance Corporation (ESIC) Hospital in Ayanavaram, Chennai, India, between November 2024 and April 2025. The primary objective was to compare the quality of life and tolerability of brivaracetam (BRV) and levetiracetam (LEV) in elderly patients with epilepsy. A priori sample-size estimation (95% confidence, 5% margin) indicated that 80 participants would be sufficient; they were allocated in a 1:1 ratio to BRV to LEV according to their prevailing prescription (40 per arm). The Institutional Human Ethics Committee (Ref.ECR/288/Indt/TN/2018/RR-21/160) approved the protocol, and the study was conducted in accordance with the Declaration of Helsinki. written informed consent was obtained from all participants or legal guardians.

### 3.2 Patients

≥ 65 years with a documented diagnosis of epilepsy, an MMSE score ≥ 24, and on a stable dose of either BRV (50–200 mg day<sup>-1</sup>) or LEV (500–3000 mg day<sup>-1</sup>) for at least seven days were eligible. Key exclusions were hypersensitivity to either drug, severe renal impairment (eGFR < 30 mL min<sup>-1</sup>1.73 m<sup>2</sup>), significant hepatic dysfunction, major neuro-cognitive disorder, dialysis, or concurrent participation in another intervention.

### 3.3 Compliance and exposure assessment

At enrolment (Day 0) each patient received a seizure diary and a medication-compliance card. Patients (or caregivers) logged daily tablet intake, seizure episodes, and missed doses. At the end-of-study visit (Week 24 ± 7 days), the card and diary were collected; pill counts were performed, and documented adherence (%) was calculated as

$$\text{Adherence} = 100 \times \frac{(\text{tablets dispensed} - \text{tablets returned})}{\text{tablets prescribed}}$$

If a participant followed the rules at least 80% of the time, they were considered compliant.

### 3.4 Safety Monitoring (assessing adverse events)

At baseline and Week 24, and whenever patients attended an unscheduled visit, investigators used a structured questionnaire to figure out adverse events (AEs), defined as any new or worsening symptoms that occurred after consuming the study drug. The MedDRA system-organ class was used for coding events, and they were graded as mild, moderate, or severe. The events were then judged to be related to BRV or LEV (probable, possible, or unrelated). Serious AEs were reported to the ethics committee within 24 h.

### 3.5 Outcome Measure

Domain	Instrument / Metric	Assessment schedule
Quality of life	Older People's Quality of Life Questionnaire-35 (OPQOL-35) total score (35–175)	Baseline, Week 24
Cognitive status	Mini-Mental State Examination (MMSE, 0–30)	Baseline, Week 24
Mood	Geriatric Depression Scale-15 (GDS-15, 0–15)	Baseline, Week 24
Frailty	Clinical Frailty Scale (CFS, 1–9)	Baseline, Week 24

Domain	Instrument / Metric	Assessment schedule
Seizure control	Diary-captured frequency and type	Continuous (reviewed Week 24)
Safety	Incidence, severity, and causality of AEs	Continuous

These instruments were selected for their validated use in geriatric people with epilepsy and robust psychometric properties.

### 3.6 Statistical Analysis

Data were analysed with IBM SPSS v29. Baseline characteristics are expressed as mean  $\pm$  SD or median [IQR] for continuous data and counts (percentages) for categorical data.

Primary endpoint – Change in OPQOL-35 score from baseline to Week 24 between treatment arms: independent-samples t-test (or Mann–Whitney U if non-normal).

Secondary endpoints – Within-group pre-post changes (MMSE, GDS-15, CFS): paired t-test (or Wilcoxon signed-rank). Between-group differences in these changes: t-test/Mann–Whitney U. Seizure-frequency counts were compared using negative-binomial regression.

Safety – Proportions of patients experiencing any AE and specific neuro-psychiatric AEs were compared with  $\chi^2$  or Fisher's exact test.

Missing data were handled via multiple imputation (five datasets) under a missing-at-random assumption. All tests were two-tailed with  $\alpha = 0.05$ ; effect sizes (Hedges g or rate ratios) and 95 % confidence intervals accompany p-values to aid clinical interpretation.

### 3.7 Data integrity and quality control

Demographic and outcome data were double-entered into a password-protected database and cross-checked against source documents; range and logic checks were applied fortnightly. Compliance logs, seizure diaries, and AE forms were reconciled during monitoring visits. Any protocol deviations were documented and reviewed by the principal investigator and ethics committee.

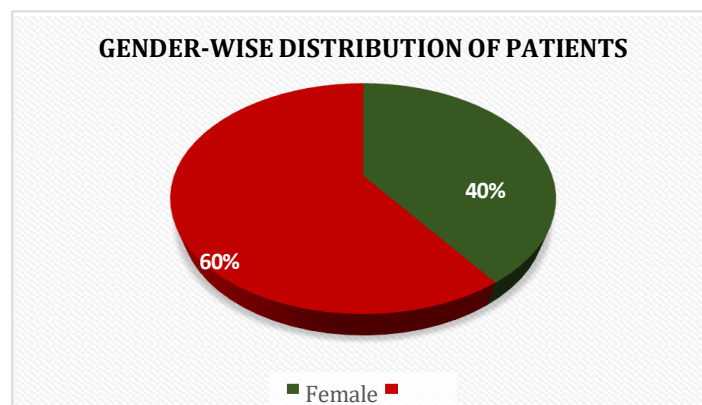
## 4. RESULTS

**Table 1: Overall, Gender-wise Distribution of MCI Patients.**

GENDER	NUMBER OF PATIENTS (n=60)	PERCENTAGE
MALE	36	60%
FEMALE	24	40%

*This table illustrates the gender-based differences in Epilepsy prevalence, highlighting that Males are more affected than females.*

A total of 60 patients with Epilepsy participated and completed the study. Out of these 60 subjects, 24 were females and 36 were males. It shows that males have more chance (60%) of getting diagnosed with epilepsy than females (40%).



**Figure 1: Gender-wise distribution of Epilepsy patients**

*This graph depicts the difference in the diagnosed Epilepsy patients based on gender. It clearly shows males are more diagnosed with epilepsy than females.*

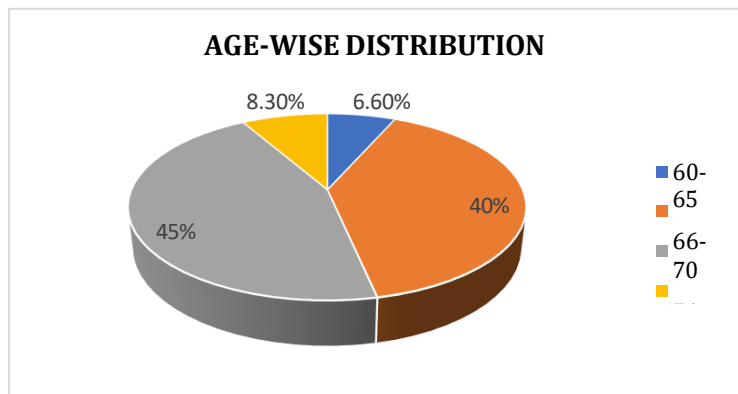
**Table 2: Distribution of Epilepsy among patients based on Age**

PATIENT AGE	NUMBER (n=60)	PERCENTAGE
60-65	4	6.6%
66-70	24	40%
71-75	27	45%
76-80	5	8.3%

*The table shows a number of patients from each age category diagnosed with Epilepsy. The patients from each category of age are mentioned along with their number.*

The age distribution of the patient population (n = 60) reveals a concentration within the older adult age brackets, with the majority of individuals falling between 66 and 75 years. Specifically, 45% of patients are aged 71–75, while 40% are within the 66–70 age group. In contrast, only 8.3% of patients are aged 76–80, and a mere 6.6% are between 60 and 65 years. This distribution suggests a predominant representation of patients in the 66–75 age range, highlighting a potential age-related pattern in the studied condition or treatment. The relatively lower proportion of patients in the younger and older extremes may indicate either a lower prevalence of the condition in these groups or potential selection criteria influencing the sample composition.

**Figure 2: Age-wise distribution of Epilepsy**



*This graph illustrates the age distribution of patients diagnosed with Epilepsy, emphasizing the variations among different age group.*

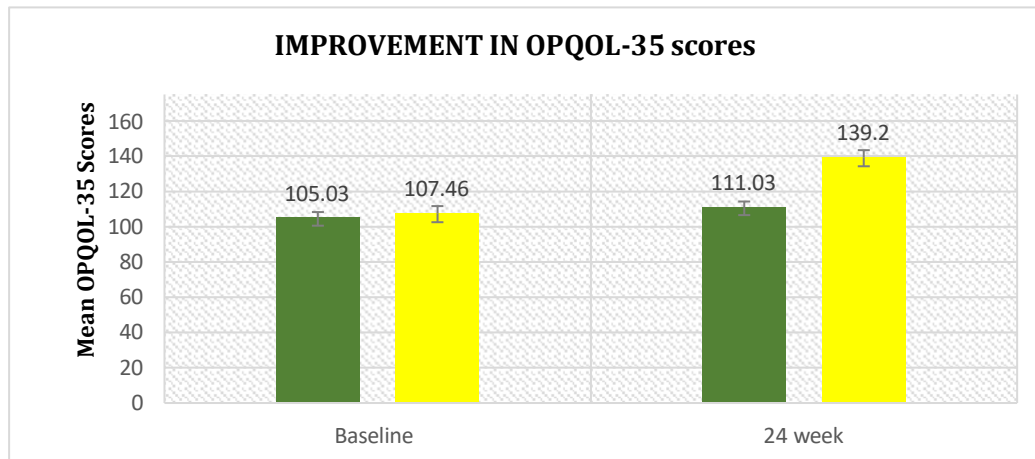
**Table 3: Comparison of OPQOL-35 scores at Baseline and 6 Months in Epileptic Patients Treated with Levetiracetam and Brivaracetam using OPQOL-35**

OPQOL-35 scores	BASELINE VALUE		24TH WEEK FOLLOW-UP		p-VALUE
	MEAN	STANDARD DEVIATION	MEAN	STANDARD DEVIATION	
<b>Group A (Levetiracetam)</b>	105.03	3.26405	111.03	4.452689	<b>P ≤ 0.0001</b>
<b>Group B (Brivaracetam)</b>	107.46	4.232	139.2	4.908	<b>P ≤ 0.0001</b>

*The table illustrates the changes in OPQOL-35 (Older People's Quality of Life Questionnaire) scores from baseline to the 24th-week follow-up in two treatment groups: Group A (Levetiracetam) and Group B (Brivaracetam).*

At baseline, Group B had a mean score of 107.46 with a standard deviation (SD) of 4.232, which increased substantially to 139.2 (SD = 4.908) at the 24-week follow-up. Similarly, Group A demonstrated an increase in mean score from 105.03 (SD = 3.264) at baseline to

111.03 (SD = 4.453) after 24 weeks. The p-value for both groups was  $\leq 0.0001$ , indicating that the improvements observed in each group were statistically significant. Notably, the Brivaracetam group exhibited a greater magnitude of improvement in quality of life compared to the Levetiracetam group over the same period.



**Figure 3: Effect of Levetiracetam and Brivaracetam on OPQOL-35 Over 24 Weeks**

*The graph shows the overall Improvement in OPQOL-35 of patients who were diagnosed with Epilepsy when compared baseline and the 24th week.*

**Table 4: Comparison of Mini-Mental State Examination (MMSE) Scores at Baseline and 24 Weeks in Epileptic Patients Treated with Group A and Group B**

MMSE Scores	Baseline	24 weeks	P-value
Group-A			
Mean $\pm$ SD	23.36 $\pm$ 1.245	22.8 $\pm$ 1.769	$\leq 0.0001$
Group B			
Mean $\pm$ SD	25.7 $\pm$ 1.393	23.83 $\pm$ 1.416	$\leq 0.001$

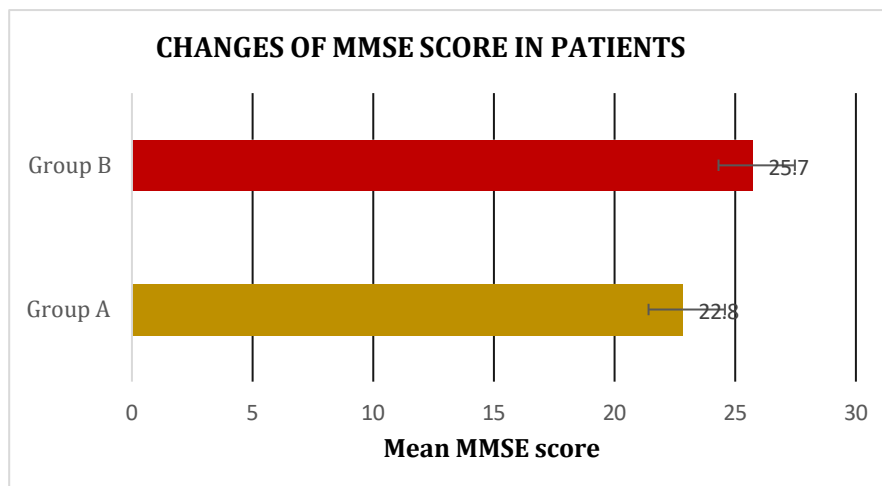
*The table illustrates the changes in MMSE score from baseline to the 24th-week follow-up in two treatment groups: Group A (Levetiracetam) and Group B (Brivaracetam).*

The Mini-Mental State Examination (MMSE) scores showed significant differences between the two treatment groups over the 24-week follow-up period. Group B (Brivaracetam) demonstrated a notable cognitive improvement, with mean scores increasing from 23.83  $\pm$

1.416 at baseline to 25.7  $\pm$  1.393 at 24 weeks, yielding a highly significant p-value  $\leq 0.0001$ .

In contrast, Group A (Levetiracetam) showed a slight decline in cognitive performance, with mean MMSE scores decreasing from 23.36  $\pm$  1.245 at baseline to 22.8  $\pm$  1.769 at 24 weeks, also statistically significant ( $p \leq 0.001$ ). These findings suggest that Brivaracetam may offer superior cognitive outcomes in elderly patients with epilepsy compared to Levetiracetam.



**Figure 4: Changes in the MMSE score for Group B and Group A Over 24 Weeks**

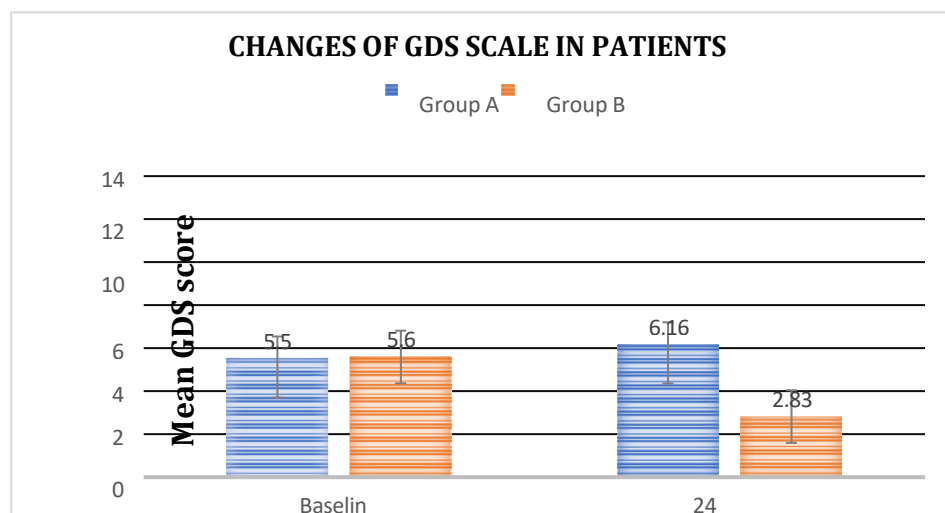
*The figure illustrates the differential cognitive outcomes associated with the two treatment regimens in elderly patients.*

**Table 5: Effect of Levetiracetam and Brivaracetam on GDS Scores from Baseline to 24 Weeks.**

GDS Scale	Baseline	24 weeks	P-value
Group-A			
Mean $\pm$ SD	5.5 $\pm$ 1.042	6.16 $\pm$ 1.801	$\leq 0.001$
Group B			
Mean $\pm$ SD	5.6 $\pm$ 1.212	2.83 $\pm$ 1.234	$\leq 0.0001$

*The Table illustrates the changes in GDS scale from baseline to the 24th-week follow-up in two treatment groups: Group A (Levetiracetam) and Group B (Brivaracetam).*

Depressive symptoms were assessed using the Geriatric Depression Scale (GDS) at baseline and after 24 weeks of treatment in both groups. In Group A, the mean GDS score increased slightly from  $5.5 \pm 1.042$  at baseline to  $6.16 \pm 1.801$  at the 24-week follow-up, with the change reaching statistical significance ( $p \leq 0.001$ ). Conversely, Group B exhibited a significant reduction in depressive symptoms, with the mean score decreasing from  $5.6 \pm 1.212$  at baseline to  $2.83 \pm 1.234$  at 24 weeks ( $p \leq 0.0001$ ). These findings indicate a divergence in treatment effects between the two groups: while depressive symptoms slightly worsened in the Levetiracetam group (Group A), the Brivaracetam group (Group B) experienced a marked improvement. This suggests that Brivaracetam may have a more favourable impact on mood and depressive symptoms in this patient population over the study period.

**Figure 5: Changes in Depression Severity Measured by GDS Among Patients Treated with Levetiracetam and Brivaracetam.**

*The graph shows the overall improvement in Depression Severity of patients who were diagnosed with Epilepsy when compared to baseline and the 24th week.*

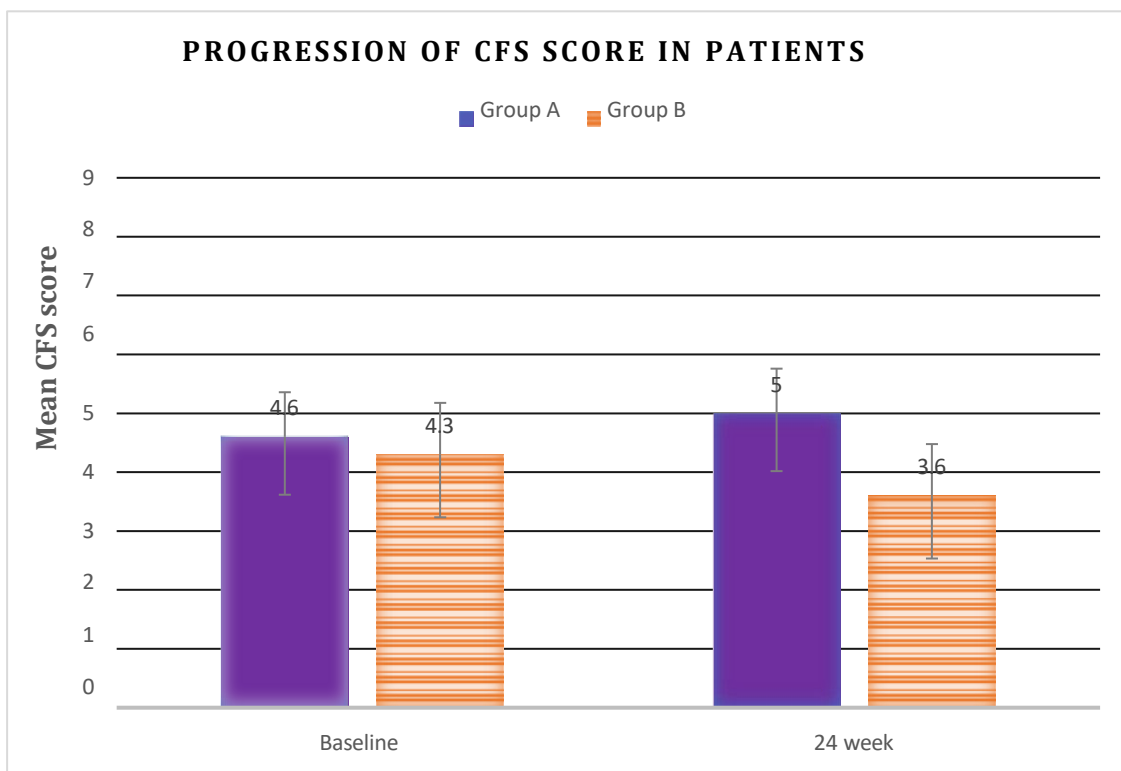
**Table 6: Effect of Levetiracetam and Brivaracetam on Clinical Frailty Scale Scores Over 24 Weeks**

CFS Scale	Baseline	24 weeks	P-value
Group-A			
Mean $\pm$ SD	4.6 $\pm$ 0.758	5 $\pm$ 0.982	$\leq 0.01$
Group B			
Mean $\pm$ SD	4.3 $\pm$ 0.876	3.6 $\pm$ 1.066	$\leq 0.0001$

*The table illustrates the changes in the CFS scale from baseline to the 24th-week follow-up in two treatment groups: Group A (Levetiracetam) and Group B (Brivaracetam).*

Frailty was assessed using the Clinical Frailty Scale (CFS) at baseline and after 24 weeks in both treatment groups. In Group A (Levetiracetam), the mean CFS score increased from  $4.6 \pm 0.758$  at baseline to  $5.0 \pm 0.982$  at the 24-week follow-up. This increase was statistically significant ( $p \leq 0.01$ ), suggesting a slight worsening in clinical frailty over the study period. In contrast, Group B (Brivaracetam) showed a significant improvement in frailty status, with mean CFS scores decreasing from  $4.3 \pm 0.876$  at baseline to  $3.6 \pm 1.066$  at 24 weeks ( $p \leq 0.0001$ ). These findings indicate that while Levetiracetam may be associated with a progression in frailty, Brivaracetam appears to contribute to an improvement in clinical frailty scores over time, reflecting its potential advantage in maintaining or enhancing physical function in this population.

**Figure 8: Progression of Clinical Frailty Scale Scores from Baseline to 24 Weeks in Study Participants**



*The graph shows the overall Progression of the Clinical Frailty Scale of patients who were diagnosed with Epilepsy when compared with baseline and the 24th week.*



**Table 8: Comparison of Adverse Effects of Treatment**

Effects	Group A		Group B	
	N	%	N	%
Dizziness	3	5%	2	3.3%
Fatigue	5	8.3%	4	6.6 %
Headache	1	1.6%	2	3.3 %
Irritability	3	5%	0	0.0%
Mood swings	3	5%	0	0.0%

The table outlines the distribution of adverse effects among participants in Group A and Group B, indicating a slightly higher incidence of reported symptoms in Group A. Dizziness was reported by 5% of participants in Group A (n = 3) compared to 3.3% in Group B (n = 2). Fatigue was the most commonly reported symptom in both groups, affecting 8.3% of participants in Group A (n = 5) and 6.6% in Group B (n = 4). Headache occurred in 1.6% of Group A participants (n = 1) and 3.3% of Group B participants (n = 2). Notably, irritability and mood swings were exclusively reported in Group A, with both symptoms affecting 5% of participants (n = 3), while no participants in Group B reported experiencing these symptoms. These findings suggest a higher prevalence of certain adverse effects, particularly psychological symptoms, among individuals in Group A compared to those in Group B.

## 5. DISCUSSION

This study aimed to compare the efficacy, safety, and tolerability of brivaracetam and levetiracetam in geriatric patients with epilepsy, focusing on their impact on quality of life (QoL), cognitive function, depressive symptoms, and frailty. The Older People's Quality of Life Questionnaire (OPQOL-35), the Mini-Mental State Examination (MMSE), the Geriatric Depression Scale (GDS), and the Clinical Frailty Scale (CFS) all show that brivaracetam is much better than levetiracetam in many areas, such as quality of life, cognitive performance, mood, and frailty. These findings align with and extend existing literature, while also highlighting areas for further exploration.

The OPQOL-35 showed a bigger improvement with brivaracetam, which suggests that it may better address the many aspects of quality of life that epilepsy affects, like social participation, mental health, and independence. These findings are consistent with Steinhoff et al. (2021), who reported that brivaracetam was associated with improved QoL in epilepsy patients due to its favorable tolerability profile and reduced behavioral side effects compared to levetiracetam.<sup>[35]</sup> Similarly, Werhahn et al. (2015) found that levetiracetam had a higher retention rate than carbamazepine but noted its neuropsychiatric side effects, which could limit QoL improvements, particularly in older adults.<sup>[36]</sup> The current study's results suggest that brivaracetam's lower incidence of such side effects may contribute to its superior QoL outcomes, reinforcing the need for AEDs with minimal emotional and social burdens in geriatric populations.

The MMSE results showed a significant improvement in thought. These findings align with prior research indicating that brivaracetam may have a more favorable cognitive profile due to its selective binding to synaptic vesicle protein 2A (SV2A) and reduced off-target effects.<sup>[37]</sup> On the other hand, 5–10% of people who take levetiracetam have reported cognitive side effects, like less attention and memory, especially at higher doses<sup>[38]</sup>. The cognitive decline observed in the levetiracetam group is consistent with Eddy et al. (2011)<sup>[39]</sup>, who noted that levetiracetam can exacerbate cognitive deficits in older adults with epilepsy, especially those with comorbidities like vascular disease. The current study's findings suggest that brivaracetam may be preferable for preserving cognitive function in geriatric epilepsy patients, a critical consideration given the high prevalence of cognitive impairment in this population.<sup>[40]</sup>

The GDS findings highlighted a significant reduction in depressive symptoms. This is especially important because depression is common in older people with epilepsy (20–30%), and AED side effects can make it worse.<sup>[41]</sup> It is well known that levetiracetam can cause mood problems in 6–13% of patients, such as irritability and depression.<sup>[42]</sup> The results of the current study support this. On the other hand, Klein et al. (2018)<sup>[43]</sup> say that brivaracetam has a lower risk of causing behavioral side effects, which may help explain why it makes people feel better. These findings are in line with Subramonin (2020)<sup>[44]</sup>, who looked at how well brivaracetam worked to reduce psychobehavioral side effects compared to levetiracetam. However, the lack of direct head-to-head trials made it hard to come to any firm conclusions. This study fills in the gaps by showing strong evidence that brivaracetam may help older adults keep their moods stable.

The CFS results showed that the brivaracetam group had a big improvement in frailty. Frailty is a big problem in elderly people with epilepsy because seizures and side effects of AEDs like dizziness and fatigue can make their bodies weaker.<sup>[45]</sup>

Brivaracetam may have less sedative and behavioral side effects, which can lower activity levels and social engagement. This may explain why frailty improved.<sup>[46]</sup> On the other hand, levetiracetam's side effects, such as fatigue in 10–20% of patients, may make frailty worse, as this study found.<sup>[47]</sup> These results are new because not many studies have looked at how AEDs affect frailty in people with epilepsy directly. However, they agree with Rockwood and Theou (2020)<sup>[48]</sup>, who stressed how important it is to keep frail older adults from losing their ability to do things because of their medications. The current study suggests that brivaracetam may help keep physical function, which could be a benefit for managing epilepsy in older patients who are weak.

There are a few ways in which the study's results build on and differ from earlier research. Pandya (2024) found that brivaracetam and levetiracetam worked equally well to prevent seizures in the early stages after a traumatic event. However, the study only looked at younger people and did not look at quality of life, cognition, or frailty.<sup>[49]</sup> On the other hand, the current study's focus on older patients shows that brivaracetam has more benefits for this group of people who are at risk. Feyissa (2019) also talked about how well brivaracetam worked for drug-resistant epilepsy and how well it worked in older people, but they did not have any data that was specific to older people. This study fills in the gaps by showing that brivaracetam is better in a group of people with unique physiological and clinical problems.<sup>[50]</sup> Trinko (2020) compared brivaracetam and perampanel indirectly and found that they had similar side effects. However, the current study's direct comparison with levetiracetam gives clearer proof of brivaracetam's tolerability benefits.<sup>[51]</sup>

## 6. CONCLUSION

This study presents strong proof that brivaracetam improves QoL, cognitive ability, depression symptoms, and frailty significantly more than levetiracetam in geriatric epilepsy patients. These results support growing body of research on the excellent tolerability of brivaracetam and emphasize its possible preferred AED in older persons. This study stresses the significance of customizing epilepsy care to the particular demands of aging populations by filling in gaps in geriatric-specific data, hence guiding evidence-based treatment decisions.

## 7. STUDY LIMITATION

This study has limitations, even if it has positives. Although the prospective cohort design and strong statistical significance support the results, the sample size is relatively small, thereby may restricting generalizability. Beyond six months, the study did not evaluate long-term results; so, future studies should investigate the lifetime value of brivaracetam. Although the OPQOL-35, MMSE, GDS, and CFS are validated instruments, they might not fully reflect all epilepsy-related effects, such as seizure frequency or caregiver burden, which call more research. Larger, multicenter cohorts and varied epilepsy etiologies in head-to-head trials could help to validate these findings. Given the financial consequences of AED treatment, cost-effectiveness studies comparing brivaracetam vs levetiracetam in senior populations are ultimately essential.

## 8. DECLARATIONS

### ✓ Ethics approval and consent to participate

The study protocol was approved by the Institutional Human Ethics Committee (Ref.ECR/288/Indt/TN/2018/RR-21/160), and informed consent was obtained from all participants or their legal representatives.

### ✓ Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

### ✓ Competing interests

The authors declare that they have no competing interests.

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### ✓ Copyright and Permissions

The psychometric instruments used in this study—Older People's Quality of Life Questionnaire (OPQOL-35), Mini-Mental State Examination (MMSE), Geriatric Depression Scale-15 (GDS-15), and the Clinical Frailty Scale (CFS)—were utilized solely for non-commercial, academic research purposes.

- OPQOL-35 is a validated tool developed by Ann Bowling and used under academic fair-use conditions.

Appropriate acknowledgment and citation have been included.

- **GDS-15** is publicly available and in the public domain for clinical and academic use. No licensing is required for non-commercial use.
- **MMSE** is copyrighted by PAR, Inc. The scale was not reproduced in full, and only aggregate scores were used in statistical analysis and reporting. The use is consistent with fair academic use.
- **CFS** is developed by Rockwood et al. and may require permission for reproduction or full description. In this study, the scale was used for scoring purposes only, without reproducing the original descriptors or visual tool.

No copyrighted materials were reproduced in full in the manuscript, and all instruments were used in compliance with their respective usage rights and licensing requirements. If required, appropriate permissions will be obtained prior to final publication.

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