



DIFFERENCES OF DEPRESSION LEVELS IN TEMPORAL LOBE EPILEPSY AND EXTRA TEMPORAL LOBE EPILEPSY PATIENTS : CASE STUDY IN POST EPILEPSY SURGERY PATIENTS

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ABSTRACT

Introduction: Depression is a common condition in epilepsy patients, especially temporal lobe epilepsy both before and after epilepsy surgery. However, not many studies have examined the depression status of patients undergoing surgery outside the temporal lobe (extratemporal resection). Differences in levels of depression between temporal lobe epilepsy (TLE) and extra-TLE patients are also not well known, so the effect of surgery on mood disorders in this group of epilepsy patients needs to be further investigated. **Aim:** This study aims to study whether there are differences in depression rates for TLE and extra-TLE patients in case studies of post-epileptic surgery patients. **Method:** The design of this study was cross sectional by conducting research on patients with temporal lobe epilepsy (n = 29) and extra temporal epilepsy patients (n = 24) from 1999 to 2019. The study was conducted at the Hospitals in Semarang. Researchers recorded depression levels using the Beck Depression Inventory - II (BDI-II) after the patient had surgery. The collected data will be analyzed using the parametric 2 independent samples t test. **Results:** 53 patients who were subject were 29 TLE patients (54.7%) and 24 Extra TLE patients (45.3%). TLE patients who had normal BDI-II results were 14 patients (48.3%), mild depression by 6 patients (20.7%), moderate depression by 8 patients (27.6%) and severe depression by 1 patient (3,4%) while the Extra TLE patients showed normal results of 11 patients (45.8%), mild depression of 8 patients (33.3%), moderate depression of 4 patients (16.7%) and severe depression of 1 patient (4.2%). 2 independent samples t test showed insignificant results, namely $p = 0.831$. **Conclusion:** There are differences of depression level between TLE and Extra TLE cannot be confirmed, because there are many factors such as the duration of epilepsy and seizure frequency that influence patients. Multifactorial explanation for the depression in patients with TLE and extra TLE must be investigated.

Keywords: TLE (Temporal Lobe Epilepsy), extra-TLE, Depression

INTRODUCTION

Epilepsy is a chronic disease related to the level of disability and functional that is most often found in developing societies in countries.¹ As many as 80% of people with epilepsy are found in developing countries like

Indonesia². People with epilepsy often suffer from mood disorders like depression. Depression in epilepsy patients occurs 30% - 50%.³

Patients with temporal lobe epilepsy (TLE) tend to have higher levels of affective and mood disorders such as



depression than other epilepsy.⁴ This is due to the main involvement of the limbic system both in the generation of seizures in TLE and in the regulation of mood effects and mood.⁵ Patients with extra temporal epilepsy (extra TLE) are not known with certainty about the magnitude of depression levels after epilepsy surgery because there are no previous research studies discussing the level of epilepsy post-epilepsy surgical depression in extra TLE patients especially in Indonesia.

Depression given the high prevalence and clinical significance of existing psychiatric diseases in epilepsy patients, the effect of surgery on psychiatric symptoms is highly relevant.⁶ Previous studies have reported development of depression after epilepsy surgery.⁷ The study was designed to examine the effect of epilepsy surgery on depression in patients with TLE and the results were different levels of depression in TLE patients after surgery.⁸

Knowing the relationship between epilepsy and depression, research is needed to understand the level of depression of temporal lobe epilepsy and extra temporal patients in post epileptic surgery patients. We suspect that there are differences in

depression between TLE and extra TLE patient after epilepsy surgery .

MATERIALS AND METHOD

Research Design and Study Variables

This research used a cross sectional design of two independent groups. It was held in Hospitals in Semarang. The dependent variable of this research is depression rates and the independent variable of this research is the temporal lobe epilepsy and extra temporal lobe epilepsy after epilepsy surgery.

Participants

Participants were patients with TLE and extra TLE who have undergone all the examination procedures before complete surgery, the results of epileptogenic focus examinations from patients can be ascertained, patients who have an IQ level of more than 70, patients over 9 years old, patients have been tested for depression using BDI-II and the results can be interpreted clearly. Participants were selected by consecutive sampling. Based on the calculation of sample size, the minimum samples needed for each group was 20 people.^{7,9} Total sample was 53 people who included inclusion criteria.



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Tools and Materials

Tools and materials that will be used in this study are patient medical records, questionnaires, informed consent paper, notebooks, stationery, and office equipment.

Procedure

Some of the stages in this study include : taking care of ethical clearance, taking medical records of epilepsy surgery patients, making selections based on criteria determined by previous researchers, determining temporal and extra temporal lobe epilepsy patients, sending BDI-II depression test questionnaires to TLE and extra TLE patients, recorded the results of depression tests for TLE and extra TLE patients after surgery, compared the results of depression tests for TLE and extra TLE patients after surgery in patients with temporal lobe epilepsy and extra temporal patients.

Ethics Approval

Prior to data collection, ethical approval was obtained from the Medical Research Ethical Committee of Kariadi. The Ethical Clearance of this research was No. 127/EC/KEPK/FK-UNDIP/V/2019.

Data Analysis

The data obtained were processed using a computer program and firstly analyzed with Kolmogorov-Smirnov normality test. The hypothesis about differences in depression rates on TLE between extra TLE was tested using the parametric independent samples t test because data was normally distributed. Data said to be significant if $p < 0.05$.

STUDY RESULTS

Characteristic of the Participant

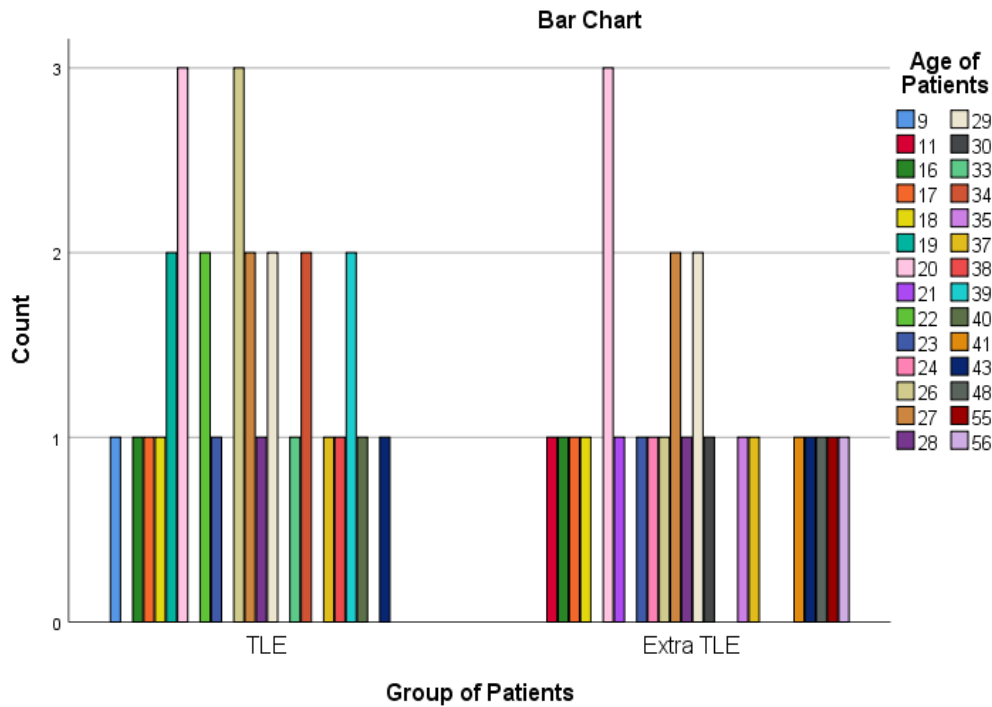
The study was held in March 2019. Participants consisted of 53 patients epilepsy of Kariadi Hospital and Tlogorejo Hospital that fulfilled the inclusion and exclusion criteria. There were 31 males and 22 females from the 53 participants of the research consisting of 29 patients (54.7%) as a group of temporal lobe epilepsy patients (TLE) and 24 patients (45.3%) as a group of extra temporal epilepsy patients (extra TLE). The research sample was obtained from questionnaires and medical records of epilepsy surgery patients from 1997-2017, the selected subjects were included in the inclusion criteria. The description of the sample used in this study can be seen in the following graphs one and table one.



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Table 1. Sociodemographics aspect

Characteristics	Frequency	
	TLE n (%)	Extra TLE n (%)
Sex		
Male	15 (51,7)	16 (66,7)
Female	14 (48,3)	8 (33,3)
Schooling		
Left Behind	2 (6,8)	1 (4,1)
Appropriate		
- Elementary	1 (3,4)	1 (4,2)
- Junior High	1 (3,4)	2 (8,3)
- Senior High	13 (44,8)	11 (45,8)
- College	12 (41,4)	9 (37,5)
Employment situation		
Unemployed	4 (13,7)	2 (8,3)
Student/Housekeeping	10 (34,4)	13 (54,1)
Employed	15 (51,7)	9 (37,5)
Marital Status		
Married	11 (37,9)	6 (25,0)
Single	14 (48,2)	15 (62,5)
Divorced	4 (13,7)	3 (12,5)



Graphic 1. Age of TLE and Extra TLE Patients

It can be seen from the graph that there are 29 TLE patients and 24 Extra TLE patients with the average age of the patients being 27.94 years old, the average TLE patients at 26.90 years old and Extra TLE patients at 29.21 years old. From the data analysis, it was found that the youngest age of TLE patients was at 9 years old and the oldest age was at 43 years old, while the youngest age of Extra TLE patients was at 11 years old and the oldest age was 56 years.

BDI-II Score Measurement Results

Table 2. BDI-II score in the TLE and extra TLE group

GROUP	BDI-II Score				Total
	Normal (0-9)	Mild Depression (10-15)	Moderate Depression (16-23)	Severe Depression (24-30)	
TLE	14	6	8	1	29
Extra TLE	11	8	4	1	24
Total	25	14	12	2	53



Table 3. Analysis of BDI-II score in the TLE and extra TLE group

BDI Score	Group		P
	TLE (n=29) (mean±SD)	Extra TLE (n=24) (mean±SD)	
Differences of depression score	9,90±0,953	10,33±0,884	0,831

Analysis of 2 independent samples t tests conducted showed a significance value (p) of 0.831. These results indicate that the independent variable does not significantly influence the dependent variable because p is considered significant if it is less than 0.05.

Although the results of the data analysis were not significant, there were differences in the mean depression score, namely the TLE depression score of 9.90 while the Extra TLE depression score was 10.33, which means that depression scores were higher in Extra TLE patients than in TLE patients. Comparison of the number of mild to severe depression there is more in Extra TLE patients but the number of moderate to severe depression is more in TLE patients.

DISCUSSION

TLE patients did not show more indications of mild to severe depression as many as 15 out of 29 people or around 51.7% whereas Extra TLE patients were 13

out of 24 people or around 54.1%, but moderate to severe depression in TLE patients was more than numbered 9 of 29 people or around 31.0% while extra TLE patients only show 5 out of 24 people or around 20.8%, this shows that the number of mild to severe depression is more prevalent in extra TLE patients while indications of moderate to severe depression are more prevalent in TLE patients.

The etiology of depression is multifactorial, it can be due to organobiological factors, genetic factors, psychosocial factors and personal factors.¹⁰ Depression that affect the limbic structure (amygdala) in the temporal lobe can cause changes in a person's personality and affect.¹¹

However, in the analysis of interictal EEG recordings, aimed at localizing the focus and possibly the side and their correlation with mood disorders, epileptic patients with depression more commonly exhibited theta waves in the left



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temporal area and increased delta waves in the left or right frontal areas as well.¹² Increased theta waves in temporal areas are common in nondepressed patients with epilepsy, and are usually ascribed to disturbances in the functioning of subcortical structures.¹³ In depressed patients, the more frequent occurrence of focal changes in the left temporal area is highly correlated with clinical exacerbation of mood disturbances. Left hemisphere temporal foci are responsible for disturbances of mood and emotions. Now, it is more commonly believed that depression is influenced not only by temporal lobe dysfunction (especially the left temporal lobe), but also by frontal lobe dysfunction.

A frequently cited reason for the alleged excess psychopathology in TLE is the claimed excessive involvement of the limbic system in temporal mesial epilepsy. It has been suggested that activation of the limbic system during seizures is related to interictal psychopathology because the involvement of repeated seizures of limbic tissue can cause kindling-like processes that can change the process limbic function interactively.¹⁴

However, only a small number of TLE patients have significant depression

and the influence of the extensive limbic system on seizures of extra TLE patients, especially those from the cingular region of the anterior frontal lobe, is now widely recognized.¹⁵ It is suspected that changes that should occur in limbic function may not directly cause pathology but can increase susceptibility to psychological problems.¹⁶

In another study mentioned that depression in patients with TLE is largely caused by endogenous factors. The findings indicate that an increase in depressive scores is caused by a reduction in abnormal ictal (and possibly interictal) epilepsy rather than removal of tissue from or deafferentation of neurons in the temporal lobe. This means that in TLE patients, depression appears to be related to pathological dysfunctional processes rather than persistent structural defects.⁸

Extra TLE can also occur with mania and depression including those that occur in frontal lobe epilepsy (FLE). Mood changes can occur in different extra TLE seizure phases, although this is not as high as TLE.¹⁷ Depression symptoms found in extra TLE patients are significantly related to bilateral decreases in glucose metabolism in the inferior frontal lobe or in other words hypometabolism in the frontal



lobes in epilepsy patients who are depressed.¹⁸

In this sample group that contained clinical and characteristic differences, the previous hypothesis that patients with TLE would show more psychiatric symptoms or mood disorders compared to extra TLE patients, could not be confirmed. Research data also do not show the expected psychiatric symptoms, especially in depressive symptoms in which the limbic structures of temporal mesial epilepsy patients should be most prominently involved. Of course, this finding must be interpreted with caution because even though the results of the analysis of the data obtained are insignificant, there are still differences in the degree of depression in TLE patients where TLE patients still have a higher prevalence of depression than extra TLE patients.

It seems that temporal lobe epilepsy cannot be considered a higher risk condition for developing different psychiatric problems. Concomitant factors, such as duration of the epilepsy, seizure frequency, and frontal lobe dysfunction may play an important role. Our findings support the hypothesis of a multifactorial explanation for the psychiatric symptoms in patients with epilepsy. Despite the

growing evidence that several factors may contribute to psychiatric disorders in epilepsy, these factors are frequently not controlled for in studies of epilepsy and psychopathology. Apart from these (brain related) epilepsy factors, the psychosocial impact of having a chronic epileptic condition (e.g., unemployment, stigmatization) should also not be underestimated and should be more integrated in future studies on psychopathology.⁵ Continued investigation of these factors is certainly recommended.

CONCLUSION AND SUGGESTIONS

Conclusion

Temporal structures may have a role in the pathogenesis of major depression in epilepsy. However, according to the Hermann and Withman model predisposition for psychiatric disorders in epilepsy may be the result of a combination of a complex variety of individual and seizure related factors.

Suggestions

Suggestions obtained from the results of the research in relation to differences in depression rates of patients with temporal lobe epilepsy and extra temporal patients who carried out case studies in post-epileptic surgery patients



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are further research needs to be done on the differences in depression rates of patients with temporal lobe epilepsy and extra temporal post epilepsy surgery, we need for more complete data on the patient's cognitive status and mental status of patients before and after surgery to provide information during data collection, need to be completed again about the data when surgery was performed, the frequency of seizures, age and address and telephone numbers of patients and their immediate family so that it is easier to do data collection and easier to communicate with patients and families, there is a need to describe the patient's neuroimaging information so that the location of the lesion obtained is clear and the patient category can be more specific, classification of the subtypes of TLE and extra TLE also needs to be done to facilitate and provide additional information about the effect of depression on the location of lesions obtained. It is hoped that research will not only be conducted at hospitals in Semarang so that the samples obtained will be more numerous and the results can be more generalized,

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REFERENCES

1. De Lemos Zingano B, Guarnieri R, Diaz AP, et al. Validation of diagnostic tests for depressive disorder in drug-resistant mesial temporal lobe epilepsy. *Epilepsy Behav.* 2015;50:61-66. doi:10.1016/j.yebeh.2015.06.004
2. Catur N, Maryanti W, Psikologi F, Gadjah U. Epilepsi dan Budaya. 2016;24(1):22-31. doi:10.22146/bpsi.16358
3. Górska N, Słupski J, Cubała WJ, Wiglusz MS, Gałuszko-Węgielnik M. Antidepressants in epilepsy. *Neurol Neurochir Pol.* 2018:1-5. doi:10.1016/j.pjnns.2018.07.005
4. Tracy JI, Lippincott C, Mahmood T, et al. Are depression and cognitive performance related in temporal lobe epilepsy? 2007;48(12):2327-2335. doi:10.1111/j.1528-1167.2007.01254.x
5. Swinkels WAM, Boas WVE, Kuyk



- J, Dyck R Van, Spinhoven P. Interictal Depression , Anxiety , Personality Traits , and Psychological Dissociation in Patients with Temporal Lobe Epilepsy (TLE) and Extra-TLE. 2006;47(12):2092-2103. doi:10.1111/j.1528-1167.2006.00808.x
6. CL H. The comorbidity of depression and epilepsy: epidemiology, etiology, and treatment. *Neurology*. 2002;59:48–55.
7. Reuber M, Andersen B, Elger CE, Helmstaedter C. Depression and anxiety before and after temporal lobe epilepsy surgery. *Seizure*. 2004;13(2):129-135. doi:10.1016/S1059
8. Reuber M, Andersen B, Elger CE, Helmstaedter C. Depression and anxiety before and after temporal lobe epilepsy surgery. *Seizure*. 2004. doi:10.1016/S1059-1311(03)00073-6
9. Marpaung V. Depresi Pada Penderita Epilepsi Umum dengan Kejang Tonik Klonik dan Epilepsi Parsial Sederhana. *FK USU*. 2001:93.
10. Elvira S, Hadisukanto G. *Buku Ajar Psikiatri*. 2nd ed. (Elvira S, ed.). Jakarta: Badan Penerbit Fakultas Kedokteran Universitas Indonesia; 2014.
11. Kanner AM. Depression and epilepsy: A bidirectional relation? Can a Bidirectional Relation between Epilepsy and Psychiatric Disturbances Be Demonstrated. 2011;52:21-27. doi:10.1111/j.1528-1167.2010.02907.x
12. Grabowska-grzyb A, Joanna J, Nagan E, Fiszer U. Risk factors for depression in patients with epilepsy. 2006;8:411-417. doi:10.1016/j.yebeh.2005.12.005
13. Tavares TP, Puka K, Smith M Lou. Emotional functioning: Long-term outcomes after pediatric epilepsy surgery. 2015;56(5):745-753. doi:10.1111/epi.12956
14. Robertson M. Epilepsy and mood. *Epilepsy, Behavior Cogn Funct*. 1988:145-151.
15. HA Ring RW. Depression in epilepsy: biological links. *Biol Psychiatry*. 1991;2:215-218.
16. RE Adamec. Does kindling model anything clinically relevant? *Biol Psychiatry*. 1990;21:249-279.



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Yuriz Bakhtiar, Dimas Sindhu Wibisono

17. Roper, SN. Surgical treatment of the extratemporal epilepsies. *Epilepsia*. 2009;50:69-74.
18. EB B, Altschuler L, Leiderman D, Devin sky O, Theodore W. Cerebral metabolism and de- pression in patients with complex partial seizures. *Achieves Neurol*. 1992;49:617-623.