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ASSOCIATION BETWEEN SEVERITY AND DEPRESSION IN PARKINSON'S PATIENTS

Popy Paramitha*¹, Aida Fithrie² & Hafin Soraya Hutagalung²

¹Resident Department of Neurology, Faculty of Medicine, University of North Sumatera

²Department of Neurology Staff, Faculty of Medicine, University of North Sumatera

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Abstract

Background: Parkinson disease (PD) has motor manifestations namely resting tremor, rigidity, bradykinesia and postural instability. In addition, non-motor symptoms such as psychiatric symptoms such as depression, anxiety, hallucinations, psychosis, delusions and sleep. Accompanying depression is the most common nonmotor symptom in Parkinson's. Depression in Parkinson's occurs in about 40% of patients and on average there is major depression and minor depression.

Objective: To determine the relationship of severity with depression in Parkinson's patients.

Method: This study used a cross sectional design. Sampling was conducted at H. Adam Malik General Hospital Medan and network hospital. The study sample was taken as many as 25 subjects consecutively, with primary data sources obtained from all patients who had been diagnosed with Parkinson's disease based on the UKPD Society Bank's Clinical Criteria for Probable Parkinson's Disease criteria. Data analysis using the Spearman correlation test.

Results: The demographic characteristics of the study subjects were 19 (76%) men and 6 people (24%) women, with the oldest age being 77 years and the youngest 49 years, mean age was 61.52 ± 6.97 years. The majority of the patients are senior high school, self-employed, and the Batak ethnic group. There is a significant relationship between the MDS-UPDRS subscale and the level of depression in Parkinson's patients with a p value <0.05 .

Conclusion: There is a significant relationship between severity and depression in Parkinson's patients.

Introduction

Parkinson disease (PD) is a chronic progressive neurodegenerative disease involving motor signs and symptoms such as rigidity, bradykinesia, rest tremor and postural instability. Parkinson's disease is a neurodegenerative disease caused mainly by the loss of dopaminergic cells in the substantia nigra (SN).¹

Parkinson disease (PD) has motor manifestations, namely resting tremor, rigidity, bradykinesia and postural instability. In addition, non-motor symptoms were also found, such as psychiatric symptoms such as depression, anxiety, hallucinations, psychosis, delusions and sleep disturbances which could be caused by anti-Parkinson medication itself or as part of the natural course of the disease. There are also symptoms of decreased cognitive function, sensory disturbances, and restless leg syndrome, olfactory disturbances, decreased ability to focus on vision and autonomic disorders.² It is estimated that around 16 - 70% of sufferers experience neuropsychiatric problems, such as depression, apathy, anxiety disorders and psychosis.²

In a comprehensive literature review of 45 depression studies in PD conducted from 1922 to 1998, the overall prevalence of depression in PD was estimated to be 31% for all PD. The prevalence range of PD depression varies with methodology and may be around 40%, with an annual incidence rate of 1.9% and a cumulative incidence of 8.4%.³

Studies using a stronger methodology found a lower but still clinically significant number of depression prevalence of PD.⁴ In a study conducted by Herath et al, in 2016, obtained from 75 patients (male 54 years old (75%), mean age 63.6 years, SD \pm 8.8). The mean HAM-D score in the sample was 7.6 (SD \pm 4.3, range 0-23). According to the scale, 36 patients (48%) showed symptoms of depression (mild; 30, moderate; 5, very severe; 1).⁵

Various studies on the factors that affect the quality of life of Parkinson's sufferers have been widely conducted, whereas in Indonesia there are still very few studies on the level of depression in Parkinson's patients, especially



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research that looks at a factor that is not a single predictor but also its impact if some of these factors are found on quality of life Parkinson's patient's. ²

Method

Study sample

The study sample was taken from patients with Parkinson disease in Adam Malik General Hospital Medan and network hospital with consecutive sampling techniques. The research subjects consisted of 25 Parkinson patients who had been diagnosed with Parkinson's disease based on the UKPD Society Bank's Clinical Criteria for Probable Parkinson's Disease criteria.

Study design

This study is a cohort design without treatment. Parkinson's disease severity was assessed by history and physical examination using the MDS-UPDRS scale, with a measuring score of 0-199 (the higher the score, the worse) and a numerical measuring scale. Depression was assessed by history and physical examination using the Hamilton Rating Scale of Depression (HAM-D). With the measurement results there is no depression, if the score is 0 - 6; mild depression, if the score is 7-17; moderate depression 18-24; major depression > 24, and ordinal measuring scale.

Statistical analysis

Data from the research were analyzed statistically using the SPSS Windows computer program (Statistical Product and Science Service) version 22.0. Univariate analysis in this study was conducted to analyze the characteristics of one variable by conducting a descriptive test. Bivariate analysis in this study was conducted to analyze the relationship between research variables, in this case to determine the relationship between severity and depression level of Parkinson's disease between the Spearman correlation test to determine the significance and r correlation.

Result

Patients Parkinson at H. Adam Malik Hospital Medan and network Hospital in December 2019 until Juni 2020, there were 25 patients with the inclusion and exclusion criteria.

Based on the characteristics of the 25 research subjects, the age of all research subjects had a mean of 61.52±6.97 years with the largest age ranges at the ages of ≥49 - 59 years and ≥60 - 70, were 11 subjects (44%). The research subjects were male, as many as 19 subjects (76%). The education level of the most research subjects was Senior High School, as many as 11 subjects (44%). Respondents occupation were mostly entrepreneur with 10 subjects (40%). Most of the ethnic groups of the research subjects were the Batak ethnic groups as many as 10 subjects (40%). For complete data about the characteristics of the subject of this study are presented in table 1 below.

Table 1. Demographic Characteristics of Research Subjects (n = 25)

Characteristics	Frequency n=25	Percentage (%)
Age, average ± SD (years)	61,52±6,97	
Age group		
- ≥49 – 59 years old	11	44
- ≥60 – 70 years old	11	44
- ≥71 – 81 years old	3	12
Sex		
- Female	19	76
- Male	6	24
Education		
- Primary School	1	4
- Junior High School	5	20
- Senior High School	11	44
- Diploma	3	12
- Bachelor Degree	5	20
Occupations		



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- Entrepreneur	10	40
- Private Employees	6	24
- Retired	3	12
- Government Employees	1	4
- Housewife	2	8
- Farmer	2	8
- Jobless	1	4
Ethnic Group		
- Batak	10	40
- Malay	4	15
- Java	7	28
- Karo	3	12
- Minang	1	4

Based on the result statistical analysis of the spearman correlation test of 25 research samples, it was found that there was a significant relationship between severity and depression level ($p < 0.001$). Adaptive correlation r value obtained is 0.664, indicating a positive correlation with strong correlation strength. This can be seen in table 2 below.

Table 2. Assosiation Severity Level with Depression Level In Parkinson's Disease

	<i>Hamilton Rating Scale (HAM-D)</i>				<i>r</i>	<i>p</i>
	<i>Berat</i>	<i>Sedang</i>	<i>Ringan</i>	<i>Tidak ada depresi</i>		
MDS- UPDRS	5 (20)	9 (36)	7 (28)	4 (16)	0,664	<0,001

In this study, the severity level was assessed using the Movement Disorder Society - sponsored revision of the Unified Parkinson's Disease Rating Scale (MDS-UPDRS), while the depression level was assessed using the Hamilton Rating Scale (HAM-D) score. Based on the spearman correlation test of 25 samples, it was found that there was a positive and significant correlation between the MDS-UPDRS subscales I, III and V with the level of depression in Parkinson's disease ($p < 0.05$). With the strength of the positive correlation which is equally strong. The correlation value obtained (I: $r = 0.602$, III: $r = 0.608$, V: $r = 0.712$).

The MDS-UPDRS II and IV subscales had a significant association with depression rates in Parkinson's disease ($p < 0.05$). With the strength of positive correlation which are both classified as moderate. The correlation value obtained (II: $r = 0.486$, IV: $r = 0.579$).

Based on the statistical analysis of the spearman correlation test on 25 research samples, it was found that there was a significant relationship between the MDS-UPDRS VI score and the Hamilton Rating Scale ($p < 0.05$). The correlation r value obtained is -0.590, indicating a negative correlation with moderate correlation strength. This can be seen in table 3 below.

Table 3. Assosiation between Movement Disorder Society - sponsored revision of the Unified Parkinson's Disease Rating Scale (MDS-UPDRS) Subscale and Depression Levels in Parkinson's Disease

	<i>Hamilton Rating Scale (HAM-D)</i>	
	<i>r</i>	<i>p</i>
UPDRS I	0,602	<0,05
UPDRS II	0,486	<0,05
UPDRS III	0,608	<0,05
UPDRS IV	0,579	<0,05
UPDRS V	0,712	<0,05
UPDRS VI	-0,590	<0,05

Discussion

The mean age characteristics of Parkinson's patients in this study were 61.52 ± 6.97 years, with the largest age ranges at $\geq 49 - 59$ years and $\geq 60 - 70$, which were 11 subjects ($44\%^2$) is relevant to previous research conducted by Ginting et al, in 2018 found that most subjects were in the 50-78 year age group, with an average age of 61.25



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± 7.48 years.⁶ Parkinson's disease is most commonly found in the elderly and is rarely found under the age of 30, the peak occurs in the sixth decade of life.² Parkinson's disease is mainly found in individuals aged > 65 years, the incidence is around 1%, with the main risk factors including old age, male sex, and exposure to pesticides while smoking and caffeine consumption are associated with a lower risk of Parkinson's disease.⁷

The aging process induces pre-Parkinsonism stage and cellular mechanisms of dopaminergic neuron death to be accelerated or aggregated in Parkinson's disease along with genetic and environmental factors. The pathophysiology of Parkinson's disease is also related to the process of oxidative stress due to mitochondrial dysfunction which causes the production of ROS and mediates lysosome autophagy. With increasing age, the accumulation of mitochondrial damage and degradation by the lysosome system is associated with dopamine neuron cell damage.⁸

In this study, sex characteristics of Parkinson diseases were found as many as 19 male subjects (76%) were more than female as many as 6 subjects (24%). Wooten et al, in 2004, there were found that the incidence of Parkinson's disease was 1.5 times higher in males than in females.⁹ The cause of the higher risk in men than women is not clear, but it is probably due to the hormonal factor estrogen which plays a neuroprotective role in women.¹⁰ The possibility of chemical exposure and X chromosome recessive gene susceptibility in males may be associated with a higher risk of Parkinson's disease.¹¹

In this study, it was found that the most education was Senior High School (SMA) compared to Diploma and bachelor degree. Most jobs are self-employed and private employees. This research is relevant to previous research conducted by Ginting et al, in 2018 where 10 people from a total of 24 Parkinson's patients studied were self-employed (41.7%) and most patients were high school students (45.8%).⁶ Incidence of Parkinson's disease was lower in the low socioeconomic group. This is associated with smoking and physical activity. Where smoking is most often found in low socioeconomic communities and is inversely associated with the risk of Parkinson's disease. Physical activity is associated with a reduced risk of Parkinson's disease.¹²

The nicotine content in cigarettes is inversely related to the incidence of Parkinson's disease. Anatomically the cholinergic nicotine system and the dopaminergic neurotransmitter are interconnected in the striatum. Nicotine and its receptors play a role in regulating striatum activity and mediating behavior through the dopaminergic system by activating nicotinic acetylcholine receptors on the dopaminergic terminal and modulating dopamine release. In addition, in experimental studies found that nicotine and its agonists are useful to protect 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP) which induces striatum and nicotine damage is also associated with improved motor function in animal models with Parkinson's disease. Nicotine and its agonists can reduce levodopa induced dyskinesia.¹³

In the results of this study, there was a significant relationship between the severity and the level of depression in Parkinson's patients ($p < 0.001$), with a positive correlation and strong correlation strength.

This is relevant to research conducted by Duefies et al, in 2015 reporting that there was a significant relationship between Parkinson's severity based on the MDS-UPDRS score and depression level ($p < 0.0001$).¹⁴

In a study conducted in India, 126 Parkinson's patients found a significant association between severity and depression rates in Parkinson's patients ($p < 0.05$). Depression is more common in patients with disabilities and higher psychosis with a longer duration of illness and older age.¹⁵

Depression is one of the most common and persistent nonmotor syndromes that occur in 35% of patients diagnosed with PD. Cognitive decline is a factor associated with worsening illness and depression. Symptoms of Activities of Daily Living (ADL) in Parkinson's and female gender may be an important factor in the increase in depressive symptoms.¹⁶

There is also a role for changes in serotonin function as a cause of depression in PD. Decreased density of the midbrain serotonin transporter. Decreased cerebrospinal fluid (CSF) in the metabolism of 5-hydroxyindole acetic acid (5-HIAA) serotonin has also been associated with both idiopathic major depression and depression in PD. The decrease in serotonin in CSF may be related to a dysfunction of the serotonin transporter that removes serotonin from the synaptic cleft. Genetic abnormalities in the short-arm allele coding for the serotonin transporters are found in major depression. The same functional polymorphisms in the premotor region of the



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serotonin transporter gene associated with anxiety in non-PD patients were also associated with higher rates of anxiety patients and Parkinson's patients with depression.¹⁷

Increased severity of disability, mainly due to akinesia, was associated with developing minor depression but not major depression. Some of the symptoms that have a strong correlation with depression include bradyphrenia, blocked thinking, and apathy. Severe depression occurs in 40 to 60% of patients with advanced PD who do not receive antiparkinsonian treatment, regardless of length of illness or degree of physical disability. Physical improvement after successful PD treatment does not consistently reduce depression.¹⁸

Dissnayaka et al, in 2011, stated that a decrease in ADL was more strongly correlated with depression than the motor disability observed in motor severity measures.¹⁹ Parkinson's sufferers with depression report poor disability status as a reflection of poor perceptions of disability. The association between decreased ADL and depression may also reflect decreased quality of life in Parkinson's patients.

From the results of this study, a significant relationship was found between the Movement Disorder Society - sponsored revision of the Unified Parkinson's Disease Rating Scale (MDS-UPDRS) subscale and the level of depression assessed by the Hamilton Rating Scale (HAM-D) in Parkinson's patients ($p < 0.001$), with moderate and strong correlation strength.

This is relevant to the study of Gallagher et al, in 2011, in which 96 Parkinson's patients found that the MDS-UPDRS I score had a significant relationship with the level of depression ($p < 0.0001$), with a value of $r=0.72$.²⁰

The results of a cross-sectional study in China showed a significant relationship between MDS-UPDRS II and MDS-UPDRS V with depression levels in Parkinson's patients ($p < 0.001$). Depression is associated with a complex combination of dopaminergic and non-dopaminergic disorders. Where dopaminergic dysfunction plays the most role and this is proven by previous biomarker and neuroimaging studies.⁴

In the study of Duefies et al, in 2015 there was a significant relationship between the severity of motor extremity subscale of the MDS-UPDRS III and the level of depression in Parkinson's patients ($p < 0.0001$).¹⁴

Studies in Brazil found that the MDS-UPDRS VI subscale score of Schwab and England Activities of Daily Living scale had a significant relationship with depression levels in Parkinson's patients ($p < 0.001$), with moderate negative correlation strength.²¹

This is relevant to a study in Kyoto, where out of 125 Parkinson's patients, there was a significant relationship between the IV and V MDS-UPDRS subscales with depression rates ($p < 0.001$). Parkinson's sufferers with repeated motor fluctuations are more likely to experience mood fluctuations. Depression and anxiety symptoms usually occur in an "off" state and immediately turn "on". Parkinson's sufferers who have more severe motor symptoms, more advanced Hoehn and Yahr stages, and more severe overall clinical conditions have a higher rate of depression. This may support the hypothesis of dysfunction of the nigrostriatal pathway that plays an important role in the pathophysiology of depression in Parkinson's patients, although later stages such as gait and balance disorders are usually associated with global involvement of brain disorders.²²

Conclusion

There is a significant relationship between severity and depression level in Parkinson disease patients.

Suggestion

Further research can further analyze the use of dopaminergic drugs (levodopa) in Parkinson's patients.

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