Description of Profile of Patients with Epilepsy Attended in a Tertiary Service and Presence of Depressive Symptoms

Descrição do Perfil de Pacientes com Epilepsia Atendidos em um Serviço Terciário e Presença de Sintomas Depressivos

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ABSTRACT

OBJECTIVE: The study aimed to understand the prevalence of depressive symptoms among epilepsy patients, identify demographic and clinical factors associated with higher prevalence. Additionally, the study aims to underscore the concerning statistic that a significant portion of patients with depressive symptoms are not receiving appropriate treatment with antidepressants.

METHODS: Data on demographics and medication use, and Beck Depression Inventory (BDI-II) scores were collected. A total of 73 patients participated, and both quantitative and qualitative analyses were performed.

RESULTS: In our study, 64.38% had a prevalence of depressive symptoms. This confirms existing literature that identifies depression as a frequent comorbidity in epilepsy patients. Data analysis revealed that depressive symptoms were more prevalent in female patients, those with generalized onset seizures, recent diagnoses, and those using multiple anti-seizure medications. The study emphasizes the importance of addressing newly diagnosed epilepsy patients regarding their condition, prognosis, and treatment to mitigate mood-related symptoms associated with the diagnosis. Alarmingly, only 23.39% of patients with depressive symptoms were receiving treatment with antidepressants.

CONCLUSIONS: Regular screening for depressive symptoms using validated instruments, such as the BDI-II, is crucial. Prompt treatment can improve symptom control for both epilepsy and depression, and patients should be referred to multidisciplinary teams.

Keywords: Epilepsy; Depression; Depressive Symptoms.

RESUMO

OBJETIVO: O estudo teve como objetivo compreender a prevalência de sintomas depressivos entre pacientes com epilepsia e identificar fatores demográficos e clínicos associados à maior prevalência. Além disso, o estudo visa ressaltar a preocupante estatística de que uma parcela significativa de pacientes com sintomas depressivos não está recebendo tratamento adequado com antidepressivos.

MÉTODOS: Dados demográficos e de uso de medicamentos, bem como as pontuações do Inventário de Depressão de Beck (BDI-II), foram coletados. Participaram 73 pacientes, e foram realizadas análises quantitativas e qualitativas.

RESULTADOS: Em nosso estudo, 64,38% apresentaram prevalência de sintomas depressivos. Isso confirma a literatura existente que identifica a depressão como uma comorbidade frequente em pacientes com epilepsia. A análise dos dados revelou que os sintomas depressivos foram mais prevalentes em pacientes do sexo feminino, naqueles com crises convulsivas generalizadas, diagnósticos recentes e naqueles que utilizam múltiplos medicamentos anticonvulsivantes. O estudo enfatiza a importância de abordar pacientes com epilepsia recém-diagnosticada em relação à sua condição, prognóstico e tratamento para atenuar os sintomas relacionados ao humor associados ao diagnóstico. De forma alarmante, apenas 23,39% dos pacientes com sintomas depressivos estavam recebendo tratamento com antidepressivos.

CONCLUSÕES: O rastreamento regular de sintomas depressivos utilizando instrumentos validados, como o BDI-II, é crucial. O tratamento imediato pode melhorar o controle dos sintomas tanto da epilepsia quanto da depressão, e os pacientes devem ser encaminhados para equipes multidisciplinares.

Palavras-chave: Epilepsia; Depressão; Sintomas Depressivos.

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INTRODUCTION

The association between epilepsy and depression is increasingly being described and, although significant, the exact correlation between such comorbidities remains uncertain. The type of seizure, the location of the epileptogenic focus, neurotransmitter dysfunction as well as genetic and hereditary factors, psychosocial factors, and negative effects of anti-seizure medications can influence this relationship.[1–3] Since anti-seizure medications, mainly GABAergic, can paradoxically exacerbate negative psychotropic symptoms, particularly in individuals with a history of depression, then can reduce neurotransmitters such as serotonin and norepinephrine, which may worsen depressive symptoms in these individuals.[4,5]

Depression, when present in patients with epilepsy, is associated with a worse prognosis ranging from drug response to increased morbidity and mortality.[1,7] The pathophysiological process of epilepsy and depression appears to be bidirectional, with one facilitating the occurrence of the other. This would result from the involvement of the limbic system, since the hippocampus and amygdala may be affected in both diseases and underpin the bidirectional character defended in a review article by Kanner (et al).[10] However, depression usually precedes seizures and has been associated with lower rates of seizure remission after epilepsy surgery. The limbic system (amygdala and hippocampus) appears to be involved in this association due to its role in emotional processing and propagation of seizures in temporal lobe epilepsy. Studies have shown a volumetric reduction of the hippocampus in patients with major depression, although there is still controversy regarding the relationship of the volume of the amygdala. As for epilepsy, a 2007 study, with Positron Emission Tomography (PET-CT), with 34 patients with temporal lobe epilepsy who were evaluated for depression according to DSM-IV and correlation with volumetric changes in magnetic resonance imaging showed that epileptic patients presented an increase in blood flow in the limbic system when compared to depressed patients, and that in patients with temporal lobe epilepsy, they tend to present the contralateral amygdala with increased processing, which can lead to greater processing of negative emotions. In addition, cortical volumetry studies correlate the severity of depressive symptoms in patients with epilepsy, with a reduction in brain cortical thickness.[8,10,11] The application of Beck Depression Inventory - II (scale widely validated in neurological patients) in patients with poor seizure control becomes extremely important, since, in a cohort study carried out in the United Kingdom, which evaluated the medical record of more than 10,000,000 patients, selected patients with depression (diagnosed through ICD10) and with depression through prescription (use of psychotherapy, SSRIs, dual or MAOI), patients with a diagnosis of epileptic syndrome, occurrence of 2 unprovoked seizures on different occasions and medicated with anti-seizure medication. It identified that patients with depression or previous history of depression had a higher incidence of epilepsy and greater difficulty in seizure control.[12]

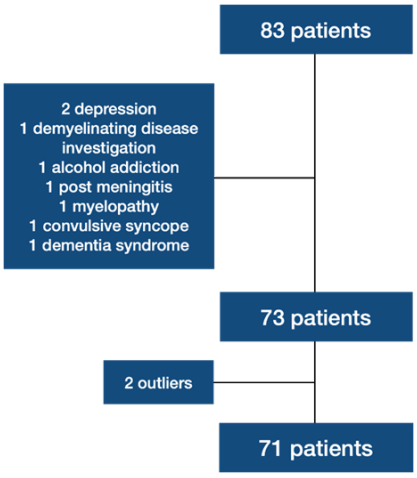
The knowledge and treatment of neuropsychiatric disorders is important since epilepsy is a chronic disease that affects more than 50 million people around the world. It is estimated that one in three patients with epilepsy will present some psychiatric diagnosis throughout life. In relation to depression, it is estimated that the incidence is 30 to 70%, which indicates it to be the most frequent comorbidity in epilepsy.[6]However, when it comes to the Brazilian population, these epidemiological data are quite scarce in the literature. Therefore, a study to evaluate possible correlations between depressive symptoms in patients with epilepsy is necessary.

Considering the difficulty in accessing specialized health services, especially Psychiatric, and the high prevalence of depressive symptoms in patients with epilepsy cited in the literature, it is important that we can recognize and evaluate the early start of treatment. However, this lack of data in our population and access to such services raises the hypothesis that patients with epilepsy have a high prevalence of depressive symptoms, possibly due to underdiagnosis. Due to this, the objectives of the study are to assess the prevalence of depressive symptoms among epilepsy patients, identify demographic and clinical factors associated with higher prevalence (such as gender, seizure type, duration since diagnosis, and treatment regimen), and highlight the need for improved management of mood-related symptoms in newly diagnosed epilepsy patients. Additionally, the study aims to underscore the concerning statistic that a significant portion of patients with depressive symptoms are not receiving appropriate treatment with antidepressants, also improving the availability of prevalence data of such symptoms and raising hypotheses of possible correlations between them, encouraging new studies.

METHODS

After approval by the Ethics and Research Committee with Human Beings, a cross-sectional study was carried out with patients attended at the Neurology Outpatient Clinic of a Specialized Outpatient Epilepsy Service. Upon arriving at the consultation and checking in, all patients over 18 years old present between May 2023 and November 2023 were approached by the researcher and invited to participate in the research, emphasizing that whether they participated in the research or not would not impact their care. After presenting the Free Informed Consent Form (FICF), a general information questionnaire (age, sex, continuous use medications) and Beck Depression Inventory - II (BDI-II), a scale widely validated in neurological patients and validated for the application in the Brazilian

population, were applied for screening depressive symptoms and the severity of these symptoms. BDI-II is composed of 21 items with four possible responses, the higher the total score, the greater the severity, with scores 14-19 (mild depressive symptoms), 20-28 (moderate depressive symptoms) and greater than 29 (severe depressive symptoms) according to Gorenstein, C. In addition, data on sex, age, time since epilepsy diagnosis, and medication use were also collected. All data were organized in an Excel® spreadsheet (only researchers involved in the study had access to the information, in order to minimize loss or circulation of information among people not involved with the study). As inclusion criteria for the study, patients over 18 years old, attended at the Neurology outpatient clinic with a focus on Epilepsy, and who had a clinical diagnosis of epilepsy (defined according to the ILAE recommendation, for population-based studies, as 2 or more unprovoked seizures that occurred with an interval greater than 24 hours) were considered. As exclusion criteria, patients who did not have a diagnosis of epilepsy, or were under 18 years old. Patients with psychogenic non-epileptic seizures were not assessed in this study, which constitutes a limitation. In the spreadsheet, data were corroborated with analysis of the patient's medical record (drugs used, type of lesion, and time of diagnosis and follow-up) were considered. In total, 83 patients participated in the study, but 10 were excluded for not meeting the inclusion criteria and had their questionnaires duly discarded and tabulated data erased from the analysis. The remaining patients with epilepsy were analyzed quantitatively (use as inclusion criterion), descriptively, and correlations were made through the Stata® and XRealStats software, and for the regression and T-test analysis, outliers shown by the Box-plot were excluded. The assessment of depressive symptoms through the BDI-II and not the diagnosis of depression itself, the recruitment period for the study and the acceptance of patients for participation were the main limitations for conducting the study.



FLOWCHART 1 - DEMONSTRATION OF SELECTION AND EXCLUSION OF PATIENTS FOR THE STUDY AND STATISTICAL ANALYSIS

NOTE: The flowchart 1 illustrates the total of 83 patients participating in the study, of which 10 were excluded for having other diseases and not fitting the study's inclusion criteria. Of the remaining 73 patients, 2 were excluded for the performance of the T-test due to an outlier.

RESULTS

73 patients with epilepsy were included in the analysis, 36 males (49.32%) and 37 females (50.68%). The median age was 41.5 years, ranging from 18 to 87 years.

Almost half of the patients had been diagnosed with epilepsy for more than 10 years (43.84%).

The majority of patients, 62 (84.93%), had focal onset epilepsy, with seven patients (9.59%) having an indeterminate onset due to a lack of clear description in their medical records. When considering the suspicion of a temporal lobe lesion as the cause of epilepsy, 22 (30.14%) had suspected temporal lobe epilepsy. However, when the presence of any structural alteration in the central nervous system was assessed as a possible cause of focal onset epilepsy, 41 (56.16%) of the patients had a structural lesion and the suspicion that such a lesion was the focus for the patient's epilepsy.

When considering the use of antidepressants, only 17 (23.29%) patients were using a drug from this class of medication.

In the absolute BDI-II score, 47 (64.38%) patients had some depressive symptoms, with more than half in absolute cumulative percentages, considering the total number of patients evaluated in this study.

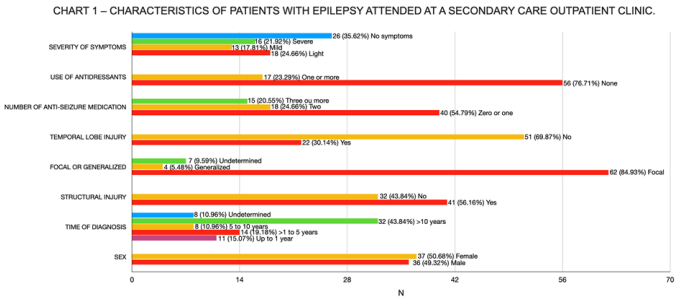


CHART 1 – CHARACTERISTICS OF PATIENTS WITH EPILEPSY ATTENDED AT A SECONDARY CARE OUTPATIENT CLINIC.

Note: chart with characteristics of 73 patients with epilepsy attended at a tertiary care outpatient clinic

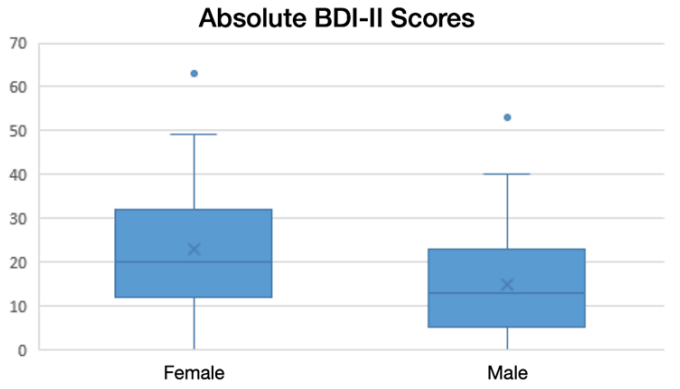


CHART 2: BOX-PLOT OF ABSOLUTE BDI-II SCORES

Note: Representation of BDI-II absolute scores. In females, the score ranged from zero to 49 points, with an outlier of 63 points, and a median of 20 points. In males, the score ranged from zero to 40 points, with an outlier of 53 points, and a median of 13 points.

Out of the 73 patients evaluated in this study, 71 were using some form of anti-seizure medication, while the remaining 2 patients were not using any anti-seizure medication. The majority of patients, 37 (52.11%), were on monotherapy with anti-seizure medication. (TABLE 1)

TABLE 1 - USE OF ANTI-SEIZURE MEDICATION BY PATIENTS WITH EPILEPSY

	N	%	MONOTHERAPY	%
CARBAMAZEPINE	29	39,73%	14	19,18%
VALPROIC ACID	26	35,62%	8	10,96%
LEVETIRACETAM	14	19,18%	5	6,85%
LAMOTRIGINE	12	16,44%	4	5,48%
PHENOBARBITAL	11	15,07%	1	1,37%
CLOBAZAM	10	13,70%	0	-
PHENYTOIN	5	6,85%	3	4,11%
CLONAZEPAM	3	4,11%	0	-
GABAPENTIN	3	4,11%	0	-
TOPIRAMATE	3	4,11%	1	1,37%
OXCARBAZEPINE	1	1,37%	1	1,37%
DIAZEPAM	1	1,37%	0	-

Note: Two patients (2.73%) diagnosed with epilepsy were not using any anti-seizure medication. One of them had been seizure-free for almost two years and the other remained without anti-seizure medication even though he had monthly seizures.

Through the T-test, with the exclusion of outliers, among the remaining 71 patients, when evaluated for the correlation between the presence of any depressive symptoms and their correlation with diagnosis time, it is suggested in this sample that patients diagnosed within the first year presented up to 10.02 average points higher on the BDI-II compared to other epilepsy patients, with a p-value <0.05. On the other hand, when considering patients diagnosed for more than 5 to 10 years, there was an average score of less than 10.04 average points on the BDI-II, with a p-value <0.05. Regarding the correlation between the presence of depressive symptoms and the number of anti-seizure medications, epilepsy patients taking two anti-seizure medications had an average score 7.30 points lower than other patients, with a p-value less than 0.05. Although statistically insignificant, the presence of three or more medications raised the average score in this sample to 22.21 average points, with a difference of 5.51 points higher when compared with the sample using three or more anti-seizure medications. When comparing the presence of depressive symptoms with focal or generalized onset, there was no statistical significance in the T-test. However, patients with generalized onset scored an average difference of 10.02 average points higher between the two samples. (TABLE 2)

TABLE 2: T-TEST FOR ASSESSMENT OF DEPRESSIVE SYMPTOMS

	N	Mean BDI-II Score	Difference Between Means	Statistical Significance (p<0.05)	Confidence Interval
DIAGNOSIS					
N -"Up to 1 year"	61	16.37	-10.02	Yes	13.39-19.35
Up to 1 year	10	26.4			14.54-38.25
N -">1 to 5 years"	57	17.35	-2.22	No	13.82-20.87
>1 to 5 years	14	19.57			13.33-25.80
N -">5 to 10 years"	63	18.92	10.04	Yes	15.69-22.14
>5 to 10 years	8	8.87			1.25-16.49
N -" More than 10 years"	39	19.41	3.59	No	15.03-23.78
More than 10 years	32	25.81			11.55-20.06
NUMBER OF ANTI-SEIZURE MEDICATIONS					
Other patients	34	16.44	-2.58	No	12.21-20.66
Use of up to 1 anti-seizure medication.	37	19.02			14.54-23.51
Other patients	53	19.64	7.30	Yes	16.00-23.28
Use of 2 anti-seizure medications.	18	12.33			7.38-17.28
Other patients	57	16.70	- 5.51	No	13.31-2.08
Use of 3 or more anti-seizure medications.	14	22.21			15.00-29.42
ONSET OF SEIZURES					
Focal or indeterminate onset	67	17.22	- 10.02	No	14.11-20.33
Generalized onset	4	27.25			9.80-44.69

Note: The legend indicates that a data cross-referencing the presence of depressive symptoms (including patients with mild, moderate, or severe symptoms) was performed with diagnosis time, the number of anti-seizure medications used, and the onset of seizures for the application of the T-test.

In the probabilistic regression assessing the presence of depressive symptoms, it was observed that men experienced lower depression rates (p 0.03), while a higher prevalence of depression was found in patients with generalized onset (p 0.01). Regarding the diagnostic duration, patients diagnosed more than 5 years before exhibited fewer depressive symptoms compared to those diagnosed within the last 5 years, although statistical significance was not achieved. (TABLE 3)

DISCUSSION

In our study, 47 (64.38%) of patients with epilepsy had a prevalence of depressive symptoms. This confirms existing literature that demonstrating depression as a frequent comorbidity, with an incidence ranging from 30% to 70%.[6] The relationship between epilepsy and depression can lead to alterations in consciousness, embarrassment, and social stigma.[4] Data analysis revealed that depressive symptoms were more prevalent in female patients, those with generalized onset seizures, recent diagnoses, and

TABLE 3: PROBABILISTIC LINEAR REGRESSION OF DEPRESSIVE SYMPTOMS

	Coefficient	p-value	Confidence Interval
Age	-.008	0.689	-.050 a .033
Male	-1.264	0.038	-2.460 a -.069
Up to 1 year	.778	0.511	-1.543 a 3.099
>1 to 5 years	.369	0.743	-1.836 a 2.574
>5 to 10 years	-2.486	0.076	-5.235 a .263
Over 10 years	-1.025	0.303	-2.974 a .924
Structural lesion presence	.252	0.704	-1.048 a 1.552
Generalized onset	2.595	0.010	.613 a 4.577
Number of anti-seizure medications	.642	0.086	.091 a 1.375
Antidepressant use	.745	0.278	-.602 a 2.093

Note: A probabilistic regression was performed, considering age, sex, diagnostic duration, presence of structural lesions, generalized onset, number of anti-seizure medications, and antidepressant use in relation to the presence of depressive symptoms (including patients with mild, moderate, or severe symptoms).

those using multiple anti-seizure medications. Alarmingly, just a minority of patients with depressive symptoms were receiving treatment with antidepressants.

Regarding sex, in this study, 37 (50.68%) patients were female. This contradicts literature data that suggest a slightly higher prevalence of epilepsy in men than in women. However, one point to consider is the resistance that males exhibit in discussing emotional issues, a resistance already mentioned in the literature and corroborated by social factors such as low virility. Therefore, the protective role of males in depressive symptoms is questionable, as this group showed a coefficient of -1.264 with a p-value 0.038.[13,14]

Focal onset was identified in 84.93% of patients, a prevalence higher than that described in the literature (approximately 60% of epilepsies). The increased prevalence may be associated with sample bias, as these patients were treated in a specialized service at a tertiary hospital with an emphasis on trauma.[15]

However, when considering the presence of depressive symptoms over time since diagnosis, patients diagnosed within 1 year showed an average score difference compared to other patients of 10.02 average points higher. This tendency reverses after 5 years of diagnosis, where the average score difference compared to other patients is 10.04 average points lower in this sample, both with a p-value < 0.05. This raises questions about disease education during the early diagnostic periods.

Regarding generalized onset, patients in this category exhibited a coefficient of 2.595 with a p-value of 0.010, suggesting an increased tendency for depressive symptoms in these patients. This raises the discussion of the severity and social impact that such seizures can have on these patients' lives. Even when considering newly diagnosed epileptic patients, the incidence of depressive symptoms related to focal onset epilepsy is 17 times higher.[6]

Despite the presence of depressive symptoms in 47 patients, only 17 (23.39%) were using some form of antidepressant. This highlights deficiencies in screening, access, and treatment for patients with psychiatric disorders within the Unified Health System (Sistema Único de Saúde), despite awareness of its impact, including treatment response in epilepsy.[1,7]

Mood disorders in epilepsy patients are multifactorial, with connections to genetic, environmental, neurological, and pharmacological factors. It is well-established that depression can be an adverse effect of long-term use of anti-seizure drugs (AEDs)[5], especially carbamazepine, phenytoin, topiramate, and gabapentin. These drugs can cause negative psychotropic effects such as depression, anxiety, and cognitive alterations, even though they are indicated for bipolar affective disorder.[3] Among the study participants, the majority (39.73%) were using carbamazepine either as monotherapy or in combination therapy, followed by valproic acid, levetiracetam, lamotrigine, and phenobarbital. Almost all were using some form of negative psychotropic medication. Analyzing the T-test (TABLE 3), there appears to be a trend toward depressive symptoms related to the use of AEDs in general. However, the sample size should be taken into account, as it may introduce bias to the data.

According to the literature, depression is a common complication following epilepsy surgery. Approximately 30% of patients may experience transient depressive symptoms in the first 3 months after the procedure. In our sample, three epilepsy patients underwent surgery for epilepsy, specifically temporal lobectomy. Among them, only one patient (33.33%) exhibited depressive symptoms, scoring moderate severity on the BDI-II. Post-surgical epilepsy patients often tend to have more severe symptoms and greater resistance to drug treatment, although this analysis was not performed in our study.[5]

We emphasize that the recruitment period for the study and the acceptance of patients for participation, just as screening for depressive symptoms through the BDI-II and not a diagnosis of depression itself may represent an important limitation of the study, we emphasize the need for further studies to clarify these relationships.

CONCLUSION

This study assessed the prevalence of depressive symptoms in epilepsy patients treated at a specialized service within a tertiary care hospital. The results revealed a 64.38% prevalence of depressive symptoms, confirming existing literature that identifies depression as a frequent comorbidity in epilepsy patients. Data analysis further

highlighted that depressive symptoms were more prevalent in female patients, those with generalized onset seizures, recent diagnoses, and those using multiple anti-seizure medications. Consequently, emphasizing the importance of addressing newly diagnosed epilepsy patients regarding their condition, prognosis, and treatment to mitigate mood-related symptoms associated with such a diagnosis. Alarmingly, only 23.39% of patients with depressive symptoms were receiving treatment with antidepressants, exposing deficiencies in access to psychiatric care within the Unified Health System. This study contributes to our understanding of the prevalence and factors associated with depressive symptoms in epilepsy patients.

The findings underscore the significance of routinely screening for depressive symptoms and initiating early treatment, when necessary, in epilepsy patients.

Regular screening for depressive symptoms should be conducted in epilepsy patients using validated instruments, such as the BDI-II. Patients with depressive symptoms should be treated promptly, as it can contribute to better symptom control for both epilepsy and depression. These patients should be referred to specialized treatment, preferably by a multidisciplinary team.

Public health policies must ensure access to and appropriate treatment for patients with psychiatric disorders, including those with epilepsy. The social and health impact on these patients, as well as in response to the treatment of epilepsy and depression, should be considered.

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