



# Factors Associated with Anxiety Scores in People with Epilepsy in Neurological Installations of Haji Adam Medan Center General Hospital

Hanny Soraya<sup>ID</sup>, Mustafa M. Amin<sup>\*ID</sup>, Muhammad Surya Husada, Elmeida Effendy<sup>ID</sup>

Department of Psychiatry, Faculty of Medicine, Universitas Sumatera Utara, Medan, Indonesia

## Abstract

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**\*Correspondence:** Mustafa M. Amin, Department of Psychiatry, Faculty of Medicine, Universitas Sumatera Utara, Medan, Indonesia. E-mail: [mustafa.mahmud@usu.ac.id](mailto:mustafa.mahmud@usu.ac.id)  
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**BACKGROUND:** Anxiety disorder is the most prevalent comorbidity that may persist chronically in individuals with epilepsy. Unfortunately, anxiety is commonly ignored and rarely reported by epileptic patient. Therefore, early intervention and proper treatment should be addressed in these people. Acknowledging risk factors related to anxiety among epileptic patients may be useful in tailoring more appropriate psychiatric support.

**AIM:** The aim of our study is to investigate risk factors related to anxiety among epileptic patients.

**METHODS:** This cross-sectional predictive analytical multivariate study was conducted through March to May 2021 in Haji Adam Malik General Hospital Medan involving 84 epileptic patients visiting Neurology outpatient clinic who fulfilled inclusion and exclusion criteria COVID-19 health protocols. Anxiety score was assessed using HADS-A self-reported questionnaire.

**RESULTS:** We found that most of our patients are female who have experienced epilepsy for around 3 years. Exacerbations occurs approximately 4 times a year with duration of 10–20 min. Finally, we found that age, seizure duration, epileptic frequency, and gender are independent risk factors for anxiety severity among epileptic patients.

**CONCLUSION:** Age, seizure duration, epileptic frequency, and gender are independent risk factors for anxiety severity among epileptic patients.

## Introduction

Anxiety disorder is the most prevalent comorbidity that may persist chronically in individuals with epilepsy [1]. Unfortunately, anxiety is commonly ignored and rarely reported by epileptic patient [2]. Epilepsy is altered brain electrophysiology, characterized by persistent presence of epileptic wave that leads to impaired cognitive, psychology, and social aspect. It may also cause injury when epileptic exacerbation presents [3]. The World Health Organization approximated that more than 50 million individuals are epileptic and that 80% of epileptic patients commonly are from middle income countries. Epileptic patients do not only face challenges from epilepsy, but also stigmatization and discrimination from those around them [4].

Studies by Fiest *et al.* in 2017 stated that prevalence of epilepsy in general is 7.6/1000 people that commonly is found in developing country [5]. Beghi in their published study in 2020 also stated that etiology, frequency, and certain risk factors may contribute to epilepsy prevalence difference worldwide

[6]. Epileptic exacerbation is also related to sudden death, it is reported that in every one cases out of 10,000 new cases poses risk of sudden death from epileptic exacerbation [7]. A report from Canadian Population-Based Study showed that coexisting psychiatry disorder is found among epileptic patient for as much as 35.5%, in which anxiety presents in 22.8% cases [6], [8]. The previous studies have shown that anxiety severity is proportionally correlated with severity of epilepsy in which more severe anxiety is related to worse prognosis of epilepsy [9], [10]. Anxiety is also one of the reasons for unemployment among epileptic patients as shown in a study by Tedrus *et al.* in Brazil. They found that out of 58 epileptic patients, 20.7% patients are no longer employed and 33.9% lost their job due to anxiety disorder [11]. Therefore, early intervention and proper treatment should be addressed in these people. Acknowledging risk factors related to anxiety among epileptic patients may be useful in tailoring more appropriate psychiatric support. Thus, the aim of our study is to investigate risk factors related to anxiety among epileptic patients.

## Methods

### Population and sample

This cross-sectional predictive analytical multivariate study was conducted through March to May 2021 in Haji Adam Malik General Hospital Medan involving epileptic patients visiting Neurology outpatient clinic who fulfilled inclusion and exclusion criteria. Sample was gathered consecutively in accordance with inclusion criteria as in the following; 1) age of 20–45-years-old, 2) diagnosed with epilepsy, 3) capable of reading and writing, and 4) fluent in Indonesian language. In the other hand, those with any ongoing or history of psychiatry morbidities, and those with any other known medical diagnosis were excluded from the study. A total of 84 subjects were given informed consent before the study, and were requested to fill in personal data on participant's form. Direct interview was conducted in accordance with COVID-19 health protocols.

### Variable Identification

Independent factors assessed in this study are the following; age, gender, education, occupation, marital status, smoking, alcohol intake, seizure duration, onset, and epileptic frequency. In the other hand, dependent variable is Hospital Anxiety and Depression Scale-Anxiety subscale (HADS-A) score.

### Measurement

Hospital Anxiety and Depression Scale (HADS) was developed by Zigmond and Snaith in 1983 to identify anxiety and depression cases in non-psychiatry clinics. HADS consists of two subscales; anxiety and depression subscale [12]. HADS is a self-reporting questionnaire, consisting of 14 questions that is scaled from 0 (never) to 3 (very often). Total score of 16 indicates severe form of disorder, 11–15 indicates moderate, 8–10 indicates mild case, and <7 indicates no form of depression or anxiety. In Indonesia, HADS has been validated by Rudy *et al.* in 2015. They also found that inter-rater agreement of HADS-A is 0.706, showing that HADS-A has a good reliability [13].

### Statistical analysis

Data collection and analysis was conducted using SPSS software version 25. Linear regression was used in this study after the following prerequisites are met; 1) normal residual spread can be proved by histogram, 2) residual mean from descriptive statistic equals to 0, 3) no outlier (as shown in case wise diagnostic), 4) constant (as shown in scatter graph between residues and independent variable), 5) independent (as shown by Durbin-Watson test), 6) no indication of multicollinearity (as proved by

Pearson and correlation test on independent variables, and 7) linearity between independent and dependent variables (as shown in scatter graph) [14]. Kolmogorov–Smirnov test was conducted initially to assess normality of the data. When data are normally distributed, Pearson test can be used, while, in the other hand, when data are not normally distributed, Spearman will be used. Only independent variables with  $p < 0.25$  that will be preceded in the study [15] (Table 1).

**Table 1: Samples demographical characteristics**

Variables	Value (n = 83)	
	Median (min–max)	n (%)
Age (years)	29 (20–45)	
Gender		
Male		40 (47.6%)
Female		44 (52.4%)
Marital Status		
Not Married		51 (60.7%)
Married		33 (39.3%)
Education (years)	12 (6–16)	
Employment		
Yes		30 (35.7%)
No		54 (64.3%)
Smoking		
Yes		21 (25%)
No		63 (75%)
Alcohol intake		
Yes		45 (53.6%)
No		39 (46.4%)
Seizure duration (minutes)	20 (10–30)	
Epileptic frequency (x/year)	4 (0–13)	
Onset (years)	2 (1–10)	

## Results

Our study found that most of epileptic patients visiting Neurology clinic at Haji Adam Malik General hospital are female (53.6%). More than half of the subjects (60.57%) are already married and employed (64.3%). Three fourth subjects (75%) are smokers and more than half of the subjects (52.4%) do not consume alcohol. We found that our subjects are in the range of 20–45 years of age and spent around 12 years to pursuit education. Most patients admitted to experience 10–20 min seizure that is usually present 4 times in a year. We also noted that in average most patients already had epilepsy for around 3 years (Table 2).

**Table 2: Model summary of first linear regression multivariate analysis**

Model	R	R Square	Adjusted R Square	Std. Error of the Estimate	Durbin-Watson
1	0.864 <sup>a</sup>	0.747	0.724	2.267	
2	0.864 <sup>b</sup>	0.747	0.727	2.253	
3	0.863 <sup>c</sup>	0.745	0.729	2.246	
4	0.861 <sup>d</sup>	0.741	0.728	2.251	1.831

After bivariate analysis was conducted, there were only seven variables that were fit to be included in multivariate analysis. Variables including occupation, onset, and marital status showed  $p > 0.25$ , thus were excluded from the study. We also found that model 3 showed highest determinant coefficient of 72.9%, yet we found that education was not significant. Therefore, we conducted another linear regression analysis, as shown in Table 3.

**Table 3: Model summary of second linear regression multivariate analysis**

Model	R	R Square	Adjusted R Square	Std. Error of the Estimate	Durbin-Watson
1	0.862a	0.742	0.722	2.273	
2	0.862b	0.742	0.726	2.258	
3	0.861c	0.741	0.728	2.251	1.831

We found that model 3 showed highest determinant coefficient of 72.8%. Kolmogorov–Smirnov test has shown  $p = 0.200$  for HADS-A indicating that this dependent variable can be included in the study.

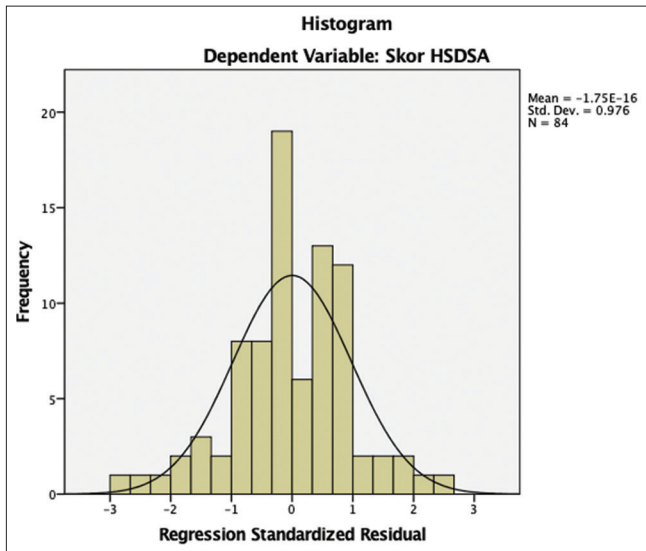


Figure 1: Histogram showing linearity

Using backward method, we generated linear regression equation as the following:  $HADS-A \text{ score} = 6.4 - 0.09 * \text{age} + 0.34 * \text{seizure duration} + 0.18 * \text{epileptic frequency} + 1.75 * \text{gender}$ . All prerequisites have also been fulfilled as shown in the Figures 1-4.

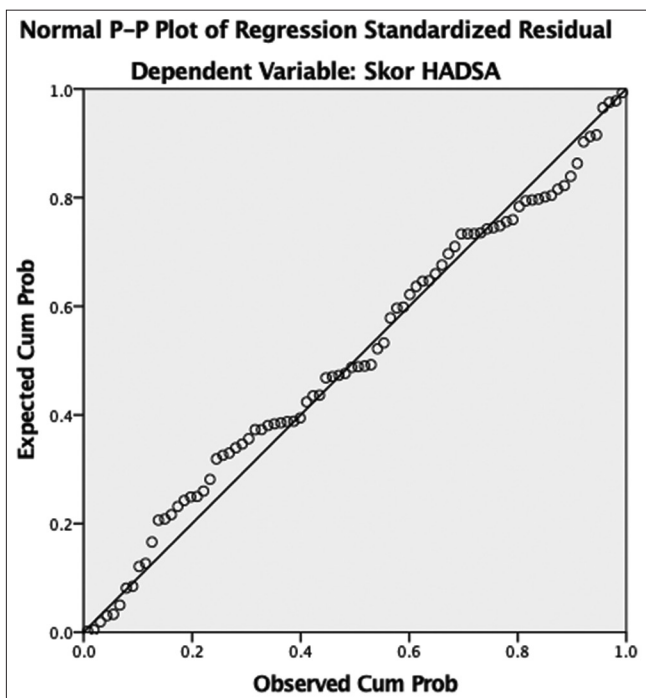


Figure 2: Normal P-P Plot showing normality of residue

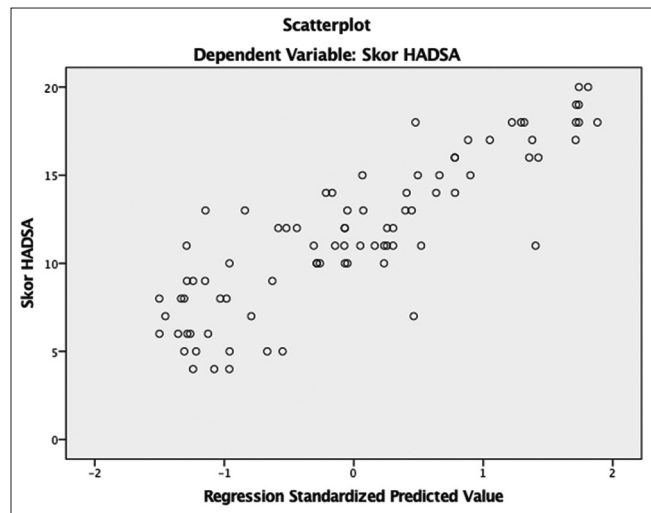


Figure 3: Scatter Plot between total HADS-A score with regression standardized predictive value

Finally, we found that age, seizure duration, epileptic frequency, and gender are independent risk factors for anxiety severity among epileptic patients (Table 4).

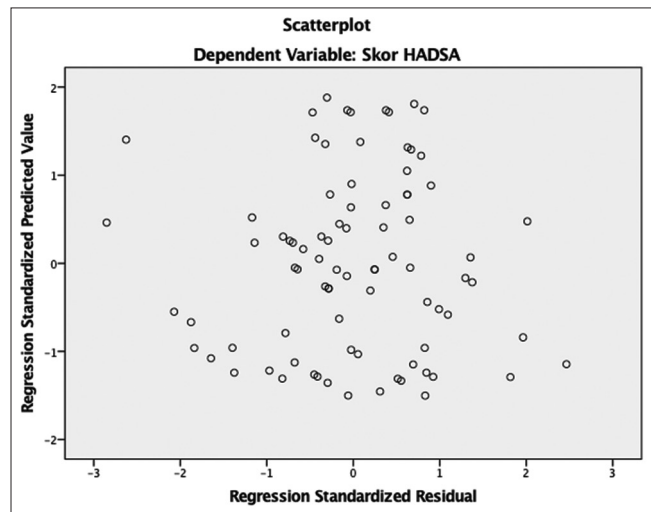


Figure 4: Scatter plot between regression standardized residual (ZRESID) dan regression standardized predicted value (ZPRED) to test constancy

## Discussion

Inhibition gamma aminobutyric acid has been linked to the development of anxiety among epileptic patients. It is found that benzodiazepine receptors are

**Table 4: Multivariate analysis**

Skor HADS-A	Correlation coefficients	Regresi multivariat $\beta$	p
Konstan		6.328	<0.001
Umur	-0.164	-0.089	0.010
Durasi kejang	0.584	0.338	<0.001
frekuensi epilepsi	0.157	0.178	0.017
Jenis kelamin	0.204	1.748	0.003

Adjusted  $R^2 = 72.8$ .

also decreased on the temporal region along with the development of sclerosis on the hippocampal region that both are shown to induce anxiety in epileptic patients [16]. Another possible explanation on how anxiety may develop in epileptic patients could be the presence of impaired amygdala. Experimental studies have shown that amygdala, as well as its central nucleus are responsible to fear and anxiety. Stimulation of this structure during partial complex seizure on temporal area has shown to produce anxiogenic effect [17].

In our study, average age of epileptic patient shows weak correlation to total HADS-A score. Our finding is in line with a study by Faravelli *et al.* from Italy that showed higher incident of epilepsy in women. This is supported by the fact that current study has found that hormonal fluctuation among women has led to increased prevalence of epilepsy [18]. Our subjects average age is also similar with those in another study by Maroufi *et al.* in 2014 and also showed negative correlation to HADS-A score. Younger age is shown to be related to higher risk of anxiety among epileptic patients, mainly due to patient's ability to anticipate the exacerbation of epilepsy. Older patients are more composed as they have had more experience in overcoming exacerbation related anxiety [19]. Another study from Liu *et al.* showed positive correlation between seizure duration and HADS-A score which is also in line with our finding. Moreover, epileptic frequency is also shown to be correlated with anxiety [20].

### Study limitation

This study is first to assess factors related to anxiety among epileptic patients in Medan, North Sumatera by using HADS-A questionnaire. Yet, we are also aware that our study is limited as it was only conducted at one place.

## Conclusion

Age, seizure duration, epileptic frequency, and gender are independent risk factors for anxiety severity among epileptic patients. By acknowledging risk factors related to anxiety among these patients, early intervention and tailored education for both patients and their family can be done.

## Declarations

### Authors' contributions

All authors contributed equally to this work.

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### Ethics approval and consent to participate

The Research Ethics Committee approved this study at the Faculty of Medicine, Universitas Sumatra Utara with the letter number 75/KEP/USU/2021 on February 26, 2021. All participants write and sign consent to participate before attending this study. Data will not be shared to respect the privacy of the participant.

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