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Factors Influencing the Frequency and Severity of Depressive Disorder in Parkinson's Disease Patients

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Abstract

Background: *Parkinson's disease is the second most common neurodegenerative disease after Alzheimer's disease. Apart from motor features, Parkinson's disease has various non-motor symptoms such as neuropsychiatric symptoms, gastrointestinal symptoms, urogenital disturbances, and sleep disorders. Among the neuropsychiatric manifestations depression is the most common but most of the time it remains underdiagnosed and undertreated leading to worsening of symptoms of the disease and deterioration of the quality of life.* ***Objective:*** *This study aimed to determine the factors influencing the frequency and severity of depressive disorder in Parkinson's disease patients.* ***Methods:*** *This cross-sectional observational comparative study was conducted at the Department of Neurology at BSMMU, Dhaka, for 16 months following ethical approval. A total of 144 Parkinson's disease patients were enrolled in this study. Following informed written consent from patients, detailed history and thorough clinical examination were carried out along with relevant investigations. Then the frequency and severity of depressive disorders were assessed by the Bangla version Montgomery–Åsberg Depression Rating Scale (MADRS) scale. Data were collected in the semi-structured questionnaire and analyzed by SPSS software.* ***Results:*** *A total of 144 patients diagnosed with Parkinson's disease were enrolled in the study. Among the 144 patients current age range of the majority patients was 51-60 (40.3%) and the minimum age range was >70 (5.6%). The Mean (±SD) age was 56.00 ± 9.94. Among the study patients, 64% were male and 36% were female. 19.4% of patients were normal, 36.1% had mild, 29.9% had moderate and 14.6% had severe levels of depressive disorder. So overall clinically significant depressive disorder (moderate and severe) frequency of this study was 44.5%. Certain variables such as the age of onset, duration of the disease, staging of the disease, on/off fluctuations, end-off-dose wearing off, drug history of Ropinirole, and Entacapone were closely associated with depressive disorder. Among them, Early age of onset (< 50 yrs) (OR 0.380, p-value 0.029), the duration of the disease (Odds ratio 3.429, p-value 0.049), on-off fluctuation (Odds ratio 0.523, p-value 0.047), and staging of the disease (Odds ratio 4.764, p-value 0.000) are independent predictors for depressive disorder.* ***Conclusion:*** *The patients who had Early disease onset (<50 years), long duration of disease, advanced staging, and on-off fluctuations were more prone to depressive disorder.*

Keywords: *Parkinson's disease, Depressive disorder, MADRS.*

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Introduction:

Parkinson's disease is one of the most common movement disorders[1]. It is an age-related disease and shows a gradual increase in prevalence beginning after the age of 50 years and a sharp rise in prevalence after the age of 60[2]. The prevalence of Parkinson's disease in developed countries is 0·3% of the entire population[3]. The prevalence of Parkinson's disease has doubled between 996-2016 and the burden of Parkinson's disease in developing nations is expected to double again over the next generation as a result of increasing life expectancy[4]. The main pathology of Parkinson's disease is due to the degeneration of dopaminergic neurons in the substantia nigra leading to decreased dopamine release in the dopaminergic pathway[5]. In addition to motor features, Parkinson's disease is also manifested by various non-motor symptoms such as neuropsychiatric symptoms, gastrointestinal symptoms, urogenital disturbances, and sleep disorders[6]. Among the neuropsychiatric manifestations depression is the most common disorder but most of the time it remains underdiagnosed and under-treated leading to worsening of symptoms of the disease and deterioration of the quality of life. Approximately 30–40% of patients with Parkinson's disease have significant depressive symptoms. Depression can precede the onset of motor symptoms in approximately 25% of depressed Parkinsonians[7]. Evidence from a few longitudinal studies suggests that depression is often persistent in patients with Parkinson's disease and can worsen over time and it can be manifested earlier than motor symptoms[8]. Depression can precede the onset of motor symptoms in approximately 25% of depressed Parkinsonians[7]. It is also a key determinant of poor health-related quality of life in patients with Parkinson's disease[9]. The interaction between depression and Parkinson's disease is bidirectional as each of them is a risk factor for the other[10]. This disorder imposes a considerable economic burden on society; therefore, prevention plays an important role in saving resources and improving quality of life[11]. So this study was performed to find out the frequency as well as severity of depressive disorders in Parkinson's disease and also helped to identify risk factors behind it.

Materials and Methods:

After ethical clearance from the Institutional Review Board (IRB) of BSMMU, this study was conducted as cross cross-sectional observational comparative study. This study was conducted in the Movement Disorder Clinic (Outpatient) and In-Patient Department of Neurology, BSMMU, Dhaka. The study was carried out from April 2022 to September 2023. Patients with the age group of e" 18 years of both sexes, diagnosed with Parkinson's disease as diagnosed by MDS Clinical Diagnostic Criteria for PD, 2015 [12] who fulfilled the inclusion and exclusion criteria were selected as the study population. Informed written consent was taken from each patient. After taking proper history, physical and neurological examinations, and excluding other diagnoses patients were diagnosed with Parkinson's disease a total of 144 patients were selected by purposive sampling method. The frequency and severity of depressive disorder were assessed by the Bangla version Montgomery–Åsberg Depression Rating Scale (MADRS) [13] which was later confirmed by a Psychiatrist based on DSM-V criteria. The MADRS includes 10 items and uses a 0 to 6 severity scale, scored following the interview. Scoring/Interpretation: Higher scores indicate increasing depressive symptoms. Ratings can be added to form an overall score (range 0 to 60). Cut-off points include 0 to 6 – symptom absent, 7 to 19 – mild depression, 30 to 34 – moderate, 35 to 60 – severe depression[14]. Proper diagnosis and treatment were ensured for each patient. All collected data were checked and verified thoroughly to reduce inconsistency. Compilation of data was done to get a master sheet. Then data were recorded, coded, and entered into the computer. Data analysis was done in three stages. In the first stage, there are some frequency distributions and a few graphical representations of some important variables (Age, sex, residence, occupation, educational status). Continuous data were summarized in terms of the mean with standard deviation. The second stage contained the cross tables between depression levels with different factors (various demographic variables, age of onset, disease duration, Hoehn and Yahr stage, on-off fluctuations, end of dose wearing off, drug history of Ropinirole and Entcapone, etc.) to identify significant risk factors for depressive disorder. These (categorical) variables were compared by Pearson's chi-square test. *p-value* d" 0.05 was considered as significant. In the final (third) stage, how levels of depressive disorders were associated with the significant factors in

Parkinson's disease by multivariate binary logistic regression analysis. Here, *p-value* d" 0.05 was considered as significant. Results were presented as texts, frequency distribution tables, figures, and charts. Statistical analysis was done using SPSS (Statistical Package for Social Sciences) Windows version 26 software program.

Result:

Among the total 144 patients, a maximum of 40.3% had a current age range 51-60 years, and a minimum of 5.6% were found to be aged 70 years and older. The Mean (±SD) age was 56.00 ± 9.94(Table-1). The age range of our study sample was 35-80 years.

Table-I

Frequency for age of the respondents (n=144)

Categories	Frequency	Percent	Mean ± SD
31-40	14	9.7	
41-50	28	19.4	
51-60	58	40.3	56.00± 9.94
61-70	36	25.0	
70+	8	5.6	
Total	144	100.0	

Among the total study patients, 64 % were male and 36 % were female (Fig-1)

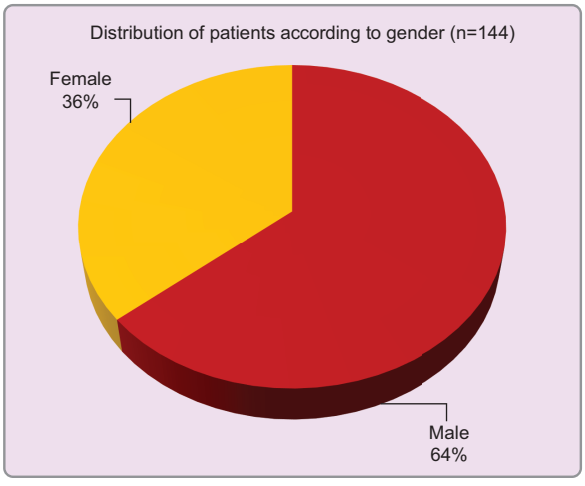

Fig.-1: *Distribution of patients according to gender (n=144)*

Out of 144 patients, 28 (19.4%) were normal, 52 (36.1%) had mild, 43 (29.9%) had moderate, and 21(14.6%) had severe levels of depressive disorder. So overall clinically significant depressive disorder (moderate and severe) frequency of this study is 44.5% (Table-II).

Table-II

Distribution of patients according to their depression frequency and severity (n=144)

Categories	Frequency	Percent
Normal(0-6)	28	19.4
Mild(7-9)	52	36.1
Moderate(20-34)	43	29.9
Severe(>34)	21	14.6
Total	144	100.0

Table-III shows an association of depressive disorder with multiple socio-demographic and clinical variables. Certain variables age of onset, duration of the disease, staging of the disease, on/off fluctuations, end-off-dose wearing off, and drug history of Ropinirole, and Entacapone were closely associated with depressive disorder.

Table-III

Socio-Demographic Variables	*p*-value
Age group	0.140
Age of onset	0.000[s]
Gender	0.155
Education level	0.902
Residence	0.422
Occupations	0.699
Clinical Variables	
Co-morbid Conditions	0.688
Family history of Parkinson's disease	0.075
Family history of depressive disorder	0.360
Duration of the disease	0.000[s]
Staging of the disease	0.000 [s]
Resting tremor	0.730
Rigidity	0.296
Bradykinesia	0.504
On/Off fluctuations	0.000 [s]
End-off-dose wearing off	0.043 [s]
Beneficial response to dopaminergic therapy	0.872
Drug history of Levodopa-Carbidopa	0.229
Drug history of Ropinirole	0.024 [s]
Drug history of Entacapone	0.033 [s]
Drug history of antidepressants	0.054
Drug history of antipsychotics	0.156
History of exposure to insecticide	0.100
History of smoking	0.933
History of alcohol	0.500

p-value measured by Chi-square test
s- Statistically significant

Table-IV

Logistic regression of depressive disorder with different significant risk factors in Parkinson's patients (n=144)

Risk factors	Odds Ratio	*p*-value	Confidence interval (95%)
Age of onset, <50 years	0.386	0.029	-1.190 to -0.040
Duration of disease	3.429	0.049	0.608 to 1.523
On-off fluctuation	0.523	0.047	-1.221 to -0.075
End-off-dose wearing off	1.545	0.451	-0.142 to 1.012
Staging of the disease	4.764	0.000	1.188 to 1.934
Drug history of Ropinirole	0.432	0.189	-1.479 to -0.201
Drug history of Entacapone	1.086	0.894	-0.535 to 0.699
Constant	.016	0.134	

The logistic regression table (Table-IV) shows that the age of onset, <50 years (Odds ratio 0.386, *p*-value 0.029), duration of the disease (Odds ratio 3.429, *p*-value 0.049), on-off fluctuation (Odds ratio 0.523, *p*-value 0.047), and staging of the disease (Odds ratio 4.764, *p*-value 0.000) are significant independent predictors for depressive disorder

Discussion

Analysis of the data revealed that out of 144 Parkinson's disease patients, the majority of (40.3%) were 51-60 years of age, and a minimum of 5.6% were found to be aged 70 years and older. The Mean (±SD) age was 56.00(±9.94) years. In this study male predominance was apparent. About 64 % of participants were male and 36 % were female. In one study, Zhu et al. found 64.5% of patients were males and 35.5% were female[15] . Possible causes of male predominance are due to exposure to toxins, head trauma, oestrogen's neuroprotective effects, mitochondrial malfunction, and the X linkage of genetic risk factors [16] . In the study people, most of them were rural 61.8%, and less than 38.2% lived in urban areas. The number of patients increased in rural areas due to environmental pesticides. Out of 172 patients, 19.4% of patients were normal, 36.1% had mild, 29.9% had moderate and 14.6% had severe levels of depressive disorder. Moderate and severe levels of depressive disorder were considered clinically significant. So a frequency of 44.5 % of patients had clinically significant depressive disorder out of 144 patients. In a previous study in Bangladesh Khalil et al found 42% depression out of 137 Parkinson's disease patients [17] . The reason for this resemblance is that participants shared the same socio-demographic traits between these two studies. In another study, Mayeux et al. showed that 47% of Parkinson's disease patients and 12% of their spouses rated themselves as significantly depressed [18]. In this study depressive disorder is closely related to the duration of the disease. Depression level is highly associated with the duration of disease of the respondents. Of those who had disease duration > 5 years, 42.4% had moderate depression and 30.3% had severe depression *(p*=0.00). Veiga et al. showed that the frequency (42%) and severity of major depression were higher in Parkinson's disease patients who had a longer disease duration [19]. In this study level of depressive disorder is highly related to the staging of the disease of the (Hoen and Yahr scale) of the respondents. Stage-1 patients had more mild depressive disorder, stage-2 patients had moderate and stage-3 patients had more severe depressive disorder (*p*=0.00). So the severity of depressive disorder is more in advanced stages. Van der Hoek et al. showed a significant difference between the different stages in the prevalence of depressive symptoms. They showed major depressive disorder was significantly more prevalent in the later stages of the disease (HY-stages 2.5–5) than in the earlier stage [20] . In this study, the patients who had on-off fluctuations and end-off-dose wearing-

off effects were more depressed. These two motor fluctuations are closely related to depressive disorder. The frequency and kind of mood shifts that take place during “on-off” intervals were evaluated by Nissenbaum et al. They discovered that 23% of individuals with 136 reported having “on-off episodes,” and that 68.7% of these said their depression was worse while “off.” [21]. In this study severity of depressive disorder was higher while patients were not using ropinirole and entacapone, probably this is due to the antidepressant effects of these two drugs. Rektorova et al. showed, that in PD patients with motor fluctuations and or dyskinesias, ropinirole reduced not only motor symptoms but also anxiety and depressive symptoms [22]. Several variables as gender, education level, residence, occupation, co-morbid conditions family history of Parkinson’s disease, family history of depressive disorder, resting tremor, rigidity, bradykinesia, beneficial response to dopaminergic therapy, drug history of Levodopa-Carbidopa, drug history of antidepressants, drug history of antipsychotics, history of exposure to insecticide, history of smoking, history of alcohol intake were performed Chi-square test with depressive disorder and found insignificant. Finally, binary logistic regression was done among the various risk factors and the age of onset, <50 years (Odds ratio 0.386, *p*-value 0.029), duration of the disease (Odds ratio 3.429, *p*-value 0.049), on-off fluctuation (Odds ratio 0.523, *p*-value 0.047), and staging of the disease (Odds ratio 4.764, *p*-value 0.000) were found significant independent predictors for depressive disorder.

Conclusion: The patients who had an Early age of onset (< 50 years), long duration of disease, advanced staging, and on-off fluctuations were more prone to depressive disorder.

Ethical Issue: All patients gave informed written consents and the study was approved by the Institutional Review Board of Bangabandhu Sheikh Mujib Medical University.

Conflict of Interest: None

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