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Risk Factors of Major Depressive Disorder in Parkinson's Disease

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Abstract

Depression in idiopathic Parkinson's disease is highly prevalent that can significantly impair the quality of life. Its exact mechanism of development is still poorly understood. It is well studied in western population but data from Asia especially in the South Asian region is limited. Considering this, to identify the potential risk factors of depression, a cross-sectional study was conducted among Parkinson's disease patients attending a tertiary care hospital in Bangladesh between July 2013-June 2014, in the Department of Neurology, Shaheed Suhrawardy Medical College and Hospital in Dhaka, Bangladesh. One hundred thirty seven cases of Parkinson's disease were enrolled, based on UK Parkinson's Disease Society Brain Bank criteria. Brain MRI was done in all cases, and patients with aphasia, significant cognitive deficits, secondary Parkinsonism were excluded. The overall prevalence of depression in the study population was 42%. There were no significant differences in gender, residence, education, smoking and marital status. In univariate analysis, age≥70 years, un-employed, right side predominantly involved, disease duration ≥5 years, sleep disturbance, postural instability, dose of levodopa ≥500 mg/day, Hoehn and Yahr stage ≥III and moderate to severe disability were significantly associated with depressive disorder. Whereas in multivariate linear stepwise regression model, age ≥70 years, (p=0.044), right side predominant involvement (p<0.001); sleep disturbance (p=0.006) and dose of levodopa ≥500 mg/day (p<0.001) were the major risk factors for depressive disorder. A significant proportion of Parkinson's disease patients suffer from depression. It was identified that depression in Parkinson's disease was significantly associated with advancing age, predominate right side involvement, sleep disturbance and higher daily dose of levodopa.

Keywords: Risk factor, Parkinson's disease, Depressive disorder

Introduction

Idiopathic Parkinson's disease (PD) is the second mostcommon neurodegenerative disease affecting about 1% of the population over the age 50, up to 4% over the age 80.[1-3] The disease is expected to rise proportionately with the increasing of aging worldwide.[4] The aetiology of PD is currently unclear and the curable treatment is still not available.[5] Depression is one of the major health problems in patients with PD.[6,7,38,39] Although, PD primarily is a movement disorder, depression in PD is difficult task and the predictors are complex and debatable.[8,38] The true prevalence of depression in PD is difficult to determine because there are no standardized assessment tools designed to evaluate depressive symptoms in the context of this disease.[9,43,44] Depending on diagnostic criteria used, the estimated prevalence of depression in PD has varied widely across studies, from 2.7% to more than 90%, with an average prevalence of about 30-40%.[3,10-13,49] Despite this high prevalence, unfortunately, depression remains frequently under recognized and often undertreated.[14,38] Overlap between symptoms andsigns of depression, with those of PD, may mask diagnosing depression or PD in its early stages.[15] This also contributes to difficulties interpreting depression rating scales and the absence of standard criteria for depression in PD.[16,17] Depression appears to be one of the most important factors impairing both subjective and objective quality of life, independent of motor deficits. Thus evaluating depression and identifying risk factors for developing depression is important.[3,18-20] Depression also has an impact on motor deficits, disability, caregiver burden, economic strain, cognitive impairment and severity of medical illness.[21,22,38,40,41] It is likely that depression in PD is multifactorial which

includes age, sex, disease severity, longer disease duration, a younger PD onset age, frequent fall, lower education level, smoking and regular use of non-aspirin bases NSAIDs or analgesics.[23-31] Whereas a recent study reported that PD patients with depression were associated with different demographic and clinical factors.[38-41] These findings emphasize the need to study the factors associated with depression in this population. It is well studied in western population but data from Asia especially sub-continent is limited. Findings from the western population cannot be directly extrapolated to the population of this region due to significant sociocultural differences. This may also be supported by the observation that rates of depression have been shown to vary widely between different countries.[1,2,4,38] However, clinical and socio-demographic risk factors for this comorbidity are not well studied. The intention of this study was to examine possible risk factors of major depressive disorder among the patients with PD in the regional context at a tertiary teaching and referral hospital of Bangladesh.

Materials and Methods

This cross-sectional study was conducted at the outpatient of Department of Neurology, Shaheed Suhrawardy Medical College and Hospital, a teaching and tertiary referral centre in Dhaka, Bangladesh, during July 2013 to June 2014. One hundred thirty seven PD patients were diagnosed clinically, based on the UK Parkinson's Disease Society Brain Bank criteria.[37,42] A written consent from all participants was taken prior to data collection. Patients with aphasia, significant cognitive deficits affecting participation and refused to participate were excluded. MRI of brain was done in all cases and secondary Parkinsonism was excluded. The Ethics Committee of the Bangladesh Medical Research Council approved the protocol.

The diagnosis of depression was based on the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV) using the structured clinical interview for DSM-IV.[50] Severity of disease was evaluated by the Hoehn and Yahr stage (H-Y I to V) and modified Rankin Scale (mRS)was used to measure disability (0-1 mild, 2-3 moderate, and 4-5 severe).[51,52] The rating was done by Neurologist based on the information obtained from the patient and care giver. A pre-designed questionnaire was used to collect socio-demographic and other clinical information. The interview was conducted in local language and assessments were made in English by the investigators. Tobacco consumption was categorised according to the WHO as: non-smoker, ex-smoker and current smoker and employed was established currently or was employed in last one year.

The data were analyzed through SPSS version 21.00. Continuous variables were expressed as mean ± standard deviation and were evaluated by the unpaired Student's t test. Similarly, categorical variables were expressed as percentage of the total and were evaluated by the chi-square test to measure the level of significance. Odds ratios and their corresponding 95% confidence limits were determined by logistic regression. A p value <0.05 was considered statistically significant. Adjusted odds ratio (adj. OR) between two groups, depression (Group A) and non-depression (Group B) were calculated. All significant variables were entered into a linear regression model in a stepwise fashion and a final fitted model was determined.

Results

One hundred thirty seven cases were enrolled, fifty-seven had depression according to DSM-IV criteria. Thus, the prevalence of depression in this population was 42%. Mean (SD) age of the depressed and non-depressed patients was 70(SD ±11.6) and 64(SD ±8.8) years respectively with a range of 45-95 years. Age was significant predictor of depression in linear regression analysis. Majority (37%) of the patients in depressed group were 70 -79 years age group. Male respondents were more in both group A and B (71.9% vs. 76.3%). In employment status, 86% in the depression group was unemployed (table I).

On the basis of residence, education, smoking status, there was no statistical significance between groups where to be found.

Right side was the major side that involves predominantly than left (81% vs. 30%). According to H-Y stage, 39% in non-depressed group in stage two and 40% in depressed group were in stage four (table II).

Table I: Socio-demographic characteristics (Group A= Depression; Group B=Non-depression)

	Group		*p*
	Group A (n=57)	Group B (n=80)	
Gender			
Male	41	61	0.568
Female	16	19	
Age			
< 50	01	03	
50-59	11	20	
60-69	12	38	0.001
70-79	21	15	
≥80	12	04	
Marital Status			
Married	48	60	0.276
Other	09	20	
Employment Status			
Employed	08	23	0.042
Unemployed	49	57	
Residence			
Urban	26	41	0.591
Rural	31	39	
Education			
Illiterate	16	22	
Primary	18	17	
Secondary	16	17	0.134
HigherSecondary	02	08	
Graduate and above	05	16	
Smoking(only inmale)			
Smoker	21	25	0. 415
Non-Smoker	20	36	

*Chi square test was done to measure the level of significance

Table II: Clinical characteristics (Group A= Depression; Group B=Non-depression)

	Group		*p*
	Group A (n=57)	Group B (n=80)	
Disability(mRS)			
Mild	12	55	
Moderate	26	21	<0.001
Severe	19	04	
Sleep disturbance			
Yes	43	33	
No	14	47	<0.001
Postural instability			
Yes	22	09	
No	35	71	<0.001
Severity (H-Y stage)			
Stage I	05	26	
Stage II	08	31	<0.001
Stage III	14	16	
Stage IV	23	05	
Stage V	07	02	
Predominant side involvement			
Right side	46	24	
Left side	11	56	<0.001

*Chi square test was done to measure the level of significance

Distribution of disability according to modified Rankin scale in Group A and B was found, mild (21% vs. 69%), moderate (46% vs. 26%) and severe (33% vs. 5%) which was statistically significant. The longest duration of PD encountered was 15 years. Mean (SD) disease duration was 6.71 (SD±3.02) and 3.48 (SD±2.02) years in groups respectively and was significant. Sleep disturbance and postural instability were found more in depressed group (table II). Mean (SD) doses of levodopa was 506.14 (SD ±176.04) and 286.56 (SD±202.75) mg/day in groups respectively, which was statistically significant.

Table III: Factors associated with depression (Unadjusted risk distribution)

Variables	Un adj. OR	95% CI	*p*
Age (years)			
<70 (Ref.)	1		
≥70	4.414	2.12 - 9.22	<0.001*
Employment Status			
Employed(ref)	1		
Un- employed	2.471	1.01 - 6.02	0.046*
Predominant side involvement			
Left side (ref)	1		
Right side	9.758	4.32 - 22.0	<0.001*
Disease duration(years)			
< 5 (ref)	1		
≥ 5	7.030	3.24 - 15.27	<0.001*
Sleep disturbance			
No(ref)	1		
Yes	4.374	2.07 - 9.26	<0.001*
Postural instability			
No(ref)	1		
Yes	4.959	2.07 -11.89	<0.001*
Drug dose of Levodopa (mg/day)			
< 500(ref)	1		
≥ 500	7.199	3.36 -15.44	<0.001*
Severity(H-Y stage)			
Upto Stage II(ref)	1		
Stage ≥ III	8.388	3.82-18.40	<0.001*
Disability(mRS)			
Mild(Ref)	1		
Moderate to severe	8.250	3.73 -18.23	<0.001*

*Statistically significant variables Unadj= Unadjusted

In univariate analysis (table-III), age ≥70 [OR=4.41, 95%CI(2.16-9.22); *p*<0.001], un-employed [OR=2.47, 95%CI(1.01-6.02); *p* =0.046], involving right side predominantly [OR=9.76, 95% CI(4.32- 22.00); *p*<0.001], disease duration ≥5 years [OR=7.03, 95%CI(3.24-15.27); *p*<0.001],having sleep disturbance [OR=4.37, 95% CI (2.07-9.26); *p*<0.001], postural instability [OR=4.96, 95%CI(2.07-11.89); *p*<0.001], daily drug dose of levodopa ≥500 mg [OR=47.20, 95% CI (3.36-15.44); *p*<0.001],H-Y stage ≥ III [OR=8.39, 95% CI (3.82-18.40); *p*<0.001],moderate to severe disability [OR=8.25, 95%CI (3.73-18.23); *p*<0.001] were statistical significant association with depression.

Table IV: Multivariate linear logistic regression: most significant factors associated with depression

Variables	Adj. OR (95% CI)	*p value*
Age (years)		
<70 (Ref.)	1	
≥70	2.823(1.03-7.76)	0.044
Predominant side involvement		
Left side(Ref.)	1	
Right side	17.134(5.55-52.93)	<0.001
Sleep disturbance		
No(ref)	1	
Yes	4.220 (1.527-11.664)	0.006
Drug dose of Levodopa (mg/day)		
< 500(ref)	1	
≥ 500	9.820(3.227-29.886)	<0.001

Adj. = Adjusted

When all significant variables were entered into a multivariate linear logistic regression mode (table IV), age ≥70 years [OR=2.82,95% CI (1.03-7.76); p=0.044], predominantly involvement in right side [OR=17.13,95% CI (5.55-52.93); p<0.001], sleep disturbance [OR=4.22, 95% CI (1.53-11.66); p= 0.006] and daily drug dose of levodopa ≥ 500 mg [OR=9.82, 95% CI (3.23-29.89); p<0.001] were the major risk factors for the development of depression.

Discussion

According to the results of this study, depression is highly comorbid with PD. These results are in accordance with Asian and Western populations.[24, 32-34.38,39,46] But studies in clinic-based samples or using different instruments have been reported a wide range of depression rates.[3,10,11,20,21,47] The prevalence of depression among PD patients depends on the population examined and the definition of depression used for the study. The present study used DSM-IV, based clinical interview, a widely used instrument for depression assessment in comparison to the majority of studies done in Asia.

It may be mentioned here in this study, it could not possible to address depression in PD patients with cognitive impairment or to the patients otherwise unable to utilize self-report instruments for data collection. Furthermore, the severity of depression was not evaluated.

Mean age of this study population had similarity with other studies.[12,14,24,34,35,38,40,48] Among the examined patient, most of the depression group was un-employed due to old age. It could not to be found an association between major depressive disorder in PD and in frequency of gender, residence, education, smoking and marital status. Another study from Asia also could not to be found any association.[38]

It was analysed to determine factors contributed for depression. In stepwise fashion, multivariate linear logistic regression model, only four factors were significantly associated with depression; advancingage, predominately rightside involvement, sleep disturbance and higher daily dose of levodopa. Findings of this study strongly predicted depression in PD patients was not surprising. The close relationship among these factors is well known in depression with PD.[24,25,27-31,38,40] It was to be found that the duration of PD symptoms was not related to depression, which supports the idea that depression might be a neuropathological process occurring concomitantly or before the degeneration of motor systems, which is similar with other study.[41]

An interesting and surprising finding was that H-Y stage and disability was not associated with depression in multivariate logistic regression model but was significant in univariate analysis. Depression was higher in H-Y stages III and above. Similar findings have been reported previously.[13,31, 38,45] It was highest in stage IV possibly because this is the stage where the debility becomes marked. Though the rise in the rate of depression would be expected to be linear as the stage and disability increases, this was not observed. This is possibly due to the inability of the severely disabled to physically attend the hospital resulting in a lesser number of patients in severe stages participating in the study which may have influenced the results. The customs of Bangladeshi society, a large number of patients who were caregiver dependent, especially elderly members are cared within a close family network without being hospitalized. Existing views about the association between the severity of PD and depression are contradictory. Some studies reported it as positive, while others showed no association.[2,17,19,36, 38,49]

Overall findings in relation to the prevalence and factors associated for depression in PD, are in keeping what is reported in Asia and western populations. This study showed some unique association of depression with PD such as higher daily dose of levodopa and predominantly involvement in right side. These findings need further inquiry whether they are replicable regionally or globally. Furthermore, the differences in depression between cultures may

be sought, and studying the phenomenology of depression in PD across cultures may be useful.

Conclusion

Among this population, a significant proportion of PD patients suffer from major depressive disorder. It was identified that depression was significantly associated with a number of socio-demographic and clinical factors including higher daily dose of levodopa, and some other weak factors. In addition, findings of this study displayed some unique features such as depressive vulnerability in the presence of predominate right side involvement and higher daily dose of levodopa. Further studies are suggested, whether there is a regional replicability of these findings and to identify possible underlying mechanisms.

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