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Anxiety and depressive disorders in people with epilepsy; A systematic review

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Abstract

Background: Epilepsy is a neurological disease that affects individuals of all ages. People with epilepsy are more susceptible to psychiatric diseases and comorbidities such as depression and anxiety disease. The existence of such co-morbidities among epileptic patients has a negative impact on the quality of life of patients and can result in worse responses to management.

Aim: To assess the presence of anxiety and depression in individuals with epilepsy by reviewing the previous studies that evaluated this subject.

Methods: Obtaining articles related to our subject required searching through PubMed, Science Direct, Google Scholar, Springer, and Scopus using different terms including "Depression, Anxiety, Epilepsy, Prevalence, Association, Correlation, Risk Factors, and Predictors." Original, English, full-text articles were eligible for inclusion in this review.

Results: In agreement with the eligible criteria, there were ten studies included in this review with a total number of 3626 individuals with epilepsy and an age range of 12-88 years. Four studies reported both anxiety and depression, whereas the remaining six studies focused on depression only.

Conclusion: There was a higher prevalence of anxiety among epileptic patients compared to depression. There were common risk factors for developing anxiety and depression among people with epilepsy, including female gender, seizure occurrence, marital status, poly-medication, epilepsy duration, and perceived stigma.

Keywords: Epilepsy, Anxiety, Depression, Associated factors.

Introduction:

Epilepsy is a neurological disease that is characterized by electrical discharges in the brain leading to recurrent seizures **[1]** and affects all ages **[2]**. The overall incidence of epilepsy was estimated to be 61.4 per 100000 person-years **[3]**. People with epilepsy are more prone to psychiatric diseases and the rates of psychiatric illness are 9% higher among this population compared to the general population **[4]**. Mood and anxiety disease are the two major psychiatric comorbidities diagnosed among up to a third of individuals with epilepsy **[5]**. Research suggests that individuals with epilepsy may be at increased risk of anxiety disorders **[6]**. Depression is the most predominant psychiatric disease and it accounts for 14.8% and 14.1% among males and females, respectively **[7]**. Depression is the most common psychiatric comorbidity in the case of epilepsy; depression affects almost one-third of cases and affects their quality of life **[8]**. In the general population, it was estimated that 9.4% and 8.2% of the individuals fulfilled the criteria for anxiety and depression, respectively in any 12-month period of time **[9]**. The existence of such co-morbidities among epileptic patients has a further negative impact on the quality of life of patients and can lead to worse responses to pharmacological and surgical management **[10]**. The previous systematic reviews conducted on anxiety and depression among people with epilepsy focused on youth **[6]** and adults during COVID-19 **[11]**, but there was no recent systematic review involving recent studies conducted on people with epilepsy. So, this systematic review was performed to identify anxiety and depression

among epileptic patients and associated factors by reviewing previous studies focused on this subject.

Method and search strategy:

In accordance with the PRISMA guidance for systematic review **[12]** this review was written. Electronic databases and websites were explored to search for articles related to the present objective; such websites included PubMed, Science Direct, Google Scholar, Springer, and Scopus. The search was limited to the articles published after 2017 till now. Different terms and keywords were used for searching through the websites, including "Depression, Anxiety, Epilepsy, Prevalence, Association, Correlation, Risk Factors, and Predictors." All the obtained titles were revised thoroughly to prevent missing potential studies.

Eligibility criteria:

The obtained articles were checked precisely for titles to include titles reporting anxiety and/or depression among epileptic patients, then the findings were examined for language to select English language studies only, and exclude those written in a non-English language. The remaining articles were checked for type to choose original articles and excluded other types of articles such as reviews, letters to editors, and case reports. The original articles were further examined to include the articles available for full-text and exclude those available for abstract only. Additionally, articles that reported incomplete or overlapped data were excluded. The description of the eligibility criteria is displayed in Figure 1.

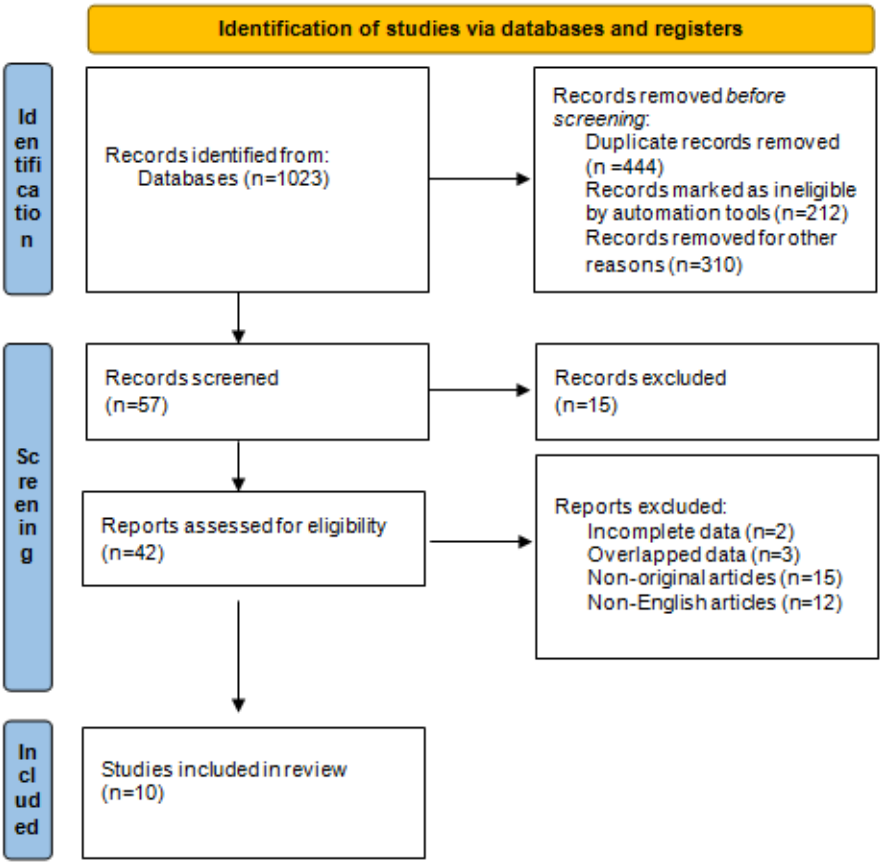


Fig1: Eligible criteria Planning

Data review and analysis:

Reviewing of the data involved reviewing the abstract to determine the data of interest for extraction and then reviewing the full-text articles to extract the pre-determined data. An Excel sheet was used for data extraction and revising, then a pre-designed table was used for data summarization under major titles.

Results:

The present review included ten eligible articles **[13-22] (Table1);** the studies were cross-sectional **[13, 15, 16, 17, 19]**, retrospective **[14]**, descriptive observational **[18]**, prospective **[20]**, consecutive cohort **[22]**, and one study didn't report the design **[22]**. There were four studies assessed depression and anxiety **[13, 15, 17, 22]**, whereas six studies assessed depression only **[14, 16, 18, 19, 20, 21]**. The tools used for the assessment of depression, included PHQ-9 **[13, 14, 16]**, NDDI **[15]**, HAD **[17]**, NDDI-E **[18, 21]**, Beck's depression inventory II **[19]**, HDRS **[20, 22]**, whereas the tools used for the assessment of anxiety, included GAD-7 **[13, 15]**, HAD **[17]**, and HRSA **[22]**.

The total number of subjects was 3626; one study was conducted on 124 patients with epilepsy and depression **[14]**, whereas the remaining nine studies enrolled epileptic patients and assessed the prevalence of depression and/ or anxiety among those patients. The age range of the participants was 12 years **[16]** to 88 years **[20]**. Regarding the duration of epilepsy, there were three studies didn't report the duration of the disease **[18, 21, 22]**, whereas the remaining seven studies reported a duration ranging between less than one year **[19]** and 34 years **[20]**.

The prevalence of anxiety among epileptic patients was reported in four studies **[13, 15, 17, 22]** and it ranged between 27.9% **[13]** and 100% **[22]**. The factors associated with anxiety included female gender (OR 1.467, P= 0.004), focal and focal to bilateral tonic-clonic seizures (OR = 1.409, P = 0.036), seizure occurrence in the last 3 months (OR = 1.445, P= 0.036) **[15]**, being a single (AOR = 1.65), using two and above antiepileptic medications (AOR = 2.27), duration of illness ≥16 years (AOR = 2.82), and perceived stigma (AOR = 2.49) **[17]**.

The prevalence of depression among epileptic patients was reported in nine studies **[13, 15, 16, 17, 18, 19, 20, 21, 22]** and ranged between 27.3% **[15]** and 67.3% **[20]**. One study reported the prevalence of chronic depression that lasted for more than one year and it was 63.7% **[14]**. The severity of depression was reported in three studies **[14, 20, 22]**; with mild depression with a prevalence of 58.9% **[14]**, and 35% **[20]**, moderate depression (33.9%) **[14]**, 34% **[20]**, and 44.7% **[22]**, and severe depression (7.3%) **[14]**, and 31% **[20]**.

The risk factors associated with depression among epileptic patients are reported as percentages or by regression analysis. Depression was more prevalent among the female gender (57.1%) **[18]**, (79%, P=0.02) **[20]**, (P=0.01) **[21]**, no school education (66.7%), working as a farmer (60%) **[18]**, unmarried status (P<0.001), disease course (P=0.01), seizure frequency(P<0.001), seizure occurrence in the last 6 months(P<0.001), and focal impaired awareness seizure(P<0.001) **[21]**, illiterates (P=0.003) and unemployed (P=0.001) **[22]**.

Depression severity was associated with education level (P=0.002), marital status (P<0.001), residency (P=0.004), duration of epilepsy (P=0.01), and controlling epilepsy (P<0.001) **[14]**. Additionally, irregular use of medications was associated with a higher risk of moderate and severe depression (P=0.03), whereas Lamotrigine agent was associated with lower rates of depression (P=0.02) **[13]**.

Regarding regression analysis, the risk factors or predictors associated with depression severity, included primary education (OR, 2.39, P=0.033) **[14]**, (AOR 3.43) **[19]**, being unable to read and write (AOR 0.4) **[16]**, (AOR 4.01) **[19]**, secondary education (AOR 2.01) **[19]**, marital status (divorced) (OR, 1.82, P=0.026) **[14]**, divorced/widowed (AOR 2.43) **[17]**, and residency inside Riyadh (OR 1.57, P=0.035) **[14]**, focal and focal to bilateral tonic—clonic seizures (OR1.531, P= 0.013), seizure occurrence in the last 3 months (OR = 1.644, P = 0.010), **[15]**, recent seizure (OR 0.23) **[20]**, treatment of epilepsy of 11 years and more (AOR 3.71) **[16]**, two or more antiepileptic medications (AOR 1.77) **[17]**, polytherapy (AOR 2.73) **[19]**, no adherence to medication (AOR = 0.216), feeling of perceived stigma (AOR = 0.244) **[16]**, (AOR 5.67) **[17]**,(OR 15.6) **[20]**, stress symptoms (AOR = 0.452) **[16]**, high perceived stress (AOR 3.21) **[19]**, very frequent seizure frequency (AOR = 2.68) **[17]**, 1-11 per year (AOR 2.34), ≥12 per year (AOR 3.49) **[19]**, current substance use (AOR = 1.82), hazardous alcohol

use (AOR = 2.84) **[17]**, poor social support (AOR = 2.04), onset of illness < 6 year (AOR = 2.40) **[19]**, financial support (OR 3.68), and controlling seizure (OR 0.23) **[20]**. On the other hand, it was found that the increase in age by one year reduced the odds of developing depression (OR 3.8) **[15]**.

Table 1: Summary of the extracted data

Author and Publication year	Study design	Studied conditions/ tools used	Characteristics of the participants	Results and main findings
Shadid et al 2024 [13]	Cross-sectional	-Depression by PHQ-9 -Anxiety by GAD-7	-N=147 epileptic patients -Age: mean=32 years -Epilepsy duration: <4->9 years *46.9% are patients for >9 years	*There 39.5% had depression and 27.9% had anxiety *Irregular use of medications was associated with a higher risk of moderate and severe depression (*P* = 0.037) *Lamotrigine medication was associated with lower rates of depression among the participants (*P* = 0.023).
Swailem et al 2024 [14]	Retrospective	-Depression by PHQ-9	-N=124 patients with epilepsy and depression -Age:18-69 years -Epilepsy duration: 1->40 years.	*There 63.7% of patients diagnosed with chronic depression that lasted for more than one year, and 36.3% had depression for less than one year *There 58.9% had mild, 33.9% had moderate and 7.3% had severe depression. *The factors associated with the severity of depression, included education level (P=0.002), marital status (P<0.001), residency (P=0.004), duration of epilepsy (P=0.01), and controlling epilepsy (P<0.001). *Multivariate analysis revealed that the factors associated with the severity, included primary education (OR, 2.39, P=0.033), marital status (divorced) (OR, 1.82, P=0.026), and residency inside Riyadh (OR 1.57, P=0.035).
Shi et al 2023 [15]	Cross-sectional	-Depression by NDDI -Anxiety by GAD-7	-N=1326 epileptic patients -Age:25-40 years -Epilepsy duration: 5-17 years.	*The prevalence of depression was 27.3% and anxiety was 31.45%. **Focal and focal to bilateral tonic-clonic seizures (OR1.531, P= 0.013) and seizure occurrence in the last 3 months (OR = 1.644, P = 0.010) were the risk factors for depression. *Female gender (OR 1.467, P= 0.004)] focal and focal to bilateral tonic-clonic seizures (OR = 1.409, P = 0.036), and seizure

				occurrence in the last 3 months (OR = 1.445, P= 0.036) were the risk factors for anxiety. *In addition, for every 1-year increase in age, the odds of developing depression were decreased by 3.8%.
Seid & Mebrahtu 2022 [16]	Cross-sectional	-Depression by PHQ-9	-N=296 with epilepsy -Age: 12->44 years -Epilepsy duration: ≤1-≥11 years	*The prevalence of depression was 34.8%. *Significant factors associated with depression, included being unable to read and write (AOR = 0.400), treatment of epilepsy of 11 years and more (AOR 3.71), no adherence to medication (AOR = 0.216), feeling of perceived stigma (AOR = 0.244) and stress symptoms (AOR = 0.452).
Nigussie et al 2021 [17]	Cross-sectional	-Depression by HAD -Anxiety by HAD	-N=556 with epilepsy -Age:18->45 years -Epilepsy duration:≤5-≥16 years.	*There 30.9% had depression and 33.1% had anxiety. *Depression was associated significantly with Being divorced/widowed (AOR = 2.43), using two and above number of antiepileptic medications (AOR = 1.77), very frequent seizure frequency (AOR = 2.68), current substance use (AOR = 1.82), perceived stigma (AOR = 5.67), and hazardous alcohol use (AOR = 2.84). *Anxiety was significantly associated with being a single (AOR = 1.65), using two and above number of antiepileptic medications (AOR = 2.27), duration of illness ≥16 years (AOR = 2.82), and perceived stigma (AOR = 2.49).
Lestari et al 2021 [18]	Descriptive observational	-Depression by NDDI-E	-N=41 patients with epilepsy -Age:18-65 years -Epilepsy duration:----	*Depression events were found among 39% *Depression events were more prevalent among females (57.1%), those with no school education (66.7%), and those working as laborers/farmers (60%).
Engidaw et al 2020 [19]	Institution-based cross-sectional	-Depression by Beck's Depression Inventory II.	-N=402 epileptic patients -Age:18-≥45 years. -Epilepsy duration:<1-≥11 years	*The prevalence of depression was 48.1%. * In multivariate analysis, educational status [unable to read and write (AOR = 4.01), primary (AOR = 3.43), secondary (AOR = 2.01], high perceived stress (AOR = 3.21), poor social support

				(AOR = 2.04), onset of illness < 6 year (AOR = 2.40), seizure frequency of [1–11 per year (AOR = 2.34), ≥ 12/year (AOR = 3.49], and polytherapy (AOR = 2.73) were independent predictors of depression among epileptic patients at *p*-value < 0.05.
Dabilgou et al 2019 [20]	Prospective	-Depression by HDRS	-N=102 epileptic patients -Age: 19-88 years -Epilepsy duration:3-34 years	*Depressive symptoms were found among 67.3% *Depression was mild among 35%, moderate among 34% and severe among 31%. *Depression was prevalent among 57.6% of males and 79% of females (P=0.02). *Risk factors of depression included financial support (OR 3.68, P=0.004), perceived stigma (OR 15..69, P=0.0000007), recent seizure (OR 3.97, P=0.001), and controlling seizure (OR 0.23, P=0.0008).
Li et al 2019 [21]	Consecutive cohort	-Depression by the Chinese version of NDDI-E	-N=461 epileptic patients -Age: mean=29.68±11.46 years -Epilepsy duration:--------	*Depression was prevalent among 29.9% *The risk factors of depression were female gender (P=0.01), an unmarried status (P<0.001), disease course (P=0.01), seizure frequency(P<0.001), seizure occurrence in the last 6 months(P<0.001), and focal impaired awareness seizure(P<0.001).
Vaswani et al 2018 [22]	------	-Depression by HRSD -Anxiety by HRSA	-N=171 epileptic patients -Age:18-60 years -Epilepsy duration:--------	*Depression was found in 61.4% of patients and of them, 44.7% had moderate severity. *Depression was significantly higher in prevalence among illiterates (P=0.003) and unemployed (P=0.001). *Anxiety was found in almost all selected patients (100%) with moderate severity among 48.5%.

PHQ-9; Patient health questionnaire-9, GAD-7; Generalized anxiety disorder scale-7, NDDI; Neurological disorders depression inventory, HAD; Hospital and Anxiety Depression Scale, NDDI-E; Neurological disorders depression inventory for epilepsy, HDRS; Hamilton Depression Rating Scale.

Discussion:

Epilepsy and depression can affect interpersonal communication, increase the risk of sudden attacks, and affect the social activities of an affected individual **[7, 23]**. Also, other psychiatric comorbidities such as anxiety are common among epileptic patients **[24]**. This review was conducted to identify anxiety and depression among individuals with epilepsy.

Depression and anxiety in epilepsy are frequently reported as distinct diseases with little or no acknowledgment of their co-existence **[25]**. In the current review, only four studies reported the co-existence of anxiety and depression among epileptic patients, whereas the remaining six studies focused on depression alone among epileptic patients. This reveals the great focus of studies on depression rather than anxiety. Similar to our findings, in a previous meta-analysis, only three out of 27 studies reported data on the co-occurrence of depression and anxiety **[26]**.

It was suggested that the pooled prevalence of anxiety and depression among studies conducted on people with epilepsy was 20.2% and 22.9%, respectively **[26]**. Such findings display that epilepsy is more prevalent among epileptic patients compared to anxiety and this was in agreement with our findings in this analysis. In a systematic review, it was found that anxiety was the major comorbidity (19.2%) followed by major repression (17.4%) **[27]**. Also, an analysis focused on youth with epilepsy included 23 studies that revealed a higher overall pooled prevalence of anxiety compared to depression with rates of 18.9% and 13.5%, respectively. Additionally, in comparison to healthy controls, significantly higher anxiety and depressive symptomatology were reported among epileptic youth **[6]**.

Anxiety is common among those with epilepsy **[24]**, with varied estimates that may be increased substantially in specialized clinical settings and may reach 50% **[28]**. In our analysis, the prevalence of anxiety exhibited a wide range of prevalence of 27.9% to 100% and this prevalence was higher than that of depression which ranged from 27.3% to 67.3%. Such findings indicate that anxiety may be a more significant co-morbidity compared to depression due to the high prevalence of anxiety compared to depression. However, there is little focus on anxiety and the associated risk factors among epileptic patients. It was suggested that in epileptic individuals, anxiety is at least as frequent as depression **[29]**. However, anxiety has received far less attention compared to depression and other comorbid diseases, despite representing a substantial burden for epileptic patients **[24]**.

Patients with anxiety often experience antiepileptic drug (AED) side effects **[24]**. In our analysis, the usage of polymedications for epilepsy increased the risk of anxiety by more than twofold (AOR 2.27) **[17]**. However, only one study reported that polymedication was a risk factor for anxiety among epileptic patients **[17]**. We could identify other risk factors associated with anxiety among individuals with epilepsy; however, such factors exhibited heterogeneity between studies and were few as the number of studies focused on epilepsy was few. The major risk factor for anxiety was the duration of epilepsy which increased the odds of anxiety by 2.82 fold, followed by perceived stigma which increased the odds of anxiety by 2.49 fold. The other risk factors of anxiety that increased its odds by less than twofold, included female gender, being single, focal, and focal to bilateral tonic-clonic seizures, and seizure occurrence. Such findings reveal that epilepsy can increase the probability of experiencing anxiety by several factors.

Depression is more prevalent among epileptic patients compared to the general population **[30]**. The reported prevalence of depression among epileptic patients varies between 10.7% and 44% **[31]**. However, the present analysis revealed a higher

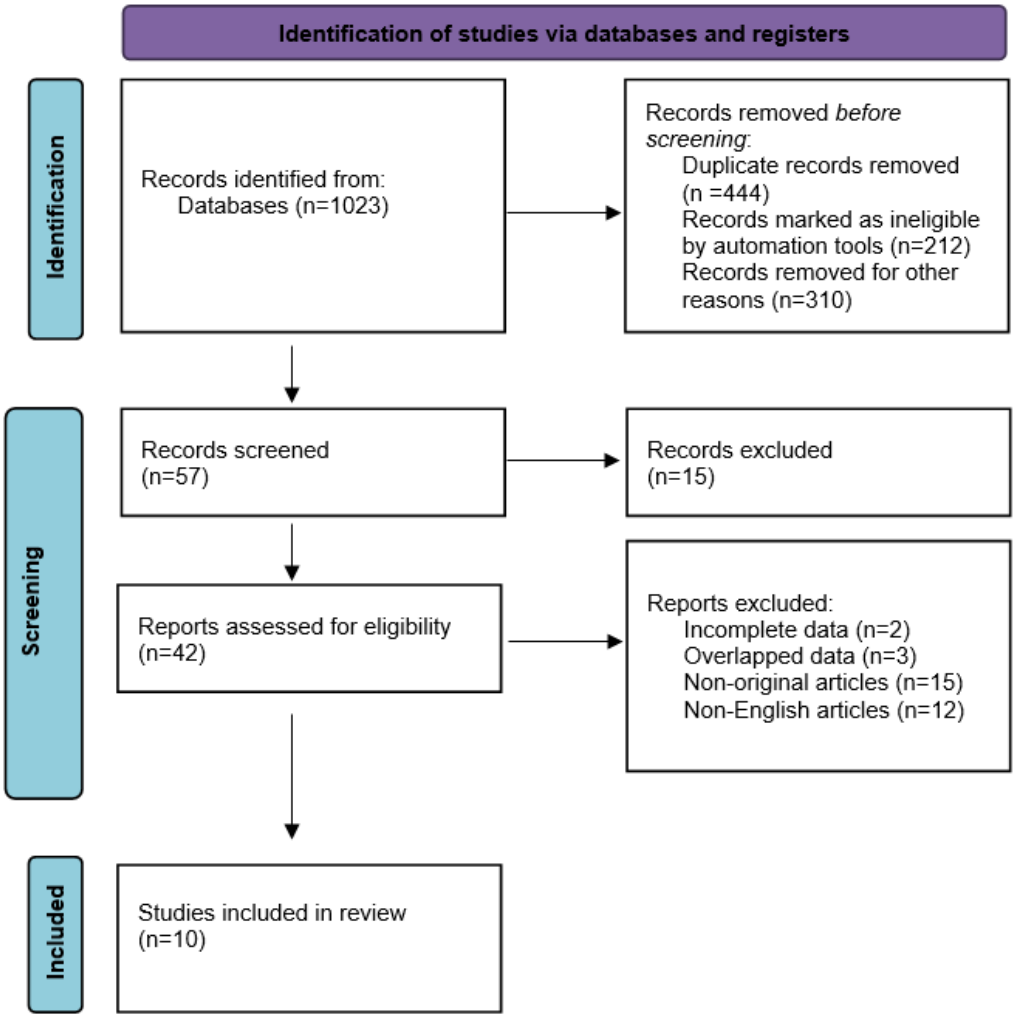
prevalence rate of depression among epileptic patients which ranged between 27.3% and 67.3%.

Epileptic seizures are rare in general with an annual incidence of 0.55% for unprovoked seizures **[32]**. In this analysis, we found that seizure frequency and occurrence were significant risk factors for depression among epileptic patients, where more frequent occurrence of seizure was associated with increased risk of depression by more than twofold. However, the risk of occurrence of seizure is restricted to time, where significant association was found between depression and seizure occurrence in the previous three and six months with an increased risk of depression by more than onefold for those who experienced seizures in the previous three months. On the other hand, recent seizure was a protective factor for depression. Furthermore, controlling seizures was a significant protective factor for developing depression (OR 0.23).

Polytherapy is an important factor; however, the association between polytherapy and depression revealed variations across the studies as some reported positive associations **[33-35]** and others none **[36]**. In our analysis, polytherapy increased the risk of depression among epileptic patients by more than onefold and more than twofold. Furthermore, non-adherence to medication was associated with moderate and severe depression and increased duration of treatment of epilepsy of 11 years, and increased risk of depression more than threefold. Hence, treatment and medication for epilepsy may cause the development of depression among epileptic patients. This in turn may return to the increased duration of medication and the need to receive several medications. A previous analysis revealed that the pooled prevalence of depression among epileptic patients was 32.71%. Additionally, the odds of depression were 2.65 for those who received polytherapy **[4]**.

Greater severity of depression with epilepsy is associated with considerable reduction of the overall seizure recovery, increased cognitive, emotional, and physical illness as well as higher seizure severity **[37, 38]**. In this review, it was found that depression severity was associated significantly with education level, marital status, residency, duration of epilepsy, controlling epilepsy, and irregular use of medication.

A previous systematic review and meta-analysis of 48 studies revealed that the pooled period prevalence of depression among epileptic patients was 27% and 34% in clinical settings **[39]**. Such rates were lower compared to the rates found in our analysis. Additionally, the previous analysis reported that the risk factors of depression, included seizure frequency, low income, perception of stigma, unemployment, female gender, unmarried status, disease course, focal-impaired awareness of seizures, and anxiety **[39]**. Such findings were close to ours, as we found that depression was significantly associated with female gender, unmarried status, disease course, unemployment, financial support, frequency of seizures, and perceived stigma. A systematic review conducted on studies during the COVID-19 period revealed that in most of the studies, the highest rate of depression was recorded among females with epilepsy and financial problems **[11]**. Additionally, we found that depression was associated with lower education or being illiterate, divorced, and widowed; low education levels increased the odds of depression by 2.01 to 4.01 fold, and being divorced or widowed increased the odds of depression by 1.82 and 4.43 folds.



*Consider, if feasible to do so, reporting the number of records identified from each database or register searched (rather than the total number across all databases/registers).
**If automation tools were used, indicate how many records were excluded by a human and how many were excluded by automation tools.
From: Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ 2021;372:n71. doi: 10.1136/bmj.n71
For more information, visit:http://www.prisma-statement.org/

Conclusion:

This review could identify that there is a great focus in the literature on depression among epileptic patients compared to the presence of anxiety among epileptic patients, despite the higher prevalence of anxiety among epileptic patients compared to depression. There were common risk factors for developing anxiety and depression among people with epilepsy, including female gender, seizure occurrence, marital status, poly-medication, epilepsy duration, and perceived stigma. The major risk factors associated with depression among this population, included lower education, residency, seizure frequency, and irregular use of medications.

References:

1-Nevitt SJ, Sudell M, Cividini S, Marson AG, Tudur Smith C. Antiepileptic drug monotherapy for epilepsy: a network meta-analysis of individual participant data. Cochrane Database Syst Rev. 2022; 4(4): Cd011412.
2-Kanner AM, Shankar R, Margraf NG, Schmitz B, Ben-Menachem E, Sander JW. Mood disorders in adults with epilepsy: a review of unrecognized facts and common misconceptions. Annals of General Psychiatry. 2024 Mar 4;23(1):11.
3-Fiest KM, Sauro KM, Wiebe S, et al.: Prevalence and incidence of epilepsy: a systematic review and metaanalysis of international studies. Neurology. 2017, 88:296-303.
4-Dessie G, Mulugeta H, Leshargie CT, Wagnew F, Burrowes S. Depression among epileptic patients and its association with drug therapy in sub-Saharan Africa: A systematic review and meta-analysis. PloS one. 2019 Mar 14;14(3):e0202613.
5-Lu E, Pyatka N, Burant CJ, et al. Systematic literature review of psychiatric comorbidities in adults with epilepsy. J Clin Neurol. 2021;17(2):176–86.
6-Scott AJ, Sharpe L, Loomes M, Gandy M. Systematic review and meta-analysis of anxiety and depression in youth with epilepsy. Journal of pediatric psychology. 2020 Mar 1;45(2):133-44.
7-Lu Y, Sun G, Yang F, Guan Z, Zhang Z, Zhao J, et al. Baicalin regulates depression behavior in mice exposed to chronic mild stress via the Rac/LIMK/cofilin pathway. Biomed Pharmacother. 2019; 116:109054
8-Maguire MJ, Marson AG, Nevitt SJ. Antidepressants for people with epilepsy and depression. Cochrane Database Syst Rev. 2021; 4(4):Cd010682.
9-Kessler, R.C.; Chiu,W.T.; Demler, O.;Walters, E.E. Prevalence, Severity, and Comorbidity of 12-Month DSM-IV Disorders in the National Comorbidity Survey Replication. Arch. Gen. Psychiatry **2005**, 62, 617–627.
10-Barco AM, Martínez MR, Restrepo D. Depression in people with epilepsy. What is the connection?. Revista Colombiana de Psiquiatría (English ed.). 2020 Jan 1;49(1):53-61.
11-Tashakori-Miyanroudi M, Souresrafil A, Hashemi P, Ehsanzadeh SJ, Farrahizadeh M, Behroozi Z. Prevalence of depression, anxiety, and psychological distress in patients with epilepsy during COVID-19: A systematic review. Epilepsy & Behavior. 2021 Dec 1;125:108410.
12- Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ 2021;372:n71.
13-Shadid AM, Alsaber N, Aldawish RA, Humaid HM, AlMubarak F, Alazwari LS, Alosaimi NS, Alkhaldi D, Alhumud MH, Shadid AM, Al Zahrani N. Depression and anxiety among patients with epilepsy: A cross-sectional study from Riyadh, Saudi Arabia. Journal of Family Medicine and Primary Care. 2024 Feb 1;13(2):549-55.
14-Swailem SK, Bamogaddam FA, Al-Attas AA. The prevalence of depression in patients with epilepsy in the Kingdom of Saudi Arabia. Cureus. 2024 Mar 5;16(3).
15-Shi W, Sun H, Peng W, Chen Z, Wang Q, Lin W, Ding M, Sun H, Wang X, Wang T, Wang X. Prevalence and risk factors of anxiety and depression in adult patients with epilepsy: a multicenter survey-based study. Therapeutic Advances in Neurological Disorders. 2023 Aug;16:17562864231187194.
16-Seid J, Mebrahtu K. Prevalence and associated factors of depression among people with epilepsy in Ethiopia: a cross-sectional study. The Egyptian Journal of Neurology, Psychiatry and Neurosurgery. 2022 Sep 6;58(1):105.

17-Nigussie K, Lemma A, Sertsu A, Asfaw H, Kerebih H, Abdeta T. Depression, anxiety and associated factors among people with epilepsy and attending outpatient treatment at primary public hospitals in northwest Ethiopia: A multicenter cross-sectional study. PloS one. 2021 Aug 13;16(8):e0256236.
18-Lestari ND, Sary NL, Ummah AK, Zulkarnain NA. Description of depression in people with epilepsy in Aceh. Age. 2021 Jun 26;18(25):14.
19-Engidaw NA, Bacha L, Kenea A. Prevalence of depression and associated factors among epileptic patients at Ilu Ababore zone hospitals, South West Ethiopia, 2017: a cross-sectional study. Annals of general psychiatry. 2020 Dec;19:1-8.
20-Dabilgou AA, Nanema D, Dravé A, Sawadogo SP, Kyelem JM, Napon C, Kaboré J. Symptoms of depression and associated risk factors in patients with epilepsy in Burkina Faso. Open Journal of Depression. 2019 Jan 10;8(1):29-40.
21-Li Q, Chen D, Zhu LN, Wang HJ, Xu D, Tan G, Zhang Y, Liu L. Depression in people with epilepsy in West China: Status, risk factors and treatment gap. Seizure. 2019 Mar 1;66:86-92.
22-Vaswani M, Haider A. Frequency of depression and anxiety among adult epileptic patients. Baqai Journal of Health Sciences. 2018 Jul 1;21(2).
23-Ping X, Qin SK, Liu SN, Lu Y, Zhao YN, Cao YF, et al. Effects of Huazhuo Jiedu Shugan Decoction on cognitive and emotional disorders in a rat model of epilepsy: possible involvement of AC-cAMP-CREB signaling and NPY expression. Evid Based Complement Alternat Med. 2019; 2019:4352879.
24-Pham T, Sauro KM, Patten SB, Wiebe S, Fiest KM, Bulloch AG, Jetté N. The prevalence of anxiety and associated factors in persons with epilepsy. Epilepsia. 2017 Aug;58(8):e107-10.
25-Grzegorzewska AM, Wiglusz MS, Landowski J, Jakuszkowiak-Wojten K, Cubała WJ, Włodarczyk A, Szarmach J. Multiple comorbidity profile of psychiatric disorders in epilepsy. Journal of Clinical Medicine. 2021 Sep 11;10(18):4104.
26-Scott, A.J.; Sharpe, L.; Hunt, C.; Gandy, M. Anxiety and depressive disorders in people with epilepsy: A meta-analysis. Epilepsia **2017**, 58, 973–982.
27-Doherty AJ, Harrison J, Christian DL, Boland P, Harris C, Hill JE, Stephani AM, Reed J, Duffield S, Marson TG, Clegg AJ. The prevalence of comorbidities in epilepsy: a systematic review. British Journal of Neuroscience Nursing. 2022 Apr 2;18(2):98-106.
28-Tellez-Zenteno JF, Patten SB, Jette N, et al. Psychiatric comorbidity in epilepsy: a population-based analysis. Epilepsia 2007;48:2336–2344
29-Hingray C, McGonigal A, Kotwas I, Micoulaud-Franchi JA. The relationship between epilepsy and anxiety disorders. Curr Psychiatry Rep. (2019) 21:40.
30-Mazarati AM, Pineda E, Shin D, Tio D, Taylor AN, Sankar R. Comorbidity between epilepsy and depression: role of hippocampal interleukin-1beta. Neurobiol Dis. 2010; 37(2):461–67.
31-Lacey CJ, Salzberg MR, D'Souza WJ. What factors contribute to the risk of depression in epilepsy?—Tasmanian Epilepsy Register Mood Study (TERMS). Epilepsia. 2016; 57(3):516–22.
32-Fiest KM, Sauro KM, Wiebe S, Patten SB, Kwon CS, Dykeman J, et al. Prevalence and incidence of epilepsy: a systematic review and meta-analysis of international studies. Neurology. 2017; 88(3):296–303.
33-Bifftu BB, Dachew BA, Tiruneh BT, Tebeje NB. Depression among people with epilepsy in Northwest
Ethiopia: a cross-sectional institution based study. BMC research notes;2015: 8: 585.

34-Tegegne MT, Mossie TB, Awoke AA, Assaye AM, Gebrie BT, et al. Depression and anxiety disorder among epileptic people at Amanuel Specialized Mental Hospital, Addis Ababa, Ethiopia. BMC psychiatry;2015: 15: 210.
35-Suljić E, Alajbegović A, Kucukalić A, Loncarević N. Comorbid depression in patients with epilepsy treated with single and multiple drug therapy. Medicinski arhiv;2003: 57: 45–46.
36-Tsegabrhan H, Negash A, Tesfay K, AberaM. Co-morbidity of depression and epilepsy in Jimma University specialized hospital, Southwest Ethiopia. Neurology India; 2014: 62: 649.
37-Cramer JA, Blum D, Reed M, Fanning K. The influence of comorbid depression on seizure severity. Epilepsia;2003: 44: 1578–1584.
38-Cramer JA, Blum D, Reed M, Fanning K. The influence of comorbid depression on quality of life for people with epilepsy. Epilepsy & Behavior;2003: 4: 515–521.
39-Qin SK, Yang ZX, Guan ZW, Zhang JH, Ping X, Lu Y, Pei L. Exploring the association between epilepsy and depression: a systematic review and meta-analysis. PloS one. 2022 Dec 15;17(12):e0278907.