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Original Research

The Relationship of Anxiety and Depression with the Frequency of Seizure Awakening in Epileptic Patients at Dr. Moewardi Hospital Surakarta

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Abstracts

Introduction: Epilepsy is the most frequent neurological disorder worldwide. Epilepsy is a disease associated with stress and anxiety, not only as a result of the disease process but also as a cause of disease recurrence. Anxiety and depression also involve stress management and often overlap with epilepsy. Determine the relationship between anxiety and depression and the frequency of seizure awakening in epilepsy patients at Dr. Moewardi Hospital, Surakarta. **Methods:** observational using a cross-sectional design with a quantitative approach and descriptive data processing. The purposive sampling method selected the 34 study subjects. Selected subjects meet the inclusion criteria and are willing to provide informed consent. The research was conducted at Dr. Moewardi Hospital. A normality test was performed with the Spearman correlation test. **Results:** The analysis of the variables indicated a significant relationship between anxiety and the frequency of seizure awakenings, as evidenced by a p-value of 0.000, which is less than 0.05. A correlation coefficient value of 0.745 indicates a strong and positive relationship category. The relationship between depression and the frequency of seizure awakening was significant because the p-value was 0.000 < 0.05. The correlation coefficient value of 0.642 indicates moderate and positive relationship categories. **Conclusion:** There is a significant relationship between anxiety and depression and the frequency of seizure awakening in epilepsy patients at Dr. Moewardi Hospital. Anxiety and depression increase the incidence of seizure awakening in epilepsy patients at Dr. Moewardi Hospital.

Keywords: Anxiety, Depression, Frequency of Seizure Awakening

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INTRODUCTIONS

Epilepsy is the most frequent neurological disorder in the entire world population, affecting about 50 million people of all ages [1]. The prevalence in developing countries was found to be higher than in developed countries. Reported prevalence in developed countries ranges from 4–7/1000 people to 5–74/1000 people in developing countries. Indonesia does not yet have exact data on the prevalence of epilepsy, but based on the results of a study by the Indonesian Association of Neurologists (PERDOSSI) in 18 hospitals in 15 cities in 2013, it was estimated that there were 2,288 epilepsy patients [2].

According to the International League Against Epilepsy (ILAE), the diagnosis of epilepsy is established when a person has two seizures without cause that occur more than 24 hours, or when a person has a single, unprovoked seizure (if the risk of recurrence is high), or when the diagnosis of epileptic syndrome has been established (by a competent doctor) [3].

As a result of the disease process and as a potential cause of recurrence, epilepsy is a unique condition that is intimately associated with stress and anxiety. Stress management is also a component of anxiety and depression, and they frequently coexist with epilepsy. Either during the seizure episode or in close proximity to it, the anxiety symptom itself may manifest as an inherent feature of the seizure phenomena. The Hypothalamic Pituitary Adrenal (HPA) axis is involved in the stress and anxiety pathway, which explains how stress can deteriorate seizure control [4].

A recent meta-analysis found that anxiety and depression disorders were prevalent in epileptic patients, with 20.2% and 22.9%, respectively. In these situations, a number of studies frequently find a connection between psychiatric disorders and epilepsy. In addition to affecting the prognosis of epilepsy by being associated with more frequent seizures, comorbid anxiety and depression in epileptic patients lowers quality of life and premature death [5].

Anxiety is a personal experience of uneasiness, terror, or foreboding. While depressive mood, loss of interest or pleasure, guilt feelings, eating or sleeping difficulties, lack of energy, and difficulty concentrating are some of the symptoms of depression. Decreased levels of the neurotransmitters dopamine, norepinephrine, and serotonin are a common pathophysiology of both epilepsy and depression. The pathophysiology of anxiety and epilepsy is related to the neurotransmitter gamma-aminobutyric acid (GABA). In people with epilepsy, the inability to suppress GABA promotes epileptogenesis [6].

Based on these things, the researcher wanted to conduct a study that aimed to determine the relationship between anxiety and depression and the frequency of seizure awakening in epilepsy patients at Dr. Moewardi Hospital, Surakarta.

METHODS

The design of this study used is observational which uses a cross-sectional design with a quantitative approach, descriptive and analytical data processing. This research was carried out at the Neurological Polyclinic of Dr. Moewardi Hospital Surakarta from July to August 2023. The population is epilepsy patients undergoing outpatient treatment at the Neurological Polyclinic of Dr. Moewardi Hospital Surakarta and how to take samples by purposive sampling.

The inclusion criteria for this study are: a). Patients who have been diagnosed with epilepsy by a neurologist based on history and EEG examination results at the Neurological Polyclinic of Dr. Moewardi Hospital Surakarta, b). Epilepsy patients who undergo outpatient treatment and receive antiepileptic therapy, c). In medical conditions, the general state is good from the examination of a neurologist, d). Age 17 years and over, e). Able to speak, read, and write in Indonesian and f). Willing to fill

out informed consent to become a research respondent.

The criteria for research exclusion are, a). Patients who refuse to be sampled, b). Patients with Psychogenic Non-Epileptic Seizures (PNES), and c). Patients who have been or are in Psychiatric therapy. The minimum sample size of the study was obtained based on the "rule of thumb" which requires a minimum sample of 30 subjects [7].

The study's independent variables were anxiety and depression which were assessed using the Hospital Anxiety and Depression Scale (HADS) questionnaire, which consisted of 14 questions of psychopathological symptoms experienced in the past month. The measurement scale used is ordinal with anxiety score criteria (HADS-A): 0-7: normal; 8-10: borderline (there may be a tendency to anxiety); 11-21: significant anxiety. Depression score (HADS-D): 0-7: normal; 8-10: limit (there may be a tendency to depression); 11-21: significant depression. This questionnaire has been validated in Indonesian by Rudy et al., in 2015 with a Kappa coefficient of 0.706 for the anxiety scale and 0.681 for the depression scale [8].

The dependent variable is the frequency of seizure awakening which is the frequency of attacks or the number of epileptic seizures (relapses) that occur in epileptic patients [9]. Seizure awakening in this study is the number of epileptic seizures that occurred in epileptics in the last 1 month. Where the frequency of seizure awakening is said: rarely <1x a month, often 1-10x a month, often once >10x a month [9]. How to assess the frequency of seizure awakening is assessed based on direct interviews with the patient or the patient's family. Ratio scale.

After the data is collected, the data will be analyzed univariately to provide an overview of population characteristics and presentation of research results descriptively and bivariate analysis of correlation tests. Analysis using SPSS software version 26. The research has received ethical approval from the Ethics Committee of Dr. Moewardi Hospital No. 1,369/VII/HERC/2023.

RESULTS

The subjects in this study totaled 34 patients. The following are the results of the frequency distributions listed in Table 1.

Table 1. Results of Frequency Distribution of Respondents Characteristics

Respondents Characteristics	Frequency (n)	Percentage (%)
Age		
<20 year	4	11.8
21-30 year	10	29.4
31-40 year	13	38.2
41-50 year	5	14.7
51-60 year	2	5.9
Duration of Treatment		
0-10 year	29	85.3
11-20 year	4	11.8
21-30 year	1	2.9
Gender		
Male	16	47.1
Female	18	52.9

Table 1. Results of Frequency Distribution of Respondents Characteristics

Respondents Characteristics	Frequency (n)	Percentage (%)
Marital Status		
Unmarried	11	32.4
Marry	23	67.6
Education		
Elementary school	4	11.8
Junior high school	3	8.8
Senior high school	24	70.6
University	3	8.8
Work		
Buruh	3	8.8
Housewives	7	20.6
Student	2	5.9
Merchant	1	2.9
Students	3	8.8
Farmer	1	2.9
Civil Servants	1	2.9
Private	8	23.5
Does not work	3	8.8
Army	1	2.9
Wiraswasta	4	11.8
Seizure Frequency 1 Month		
1x	15	44.1
2x	6	17.6
3x	3	8.8

Table 2. Results of Frequency Distribution of Anxiety and Depression

Anxiety	Frequency (n)	Percentage (%)
Normal	7	20.6
Border	5	14.7
Significant anxiety	22	64.7
Total	34	100.0
Depression	**Frequency (n)**	**Percentage (%)**
Normal	9	26.5
Border	16	47.1
Significant depression	9	26.5
Total	34	100.0

The results indicated that the majority of respondents were aged 31–40 years (13 respondents, or 38.2%). Individuals aged 31–40 years may experience the burden of social stigma in their lives due to epilepsy, which can hinder their ability to resume normal activities [6].

Of the respondents, most had been receiving treatment for epilepsy for 0–10 years (29 respondents, or 85.3%). Treatment-induced depression has a complex pathophysiology. These include potentiation of GABAergic

neurotransmission, the drug's capacity to reduce folic acid levels, and high titration dosages. Serotonin, norepinephrine, and dopamine are examples of monoamine neurotransmitters that are affected in depressive states, along with reduced GABA action. Long-term OAE usage can also lead to low folic acid levels. Depression can result from decreased levels of the monoamine neurotransmitters dopamine, norepinephrine, and serotonin [10].

In this survey, female respondents made up 18 (52.9%) of the total number of respondents; male respondents constituted the remaining 16 (47.1%). The central nervous system's neuronal excitation can be altered by ovarian steroid hormones in females. Estrogen is known to increase the excitation properties of glutamate receptors by acting as an agonist to NMDA receptors, thereby increasing brain neuron excitation that may potentially trigger a generation while decreasing the inhibitory properties of GABA neurotransmitter receptors, particularly GABAA, by altering the conductivity of Cl ions. Variations in hormone levels link to changes in seizure patterns in women with epilepsy during adolescence, menstruation, and menopause [11].

A total of 23 respondents (67.6%), or most epilepsy patients in this study, were married, while only 11 respondents (32.4%) were unmarried. Epilepsy that occurs in someone who is married can be caused by other factors that play a role, such as stress, environment, and other risk factors (predisposing factors). In addition to limited or no emotional support, poor communication can also worsen the condition [4][12].

The respondents' highest level of education in this study was high school, with 24 respondents, or 70.6%. This is caused by impaired cognitive function experienced by epilepsy sufferers themselves, so most epilepsy sufferers are only able to carry out education up to the high school level [13]. Based on job distribution, housewives (7 respondents or 20.6%) and private employees (8 people or 23.5%) had the most jobs owned by respondents in this study. This is due to health problems that make people with epilepsy dismissed from work because they have seizures, even though they have been controlled [13].

This study uses the Spearman correlation test which is a non-parametric statistical test where the test does not require assumptions or requirements that must be met, in the spearman correlation test is used when the data scale is ordinal. The following are the results of the Spearman correlation test presented in the table below.

Tabl 3. Hypothesis Test Results

Relationship	Sig.	Correlation Coefficient
Anxiety with the Frequency of Seizure Awakening	0.000	0.745
Depression with Frequency of Seizure Awakening	0.000	0.642

Based on the table above, information was obtained that in the relationship between anxiety and the frequency of seizure awakening, a significance value of 0.000 was obtained < 0.05; then H0 was rejected and H1 was accepted, which means that there is a relationship between anxiety and the frequency of seizure generation. A correlation coefficient of 0.745 means that the level of closeness of the relationship includes strong criteria. Because the value of the correlation coefficient is positive, the relationship between the two variables is unidirectional. Thus, it can be concluded that the higher the anxiety, the frequency of seizure awakenings will also be higher, while if anxiety is low, the frequency of seizure awakenings will also be low.

In the relationship between depression and the frequency of seizure awakening, a

significance value of 0.000 is obtained < 0.05; then H0 is rejected and H1 is accepted, which means that there is a relationship between depression and the frequency of seizure awakening. A correlation coefficient of 0.642 means that the level of closeness of the relationship falls into the medium criteria. Because the value of the correlation coefficient is positive, the relationship between the two variables is unidirectional. Thus, it can be concluded that the higher the depression, the higher the frequency of seizure awakening will also be, while if the depression is low, the frequency of seizure awakening will also be low.

DISCUSSIONS

The results stated that there was a relationship between anxiety and the frequency of seizure awakening in epilepsy patients. This is shown based on the results of bivariate tests that have p-values = 0.000 < 0.05, where the relationship is included in strong criteria. The results of this study are in line with previous research conducted by Sugandi et al. (2022), where there is a relationship between anxiety and depression in epilepsy sufferers [6].

Anxiety is a subjective feeling of anxiety, fear, or hunch. Depression, on the other hand, is a mental condition marked by a depressed mood, a loss of pleasure or interest, feelings of guilt, eating or sleeping disorders, a lack of energy, and a decrease in concentration. Depression and epilepsy have an interrelated pathophysiology of decreased levels of the neurotransmitters serotonin, norepinephrine, and dopamine. Anxiety and epilepsy share the same pathophysiology associated with the neurotransmitter gamma-aminobutyric acid (GABA). The inability to inhibit GABA in epileptic patients increases epileptogenesis [6][14].

Anxiety very often appears in patients with epilepsy. Epileptics experience anxiety disorders that are exacerbated by psychosocial conditions of epileptics, including concerns about the unpredictable of when seizures will occur and limited daily activities carried out by sufferers. A sense of inferiority, societal stigma, and social rejection exacerbate anxiety in people with epilepsy. This anxiety affects the nervous system related to the appearance of seizure awakening [15].

Anxiety can occur in conditions of normal response to stress, but high and prolonged exposure to stress can cause anxiety disorders. Clinical studies in epilepsy patients reveal that stress is the most frequent trigger of seizures. Increased stress and anxiety correlate with an increased risk of subsequent seizures. Disruptions in the transmission of the neurotransmitter GABA can cause anxiety and stress-induced seizures. This is the relationship between anxiety and stress in epilepsy patients [6].

The results also stated that there is a relationship between depression and the frequency of awakening in epilepsy patients. This is shown based on the results of a bivariate test that has a p-value = 0.000 < 0.05, where the relationship is included in the medium criteria. The results of this study are in line with previous research conducted by Joao et al. (2022), where there was a relationship between depression and the incidence of awakening in people with epilepsy [15][16].

Depression is known to influence on the occurrence of epileptic seizures. In a state of depression, there will be hyperventilation, where CO2 levels in the blood increase, which will cause brain cells to release abnormal electrical charges against their will. Mediators of depression such as corticosteroids and corticotropin-releasing hormone (CRH) contribute to the incidence of epilepsy. Corticosteroid hormones will quickly increase Cl- levels that enter the membrane of neurons; these changes can cause injury to the nerves, and then depolarization will occur. High levels of steroids can increase and accelerate the pathogenesis of epilepsy. CRH will increase spontaneous bursts, and then hyperpolarization suppression will occur

after excessive action potential bursts [11] [17].

Neurologically, people with depression experience changes in brain areas, including reduced hippocampal volume, decreased frontal lobe cortex thickness, and lower density in several other brain regions. Dysfunctional areas of the brain that produce serotonin are also responsible for the possibility of depression. People with epilepsy also experience various brain changes, although depressive disorders do not accompany all cases of epilepsy. In fact, preictal symptoms or antiseizure treatment (either with drugs or surgery) may trigger depressive symptoms in individuals with epilepsy [18][19].

Depression and stress in epilepsy patients who have stressful lives can increase the risk for seizures. The stress experienced by patients usually appears in the form of anticipatory anxiety and boredom from never-ending treatment. Stressors can cause prolonged activation of the HPA axis and recurrent seizures. These stressors can develop and lead to depression. Depression often appears in patients with epilepsy. Epileptic patients with depression had a 32 times higher risk of committing suicide compared to epileptic patients without depression. Changes in brain activity can trigger epileptic seizures, which may contribute to mood disorders; additionally, the stresses of life can exacerbate depression. Epilepsy becomes difficult to treat because depression causes more frequent seizures and reduces motivation to manage it effectively [6][20].

This research has experienced limitations, which should be considered by future researchers aiming to refine their studies. One limitation of this study is the use of measurement instruments for bound variables that have not been validated or standardized in the scientific literature, which can affect the validity and reliability of the results obtained. The main advantage of this research lies in its new focus, which has never been explored before, especially at Dr. Moewardi Hospital Surakarta, allowing for further research by developing other variables.

CONCLUSIONS

Based on the results of analysis and research that has been conducted on epilepsy patients at Dr. Moewardi Hospital Surakarta, the conclusion that can be drawn is that the majority of respondents have high levels of anxiety and moderate levels of depression. There is a positive relationship between higher anxiety or depression and the frequency of seizure awakening, which will also be higher.

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

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