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# DIAGNOSTIC TEST USING NEUROLOGICAL DEPRESSION DISORDERS INVENTORY FOR EPILEPSY COMPARED TO HAMILTON DEPRESSION RATING SCALE -17 AS A GOLD STANDARD

**Running Head: Diagnostic Test For Epilepsy**

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***ABSTRACT---Background****Depressionisacomorbiditywhich is most frequently ound in epileptic patients. Epileptic patients have a 5-10 timeshigher risk to sufferfrom depression compared to general population.Unfortunately, screening for depression hasn't been performed routinely in outpatient neurology clinic. Hamilton Depression Rating Scale (HDRS) is a well-known test and often used as a screening instrument, but it spares a lot of time.*

***Objectives***

*To determine the diagnostic value of Using Neurological Depression Disorders Inventory(NDDI)-E compared totheHDRS-17 as a gold standard whichwas used as a screening instrument to detect ~~the~~depressioninepilepticpatients.*

***Methods***

*This study used cross-sectional design on epilepticpatients of the 71 patientsneurology clinic and EEG unit SoetomoTeaching Hospital, Surabaya during MarchtoJune 2016. the sample in this study that consisting of 37 men and 34 women.The diagnosis of depression was performed using NDDI-E to comparedwithHDRS-17. Statistical analysis was performed by SPSS16 and cat maker.*

***Results***

*Moreover, from the statistical tests obtained; the mean age was 34.3+12,301year.Compared with HDRS-17, the Sensitivityvalue of NDDI-E was86%,and the specificityvalue was 72%, positive prediction value was 67%, negative prediction value was 89%, positive probability ratio was 3,07 %, and negative probability ratio was 0,2%.*

***Conclusion***

*NDDI-E could be used as a screening instrument to detect depression in epileptic patients.*

***Keywords---****Diagnostic Test, Neurological Disorders Depression Inventory for Epilepsy, Hamilton Depression Rating Scale-17*

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## I. INTRODUCTION

Depression is the most common comorbid mental disorder in epileptic patients.Therefore, it is important to do screening tests for depression in the patients with epilepsy. [1] Unfortunately, depression screeningis not routinely performed in outpatient neurological unit based on neurologists studies because it took longer time. [2,3] Later on, this causes the epilepsy patients with comorbid depression often undiagnosed and were not getting an appropriate treatment. [1]

Epilepsypatientshave a 5-10 times higher risk of depression than in general population. [4]The prevalence of depression in uncontrolled and controlled epilepsy patients were estimated to reach 20-55% and 3-9% respectively. [5]Anoother result in CiptoMangunkusumo National Central Teaching Hospital Jakarta found about 42% of epilepsy patients was experiencing the depression disorder. [6]The negative effects of depression in epilepsy patients were decreasing the quality of life, increasing risk of suicide, increasing of health costs, decreasingthe chance of Anti-epileptic drugs (AEDs) in controlling seizures, increasing the side effects of consuming AEDs, and worsening the outcome of epilepsy surgery.[7] One of the instruments to assess the depression of Hamilton depression rating scale was HDRs.[7]HDRS is a gold standardfor depression examination for more than 40 years.[8]

One of the instruments often used for epilepsy patients was the Neurological disorders depression inventory for epilepsywhich was first introduced by Gilliam in 2006 at New York.NDDI-E was developed from 46 instruments of depressive symptoms separated from cognitive impairment andAEDs influences. [9]NDDI-E has several advantages due to it was simple, fast and clear that consisting of 6 questions that were filled by the patients and takes only about 3 minutes. [4] Another result performed the diagnosis of NDDI-E with the gold standard of International Neuropsychiatric Interview (INI) thatshowed87.9%, 88.0% for sensitivity andspecificityconsecutively. [1] This NDDI-E has been validated in many countries and its questionnareshas been translated into 10 languages. [1] Previous Research in Indonesia has also tested the validity and reliability in assessing NDDI-E and obtained valid also reliable results in assessing thedepression in epilepsy patients. [10] Meanwhile the diagnosis test conducted by the gold standard MINI showed 87.9%, 88.0% for sensitivity andspecificityconsecutively. [11]

In Indonesia, HDRS instruments were relatively well known and more commonly used in clinical practice and depression-related research. Currently, NDDI-E diagnostic test compared with HDRS has not been performed yet in Indonesia. Therefore, the authors performed a diagnostic test to calculate the sensitivity and specificity values of NDDI-E with the gold standard of HDRS-17 in the epilepsy patients.

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## II. METHODS

71 epilepsy patientswere enrolled that consisting of 37 people (52.1%) of men and 34 people (47.9%) of women who visited to neurology and EEG outpatient unit for 4 months (March to June 2016). The average age of the subjects was 34.30 + 12.301.The inclusion criterias of this research wereage more than 18 years old, the graduated from minimum education was elementary school, follow the research consent (informed consent). While the exclusion criterias were patients with cognitive impairment MMSE <23, sex, marital status, occupational status,consumption of antiepileptic drugs, antidepressant drug consumption included as demographic and clinical data.

Subjects who have signed an approval letter will record their identity and characteristics in the form. Data collection conducted by researchers was accompanied by two-doctors and student of doctor specialist program's. The subjects was performed NDDI-E and HDRS-17 assessment separately, and its forbid to know each result of examination yet.

The following steps were performing throughanamnesis and MMSE examination.Theselection subjects was recording of all eligible subjects and all the necessary clinical data, also examination of NDDI-E and HDRS-17 was performed in the neurological and EEG unit of SoetomoTeaching Hospital sequentially. The HDRS-17 examiner was a neurologicstudentofdoctor specialist program's. Meanwhile, the NDDI-E examiner was a neurologic student of doctor specialist program'swho has currently in a stasis of the neurological and EEG unit. The collected data were analyzed with withtable 2x2, SPSS-16, and cat maker.

## III. RESULTS

this study enrolled 71 subjects that consisting of 37 (52.1%) male and 34 (47.9%) women. While for the average age of the study subjects was 34.30 + 12.301 years. The youngest subjects were 19 years old, while the oldest was 65 years old. Educational characteristics of the sample showed that 6 people with elementary education (8.5%), Junior Higheducationwas 13 people (18.3%), Senior Higheducationwas 43 people (60.6%), 3 people have been getting a diploma (4.2%), and bachelor degree was 6 people (8,5%). Marital status of samples showed that 40 samples were married (56.3%), and 31 samples were single (43.7%). While the occupational status of sampleswas39 people work (54,%), and 32 people not working (45.1%).

Additionally, some of the recorded clinical data included the amount of anti-epileptic drugs consumed, the length of epilepsy, the frequency of seizures within 1 month, and the history of taking anti-depressant medication. The distribution of research subjects based on total AEDs consumption was monotherapy of 46 patients (64.8%), dualtherapy of 22 patients(31.0%), and politherapy of 3 patients(4.2%).Characteristics of samples based on

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antidepressant drug consumption consisted of 64 subjects that not take anti-depressant drugs (90.1%) and 7 subjects taking antidepressant drugs (9.9%). The average length of samples suffering from the epilepsy was 9.86 + 11.333 years. While the average frequency of seizures in 1 month in the study subjects was 1.63 + 3.062 years.The NDDIE score for the Indonesian version has a cutoff value>11, it was said to be normal if the resulting score was between 0 - 11 and if the score>11 then patientwas depressed.[14]NDDIE score results in Table 2 obtained that the patients suffering from depression was 36 people (50.7%), while the normal patients was35 people (49.3%). Table 3 shows the cross-tabulation between the NDDIE and DRS 17 scores that resulted in the same diagnosis of 36 patients diagnosed with NDDIE depression; 24 patients (66.6%) were diagnosed as positive for depression with HDRS-17. Whereas 35 patients were diagnosed normally with NDDIE score; 31 patients (88.6%) were diagnosed not depressed with HDRS-17.

Tabel 1: The analysis diagnostic test using neurological depression disorders inventory for epilepsy compared to hamilton depression rating scale -17

| | | |
|---|---|---|
| Sensitivity | = 24/28 | = 86% (95% IK: 73% – 99%) |
| Specificity | = 31/43 | = 72% (95% IK: 59% – 85%) |
| Positive predictive value | = 24/36 | = 67% (95% IK: 51% – 82%) |
| Negative predictive value | = 31/35 | = 89% (95% IK: 78% – 99%) |
| Prevalence | = 28/71 | = 39% (95% IK: 28% – 51%) |
| Positive possibility ratio | = 86/(1-72) | = 3,07 (95% IK: 1,86 – 5,08) |
| Negative possibility ratio | = (1-86)/72 | = 0,20 (95% IK: 0.08– 0,50) |
| Accuracy | = (24+43)/71 | = 94,3% |

## IV. DISCUSSION

The samples of this study consisted of 37 men (52.1%) people and 34 women (47.9%). The number of samples was in accordance with a study conducted that males had a tendency not to express their depressive symptoms compared to women. [12]The NDDIE diagnostic test results of HDRS-17 on the cross tabulation (Table 3) by SPSS and cat maker software showed NDDIE the sensitivity compared to the HDRS-17 (as gold standard) of 86% and

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specificity of 72%.Sensitivity value of 86% indicates the ability of NDDIE as a screening instrument to detect the presence of depression by 86%.Sensitivity was the proportion of diseased samples with positive diagnostic test results across all sick samples (false positives and false positives), or the possibility that the diagnostic test results were positive when performed on a diseased group.[13]The specificity of 72% means the ability of NDDIE to diagnose the absence of depression by 72%. Specificity was the proportion of healthy subjects who give negative (true-negative) diagnostic test results compared to all non-sick subjects (true negative and false positives) or the possibility that the diagnostic test results will be negative when performed on a group of healthy samples.

Distribution of samples based on education level were; the samples that were graduated from elementary school by 8%, junior high school (27%), 61% of patients have completed high school, 4% have received diploma degree, and 8% have received bachelor degree. While the results obtained from the research that shows the samples of complete junior high school by 6%, high school by 75%, 6%have receiveddiploma, and bachelor degree of 16%.[14]

Additional, marital status in this study received 56.3% of married patients and 43.7% of unmarried patients. This result was consistent with another research in Brazil 59.8% of married samples and 40.2% of unmarried samples. [15] Occupational status in this study found 54.9% of working patients and 45.1% of unemployed patients.This result was in accordance with the studies that conductedanother research in France ie 50.8% of working samplesand 49.2% samples were unemployed.[1]

The previous research show that those with low education, unmarried, and unemployedhave a relationship with the increased incidence of depression in patients with epilepsy. [5]In this study, the number of epilepsy patients who took anti-epilepsy monotherapy drugs of 64.8%, dual therapy as much as 31.0% and Politerapi as much as 4.2%. Based on this study, the average seizure frequency in 1 month was 1.63 + 3.062. This result was in accordance with the study who got an average seizure frequency was 1.8+2.8 times a month.[19]The consumption of unit therapy (3 or more anti-epilepsy drugs) and high seizure frequency were at risk factors for increased incidence of depression in epilepsy patients. [2]

The average duration of epilepsy in this study was 9.86 ± 11.333 years. This result was shorter than the study in Germany that obtained an average length of epilepsy of 20.4±13.8 years.[20]The study conducted that mentions that the longer a person suffers from epilepsy, the greater the possibility of depression symptoms occur. [16]

Whereas, we obtained the prevalence of epilepsy patients who experienced depression by 39.4% and no depression incidence of 60.6% using HDRS-17. These results were consistent with those obtained of 28.4%.[1]While

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epidemiological studies have a result of 21.9%.[14] The prevalence of depression in this study was consistent with the epidemiology mentioned with an average of 30-35%. [17]

We found that the samples who took antidepressant drugs as much as 9.9%, while the remaining 90.1% were not taking the antidepressant drugs. Out of the 39% of subjects with a diagnosis of depression, only 9.9% took antidepressant drugs.In conclusion, most patients with depression complaints have not been diagnosed and handled properly.

The sensitivity values in this study were consistent with those who obtained with 85% sensitivity and 85% specificity.[15]These results were also not significantly different from those obtained with sensitivity 91% and specificity 89%.[18]

Positive predictive value was the probability of a person that suffering from a disease if the diagnosis test results were positive [13], This study obtained a NDP of 67%.While negative predictive value was the probability of a person not suffering from a disease if the diagnosis test results ware negative[13],This study obtained NDN of 89%. The estimated value was strongly influenced by the prevalence of the disease. This predictive value was important in assesing diagnostic tests.[19]

Another statistic of the diagnostic test was the possibility ratio which was thecomparison of proportion of sick subjects who gave positive test results with the proportion of healthy subjects who gave positive test results.Negative possibility ratio wasthe comparison between the proportion of sick subjects who gave negative test results with healthy subjects who gave negative test results.[13]In this study, the posibility ratio of 3.07 means that the comparison between the proportions of depressed patients in epilepsy who gave a positive NDDIE score with non-depressive patients in epilepsy who gave a positive NDDIE score was 3.07. The negative posibility ratio of 0.20 means that the comparison between the proportions of depressed patients in epilepsy who gave a negative NDDIE score with a non-depressive sample in epilepsy who gave a negative NDDIE score of 0.20.The positive diagnostic test results give a LR value much greater than 1,the strong negative test result will give the LR value close to 0, and the results of the medium test give the LR value around the value of 1. The LR value which was considered important was 10 or more.[13,20]

The results of this study were statistically significant. [21]NDDIE instruments have the advantage of HDRS-17 because it performed done faster and the questionnaireinstrumentsdid not include about the side effects of anti-epilepsy drugs such as concentration disorders, fatigue and sleep disturbances contained in HDRS-17. Instruments

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involving anti-epilepsy drug side-effects have the potential to increase the sensitivity of the instrument because more symptoms of depressive disorder were filtered so that the score was larger and diagnosed as a depressive disorder.[9]

The sensitivity of 86% indicates that the NDDIE examination could be used to screening for the depressive symptoms in epilepsy patients. This NDDIE will assist neurologists in detecting depressive symptoms in epilepsy patients. Thedepression in many epilepsy patients were not treated, because neurologists did not do the depression screening in their patients.[9]

However, NDDIE was not purposed to make a definitive diagnosis of depression. According to the DSM V the diagnosis of depression was way more complex and requires an observation of more symptoms than NDDIE. Additionally, episodic depression requires symptom monitoring for 2 months,Whereas there was no time span of observation on NDDIE[22]. The limitation of this study was that there was no time measurement for each examination, either NDDI-E or HDRS-17, so it could not be calculatedthe average time for each examination to find out which instruments were faster.

## V. CONCLUSSION

In conclusion, this study found a sensitivity 86%, a specificity 72%, a positive predictive value 67%, a negative predictive value 89%, a positive ratio 3.07, and a negative ratio 0,20.They indicated that NDDIE instrument could be used for screening of depression disorder in epilepsy patients, especially in neurologic outpatient unit and EEG unit in Dr. Soetomo general hospital.

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Table1: DemographicandClinic Data

| | N=71(5) SD |
|---|---|
| **Demographic Data** | |
| **Sex** | |
| **Male** | 37(52.1) |
| **Female** | 34(47.9) |
| **Mean Age** | 34.30(12.301) |
| **Educational Status** | |
| **Elementary School** | 6(8.5) |
| **Junior High School** | 13(18.3) |
| **Senior High School** | 43(60.6) |
| **Diploma** | 3(4.2) |
| **Bachelor** | 6(8.5) |
| **Marital Status** | |
| **Married** | 40(56.3) |
| **Single** | 31(43.7) |
| **Occupational Status** | |
| **Working** | 39(54.9) |
| **Not Working** | 32(45.1) |
| **Clinic Data** | |
| **Anti-Epilepsy Drugs** | |
| **Monotherapy** | 46(64.8) |
| **Dualtherapy** | 22(31.0) |
| **Politherapy** | 3(4.2) |
| **Anti-Depression Consumption** | |
| **Yes** | 7(9.9) |
| **No** | 64(90.1) |
| **The Average Duration of Epilepsy** | 9,86(11.333) |
| **Frequency of Seizures in 1 Month** | 1,63(3.064) |

Table2: Characteristics of Patients Based on NDDIE Indonesia on HDRS17

| | Frequency (person) | Percentage (%) |
|---|---|---|
| **Normal** | 35 | 49,3 |
| **Depression** | 36 | 50,7 |
| **Total** | 71 | 100 |

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Table3: Cross Tabulation (Table 2x2) of Score Result between NDDIE and HDRS 17

| Category | | HDRS 17 | | Total |
|---|---|---|---|---|
| | | Depression | Normal | |
| NDDIE | Depression | 24 | 12 | 36 |
| | | 66,6% | 33,4% | 100% |
| | Normal | 4 | 31 | 35 |
| | | 11,4% | 88,6% | 100% |
| | Total | 28 | 43 | 71 |
| | | 39,4% | 60,6% | 100% |

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