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# DEPRESSION AMONG EPILEPSY PATIENTS PRESENTING TO A TERTIARY CARE HOSPITAL AND ITS ASSOCIATION WITH ANTI-EPILEPTIC DRUGS: A CROSS-SECTIONAL, OBSERVATIONAL STUDY

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## ABSTRACT

**Background:** Epilepsy is a chronic neurological disorder frequently associated with psychiatric comorbidities, particularly depression, which significantly impairs quality of life, treatment adherence, and overall prognosis. Despite its clinical importance, depression in people with epilepsy often remains underdiagnosed and undertreated. Understanding its prevalence and associated factors is essential to comprehensive patient care. The objective is to study the sociodemographic profile of patients with epilepsy attending the Neurology Department for antiepileptic drug therapy. To examine the association between antiepileptic drug (AED) therapy and depression among people with epilepsy, compare the prevalence and severity of depression between AED monotherapy and polytherapy, and evaluate the association of individual AEDs with depression.

**Materials and Methods:** A cross-sectional observational study was conducted among people with epilepsy attending a tertiary care hospital. Eligible participants were screened for depression using the Neurological Disorders Depression Inventory for Epilepsy (NDDI-E), and the Hamilton Depression Rating Scale (HAM-D) was used to assess the severity of depression. Demographic and clinical data were collected, and statistical analysis was performed to identify correlations between depression and relevant clinical parameters.

**Results:** This cross-sectional observational study involving 157 epilepsy patients attending a tertiary care hospital identified a high prevalence of depression, with 59.9% screening positive on the NDDI-E. The majority of participants were undergoing polytherapy (59.2%), which was significantly correlated with depression compared with monotherapy ($p = 0.006$). The HAM-D assessment indicated that very severe depression was the predominant category among patients with depression. Although severe depression was more prevalent among individuals on polytherapy, the association with depression severity did not attain statistical significance ($p = 0.114$). These findings underscore the importance of routine depression screening and multidisciplinary management in patients with epilepsy, particularly those receiving multiple antiepileptic agents.

**Conclusion:** This study identified a high prevalence of depression among patients with epilepsy, with polytherapy notably associated with depressive symptoms compared with monotherapy. These findings underscore the importance of implementing routine depression screening using validated instruments such as NDDI-E and HAM-D, particularly in patients receiving

multiple antiepileptic medications. Early psychiatric intervention, coupled with a multidisciplinary approach, may enhance treatment adherence, seizure management, quality of life, and overall prognosis. Further longitudinal, multicentric research is essential to clarify the relationship between antiepileptic therapy and depression.
**Keywords:** Epilepsy, Antiepileptic drugs, Depression, NDDI-E, HAM-D, Cross-sectional study.

## INTRODUCTION

Epilepsy is one of the most prevalent chronic neurological disorders worldwide, characterised by recurrent, unprovoked seizures arising from abnormal, excessive, and synchronous neuronal activity in the brain. According to global estimates, more than 50 million people live with epilepsy, with nearly 80% of cases occurring in low- and middle-income countries.[1] In India, epilepsy is a significant public health concern due to its high prevalence, treatment gap, social stigma, and limited access to specialised neurological care in certain regions. Beyond its neurological manifestations, epilepsy substantially affects patients' psychological health, social functioning, educational attainment, employment opportunities, and overall quality of life.[2]

The primary goal of epilepsy management is sustained seizure control with minimal adverse effects. Antiepileptic drugs (AEDs) are the cornerstone of therapy and are typically initiated as monotherapy. However, approximately 30–40% of patients fail to achieve adequate seizure control with a single agent and require polytherapy.[3] Although these medications effectively reduce seizure frequency and severity, long-term therapy is often associated with neurological, metabolic, cognitive, and psychiatric adverse effects. Because AED treatment is frequently lifelong, the cumulative burden of these adverse effects becomes clinically significant. Among the psychiatric comorbidities associated with epilepsy, depression is the most clinically significant. The reported prevalence of depression among people with epilepsy ranges from 20% to 55%, depending on demographic factors, study design, diagnostic criteria, and assessment tools.[4] Hospital-based studies, particularly in tertiary care centres, often report higher prevalence rates due to referral bias and the inclusion of more severe or refractory cases.[5] In epilepsy, depression may present as major depressive disorder, dysthymia, adjustment disorder with depressed mood, or subclinical depressive symptoms that nonetheless impair functioning.[6]

The coexistence of depression in patients with epilepsy has profound clinical implications. Depressive symptoms are linked to poor seizure control, reduced adherence to antiepileptic therapy, increased healthcare utilisation, diminished quality of life, and a significantly elevated risk of suicidal ideation and suicide attempts.[7] Suicide rates among patients with epilepsy are reported to be several times higher than in the general population. Despite these serious consequences, depression frequently remains underdiagnosed and undertreated in neurological settings.[8] The relationship between epilepsy and depression is complex and bidirectional. Evidence suggests that depression may precede the onset of epilepsy and worsen seizure outcomes.[9] Neurobiological mechanisms, including dysfunction of serotonergic, noradrenergic, dopaminergic, and GABAergic pathways, may contribute to both seizure generation and mood disturbances. Structural abnormalities in limbic structures, particularly the hippocampus and amygdala, as well as hypothalamic–pituitary–adrenal (HPA) axis dysregulation, have also been implicated.[10]

Importantly, antiepileptic drug therapy itself may influence mood. Certain AEDs, including phenobarbital, levetiracetam, and topiramate, have been linked to behavioural disturbances and depressive symptoms.[11] Conversely, agents such as lamotrigine and valproate have mood-stabilising properties and are used to manage bipolar disorder.[3] Polytherapy and a higher cumulative drug burden may further increase the risk of psychiatric adverse effects. Therefore, understanding the association between specific AED regimens and depressive symptoms is crucial for optimising individualised treatment strategies. Validated screening tools, such as the Neurological Disorders Depression Inventory for Epilepsy (NDDI-E), provide a rapid, epilepsy-specific method for identifying depressive symptoms in clinical settings.[12] When used alongside structured scales such as the Hamilton Depression Rating Scale (HAM-D), these tools improve diagnostic accuracy and enable severity grading.

In the Indian context, there remains a paucity of comprehensive hospital-based cross-sectional studies examining the prevalence of depression among patients with epilepsy and its association with specific antiepileptic drug regimens. Therefore, this cross-sectional observational study conducted in a tertiary care hospital aims to determine the prevalence of depression among patients with epilepsy attending the Neurology Outpatient Department, assess the distribution of severity using validated tools, and evaluate associations with antiepileptic drug regimens. The findings of this study are expected to inform evidence-based prescribing practices, promote rational AED selection with due regard for psychiatric safety profiles, and support the integration of mental health screening into routine epilepsy care.[8]

## MATERIALS AND METHODS

**Study Setting:** Department of Neurology, Government General Hospital (GGH), Vijayawada, Andhra Pradesh.
**Study Duration:** 6 months (August 2025 to January 2026)
**Study Design:** cross-sectional observational study.
**Study Population:** Patients with epilepsy on AED therapy visiting the Neurology Outpatient Department at Government General Hospital, Vijayawada, Andhra Pradesh.
**Sample Size:** 157
**Sampling Method:** Convenience Sampling
**Study Criteria**
**Inclusion Criteria**

- Subjects willing to participate in the study by providing written informed consent
- Subjects of either gender, aged 18 years or older, diagnosed with epilepsy
- Subjects currently receiving antiepileptic drug (AED) therapy.
- Subjects with a minimum seizure frequency of at least one seizure in the past year.

**Exclusion Criteria**

- Subjects unwilling to provide written informed consent.
- Subjects under 18 years, pregnant and lactating women.
- Critically or terminally ill subjects; subjects with pre-existing psychiatric disorders or intellectual disability; and those receiving antidepressant therapy prior to initiation of AED therapy.

**Study Tools**

- Neurological Disorders Depression Inventory for Epilepsy (NDDI-E)
- Hamilton Depression Rating Scale (HAM-D).

**Ethical Approval**
The study was approved by the Institutional Ethics Committee of Siddhartha Medical College and Government General Hospital (IEC SMC & GGH), Gunadala, Vijayawada, on 7th August 2025, with ethical approval number IECSMCGGH/2025/AP/201.
**Study Procedure:** Eligible outpatients attending the Neurology Department were enrolled after obtaining informed consent. Data were collected using a standardised form developed from a literature review and expert recommendations. Collected information included socio-demographic details, diagnosis, type and duration of epilepsy, seizure frequency, comorbidities, type of AED prescribed, dosage, duration of therapy, and classification as monotherapy or polytherapy. Subjects were screened for depression using the NDDI-E, and those who screened positive were assessed for severity using the HAM-D scale.
**Statistical Analysis**
Data were entered into Microsoft Excel and analysed using IBM SPSS Statistics v27. Categorical variables were summarised as frequencies and percentages, and continuous variables as mean ± standard deviation. The association between AED therapy pattern and depression status/severity was assessed using the Chi-square test. A p-value <0.05 was considered statistically significant.

## RESULTS

**Table 1: Distribution of Socio-Demographic Characteristics of Study Participants (N = 157)**

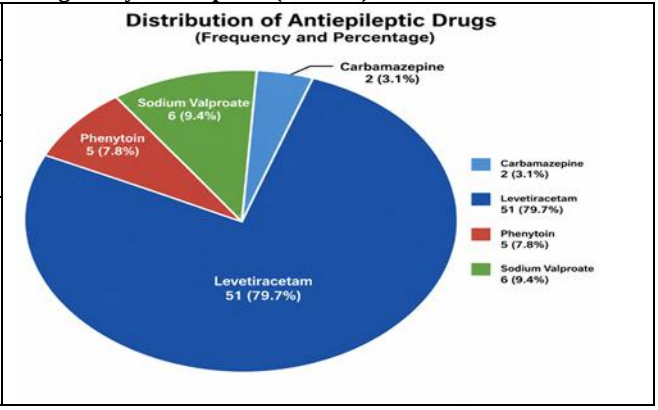
| Variable | Category | Frequency (n) | Percentage (%) |
|---|---|---|---|
| Age (Years) | 18 – 30 | 57 | 36.3 |
| | 31 – 40 | 44 | 28.0 |
| | 41 – 50 | 34 | 21.7 |
| | More than 50 | 22 | 14.0 |
| Gender | Male | 81 | 51.6 |
| | Female | 76 | 48.4 |
| Education | Illiterate | 63 | 40.1 |
| | Primary | 19 | 12.1 |
| | Secondary | 59 | 37.6 |
| | Tertiary | 16 | 10.2 |
| Occupation | Employed | 85 | 54.1 |
| | Unemployed | 72 | 45.9 |
| Marital Status | Married | 114 | 72.6 |
| | Unmarried | 41 | 26.1 |
| | Widowed/Separated | 2 | 1.3 |
| Socioeconomic Status | Lower | 12 | 7.6 |
| | Lower Middle | 39 | 24.8 |
| | Middle | 50 | 31.8 |
| | Upper Middle | 47 | 29.9 |
| | Upper | 9 | 5.7 |
| Religion | Hindu | 114 | 72.6 |
| | Christian | 29 | 18.5 |
| | Muslim | 14 | 8.9 |

The majority of participants were aged 18–30 years (36.3%), followed by those aged 31–40 years (28.0%). Those aged over 50 years formed the smallest group (14.0%). The mean age was

36.75±12.594 years. Gender distribution was nearly equal, with males accounting for 51.6% and females for 48.4%. In terms of education, 40.1% of respondents were illiterate, while 37.6% had completed secondary education. Only 10.2% had attained tertiary education. More than half of respondents were employed (54.1%), whereas 45.9% were unemployed. Most participants were married (72.6%), while 26.1% were unmarried and 1.3% were widowed or separated. Regarding socioeconomic status, the largest proportion belonged to the middle class (31.8%), followed closely by the upper middle class (29.9%). Only 5.7% were classified as upper socioeconomic status. With respect to religion, the majority were Hindus (72.6%), followed by Christians (18.5%) and Muslims (8.9%).

**Table 2: Distribution of AED Therapy and Depression Among Study Participants (N = 157)**

| Variable | Category | Frequency (n) | Percentage (%) |
|---|---|---|---|
| **AED Therapy** | Monotherapy | 64 | 40.8 |
| | Polytherapy | 93 | 59.2 |
| **Depression (NDDI-E)** | Absent | 63 | 40.1 |
| | Present | 94 | 59.9 |




Regarding antiepileptic drug (AED) therapy, the majority of participants were receiving polytherapy (59.2%), while 40.8% were on monotherapy. Screening for depression using the Neurological Disorders Depression Inventory for Epilepsy (NDDI-E) showed that 59.9% of respondents screened positive for depression, whereas 40.1% screened negative. The pie chart shows the distribution of antiepileptic drugs in monotherapy. Levetiracetam is the most commonly used drug, with 51 cases (79.7%). Sodium Valproate has 6 cases (9.4%). Phenytoin has 5 cases (7.8%). Carbamazepine has 2 cases (3.1%).

**Table 3: Depression Severity Among Participants with Depression (N = 95)**

| Depression Severity (HAM-D) | Frequency (n) | Percentage (%) |
|---|---|---|
| Mild | 18 | 18.9 |
| Moderate | 18 | 18.9 |
| Severe | 28 | 29.5 |
| Very Severe | 31 | 32.6 |

Assessment of depression severity using the Hamilton Depression Rating Scale (HAM-D) revealed varying levels of depressive symptoms among respondents. Very severe depression was the most common category, affecting 32.6% of participants. Severe depression was reported in 29.5% of respondents. Mild and moderate depression were equally prevalent, each accounting for 18.9% of participants.

**Table 4: Association of AED Therapy with Depression Presence and Severity**

A. Association Between AED Therapy and Presence of Depression (N = 157)

| AED Therapy | Depression Absent n (%) | Depression Present n (%) | p-value |
|---|---|---|---|
| Monotherapy | 34 (53.1) | 30 (46.9) | 0.006* |
| Polytherapy | 29 (31.2) | 64 (68.8) | |

The association between antiepileptic drug (AED) therapy and depression was assessed among the study participants. Among respondents receiving monotherapy, 53.1% did not have depression, while 46.9% did. In contrast, among those on polytherapy, a higher proportion (68.8%) had depression, whereas only 31.2% were free from depression. A statistically significant association was observed between AED therapy and depression (p = 0.006), indicating that participants receiving polytherapy were more likely to experience depression than those on monotherapy.

B. Association Between AED Therapy and Severity of Depression (N = 95)

| Depression Severity | Monotherapy n (%) | Polytherapy n (%) | p-value |
|---|---|---|---|
| Mild | 10 (32.3) | 8 (12.5) | 0.114 |
| Moderate | 6 (19.4) | 12 (18.8) | |

| | | | |
|---|---|---|---|
| Severe | 8 (25.8) | 20 (31.2) | |
| Very Severe | 7 (22.6) | 24 (37.5) | |

The relationship between antiepileptic drug (AED) therapy and depression severity was assessed using HAM-D scores. Among participants receiving monotherapy, 32.3% had mild depression, 19.4% had moderate depression, 25.8% had severe depression, and 22.6% had very severe depression. Among those on polytherapy, 12.5% had mild depression, 18.8% had moderate depression, 31.2% had severe depression, and 37.5% had very severe depression. Although a greater proportion of participants on polytherapy experienced severe and very severe depression than those on monotherapy, the association between AED therapy and depression severity was not statistically significant ($p = 0.114$).

## DISCUSSION

Depression is among the most prevalent psychiatric comorbidities in patients with epilepsy and markedly affects quality of life, treatment adherence, seizure management, and overall prognosis. In the current study, 59.9% of patients with epilepsy tested positive for depression using the Neurological Disorders Depression Inventory for Epilepsy (NDDI-E). This prevalence exceeds that reported in numerous previous studies, which have documented depression rates ranging from 20% to 55% among individuals with epilepsy.[13,14] Zhong et al. reported pooled prevalence estimates of 27% in population-based studies and 34% in clinical settings.[14] Similarly, Josephson et al. observed depression prevalence rates between 40.1% and 45.4% among epilepsy patients attending tertiary care centres.[13] The relatively higher prevalence identified in the present study may be due to differences in the study population, socioeconomic backgrounds, the chronicity of epilepsy, and a higher proportion of patients undergoing polytherapy.

Most participants in this study were young adults aged 18–30 years, with nearly equal numbers of males and females. These results align with Indian and international studies showing that epilepsy mainly affects young adults during their most productive years.[4,15] The socioeconomic profile indicated that many participants were illiterate and belonged to middle or lower social classes. Lower education levels and poor socioeconomic status have been linked to greater psychological distress, social stigma, and reduced access to mental health care among people with epilepsy. Tesfaye et al. found that illiteracy was significantly associated with depression among people with epilepsy.[16]

In the present study, 59.2% of participants were receiving antiepileptic drug (AED) polytherapy, whereas 40.8% were on monotherapy. Polytherapy is often prescribed for patients with refractory or poorly controlled epilepsy and may increase the risk of adverse drug effects, drug interactions, and psychological stress. The study demonstrated a statistically significant correlation between AED therapy and depression, with polytherapy associated with a markedly higher prevalence of depression than monotherapy (68.8% vs. 46.9%, $p = 0.006$). These findings align with existing literature. Gurung et al. reported that polytherapy was significantly associated with an increased risk of depression among individuals with epilepsy.[17] Similarly, Josephson et al. observed elevated rates of depression among patients receiving multiple antiepileptic drugs.[13] Moreover, Tadikonda et al. reported that patients on combinations of newer antiepileptic medications scored higher on depression assessments and experienced reduced quality of life.[18]

The relationship between polytherapy and depression may be multifactorial. Patients requiring multiple AEDs generally have more severe or refractory epilepsy, higher seizure frequency, and poorer seizure control, all of which contribute to emotional distress and depressive symptoms. Moreover, cumulative adverse neuropsychiatric effects of multiple AEDs may also play an important role. Gilliam et al. demonstrated that uncontrolled seizures were strongly associated with depression severity in patients with epilepsy.[19] Therefore, the higher prevalence of depression observed among patients receiving polytherapy in the present study may partly reflect greater disease severity rather than the isolated effect of AEDs.

Levetiracetam was the most commonly used antiepileptic drug for monotherapy in this study. Although it is often prescribed for its favourable pharmacokinetic profile and effectiveness, some studies have linked it to behavioural and psychiatric side effects, including irritability, anxiety, and depression. Mula et al. reported a link between levetiracetam treatment and depressive symptoms in patients with epilepsy, particularly those with hippocampal sclerosis.[20] Nonetheless, evidence for a direct link between specific AEDs and depression is mixed, and various patient and disease factors may also play a role.

The evaluation of depression severity using the Hamilton Depression Rating Scale (HAM-D) in the current study showed that very severe depression was the most prevalent category, accounting for 32.6%, followed by severe depression at 29.5%. Mild and moderate depression were each represented by 18.9%. These results suggest a significant burden of clinically notable depressive symptoms among epilepsy patients receiving care at tertiary medical centres. Similar observations have been documented in previous research, where moderate-to-severe depressive symptoms were frequently observed among patients with chronic

epilepsy, particularly those with inadequate seizure control and longer disease duration.[18,19]

Although participants receiving polytherapy had higher proportions of severe and very severe depression than those undergoing monotherapy, the association between AED therapy and depression severity was not statistically significant ($p = 0.114$). This finding indicates that, while polytherapy may increase the likelihood of developing depression, the severity of depressive symptoms is also likely influenced by additional factors such as seizure frequency, duration of illness, psychosocial stressors, perceived stigma, social support, and underlying neurobiological mechanisms. Prior research has similarly highlighted that depression in epilepsy is multifactorial and bidirectional.[8,14]

The findings of the present study underscore the importance of routine psychiatric screening in epilepsy clinics, particularly for patients receiving antiepileptic drug (AED) polytherapy. Early detection and management of depression are crucial for improving treatment adherence, seizure control, and overall quality of life. In tertiary healthcare settings, validated screening instruments such as the NDDI-E and HAM-D can promote prompt recognition and intervention. Consequently, integrated multidisciplinary care involving neurologists and mental health specialists is advocated to ensure comprehensive epilepsy management.

## CONCLUSION

The present study demonstrated a high prevalence of depression among patients with epilepsy attending a tertiary care hospital, with nearly three-fifths of participants screening positive for depressive symptoms. Polytherapy with antiepileptic drugs was significantly associated with depression compared with monotherapy, highlighting the potential psychological burden of multiple drug therapy. Although depression severity was higher among patients receiving polytherapy, this association was not statistically significant. The findings emphasise the importance of routine depression screening in patients with epilepsy, particularly those on polytherapy, using validated tools such as NDDI-E and HAM-D. Early identification and appropriate psychiatric intervention may improve treatment adherence, seizure control, quality of life, and overall clinical outcomes. A multidisciplinary approach involving neurologists and mental health professionals is essential for comprehensive epilepsy care. Further longitudinal and multicentric studies are recommended to better understand the causal relationship between antiepileptic drug therapy and depression.

**Limitations**

Although this study provides valuable insights, it is important to acknowledge certain limitations. Its cross-sectional design precludes establishing causality between antiepileptic drug (AED) therapy and depression. Additionally, the research was conducted at a single tertiary care hospital, which may limit the generalizability of the findings to the broader population. Moreover, critical factors such as seizure frequency, epilepsy duration, adherence to treatment, and psychosocial variables were not comprehensively examined. Future research should employ a longitudinal design, involve multiple centres, and include larger sample sizes to better elucidate the relationship between specific AEDs and depression.

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