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Psychiatric Symptoms in Patients and Caregivers with Parkinson's Disease

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ABSTRACT

Objectives: Psychiatric disorders in patients with Parkinson's disease (PD) and their caregivers play an important role in patients' treatment and follow-up. Our study aimed to examine the prevalence of psychiatric symptoms among patients with PD and their caregivers, demographic risk factors, and the influence of severity and manifestations of PD on psychiatric distress. ***Methods***: We included 125 patients with PD and 125 of their primary caregivers in this descriptive cross-sectional study. The severity of PD was evaluated according to the Hoehn and Yahr severity scale from the Movement Disorder Society-Sponsored Revision of the Unified Parkinson's Disease Rating Scale. PD patients and their caregivers completed the Symptom Checklist-25 to determine the presence of psychiatric distress. Also, demographic factors, including age, high level of education, occupation, residence, and cigarette smoking, were assessed in the PD patients and their caregivers. ***Results:*** The prevalence of psychiatric distress was 47.2% for PD patients and 18.4% for caregivers. Female sex, city residency, and medical disease were risk factors for more psychiatric symptoms in PD patients. Also, the female sex, single status, living in a village, and having a medical disease were risk factors for greater psychiatric symptoms in caregivers. PD patients in more advanced stages of disease suffered significantly from psychiatric distress, somatization, anxiety, interpersonal sensitivity, obsessive-compulsive disorder, and phobia compared to the lower severity of disease. PD patients with manifestation of postural instability showed a higher score of somatization, phobia, and psychiatric distress as compared with tremor, hypokinesia, and rigidity. ***Conclusions:*** Progression of PD influenced the psychiatric symptoms of both patients and their caregivers. A higher stage of PD is associated with higher scores of psychiatric distress, phobia, and somatization in the patients and their caregivers.

Parkinson's disease (PD) is the second most common neurodegenerative disorder. The overall prevalence of PD is 1% in the over 60s.[1] A study on the demographics of PD in Iran revealed that the most frequent age of onset of PD was between 51 and 60 years old. The male-to-female ratio among Iranian PD patients was 2.1:1.[2] PD is associated with motor symptoms such as tremor, rigidity, bradykinesia, postural instability, and impaired walking/gait. These patients experience higher levels of psychiatric distress compared to their age-matched general population.[3] Depression and anxiety appear as both primary and secondary pathologies of the disease in response to progressive disability.[4] Previous studies have reported a prevalence of 34.4% for anxiety, 34.9% for depression, and 50% for sleep disturbance in PD.[5,6] There is also evidence that depression and anxiety significantly affect the quality of life of patients with PD.[7]

Parkinson's disease caregivers (PDCs) play an important role in the treatment and follow-up of patients with PD. As caring for these patients is extremely stressful, psychiatric symptoms are also common in this group of indivuals. A study reported that 32% of PDCs had anxiety symptoms, and 51% of those had depressive symptoms.[8] Recent studies have shown a significant relationship between psychiatric symptoms in PDCs and some symptoms of PD patients like depression.[9–13]

Evidence suggests that the identification and treatment of psychiatric disorders in patients with PD and PDCs have been neglected.[14,15] To the

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best of our knowledge, this study is the first to simultaneously provide data on the psychiatric symptoms of both patients and primary caregivers and associations with severity of the PD. We sought to determine the prevalence of psychiatric symptoms among PD patients and PDCs. The study's second objective was to examine the possible association between psychiatric symptoms and sociodemographic and clinical risk factors. The study also intended to assess the influence of the severity of PD on psychiatric distress in patients and caregivers. Finally, to investigate the association between the severity of PD and psychiatric distress in patients and caregivers.

METHODS

We conducted a descriptive cross-sectional study in a group of patients with PD, who were under regular follow-up at the outpatient clinic of the teaching hospital of the Department of Neurology of Babol University of Medical Sciences in Babol (North of Iran) from May to November 2019. A total of 125 PD patients and 125 their primary caregivers were included in the study.

The sample size was determined as 150 participants in each group assuming that 65% of caregivers have psychiatric disorders[16] with 0.1 error at 95% confidence level and 80% power. A convenience sample of 150 PD patients and their caregivers was collected accordingly. Finally, 125 questionnaires were analyzed, given the inadequate response of 25 patients or their caregivers.

Patients who met the United Kingdom Parkinson's Disease Society Brain Bank (UKPDSBB) criteria for idiopathic PD were enrolled in the study.[16] PD patients who had secondary causes of a Parkinsonian syndrome, including a history of repeated strokes or head injury, Parkinson's syndrome caused by taking neuroleptics, and significant cognitive impairment preventing the patient from filling the questionnaire or providing informed consent were excluded from the study. Also, PD patients who did not have the capacity to self-report reliable information were excluded from the study to prevent possible data collection alterations.

At the time of their recruitment, one member of the research team (a medical student) explained the study to the participants and invited them to join. She explained the goals and the research questionnaires. Then she assessed the inclusion/exclusion criteria for PD. After an initial assessment of the primary inclusion/exclusion criteria and demographic information, the patients were interviewed by a neurologist to assess complementary assessments. An expert neurologist (first author) interviewed and examined the participants neurologically. The diagnosis of PD patients was made based on UKPDSBB criteria for idiopathic PD.[16,17] He evaluated and managed the PD course, obtained the clinical records of the patients, and disease information. The severity of PD was evaluated according to the Hoehn and Yahr (H&Y)[18] severity scale from the Movement Disorder Society-Sponsored Revision of the Unified Parkinson's Disease Rating Scale (MDS-UPDRS).[19] The cardinal manifestations of the symptom disease were evaluated by UPDRS. Afterward, the medical student explained the questionnaires to the PD patients and gave them the scales to be completed. PD patients filled the demographic questionnaire and Symptom Checklist-25 (SCL-25).

PDCs were also assessed for the inclusion/exclusion criteria. The primary caregiver was the person who usually lived with the patient and was directly involved in caring for the patient or directly affected by the patient's health problem.[16] PDCs who lived with the PD patients and who had an education level higher than primary school were invited to the study. However, the PDCs who did not have the capacity to self-report reliable information were excluded from the study to prevent possible data collection alterations. A total of 125 eligible PDC completed two questionnaires, including a demographic questionnaire and SCL-25.

This research was approved by the ethics committee of Babol University of Medical Sciences (IR.MUBABOLHRI.REC.1398.121). All PD patients and PDCs provided written informed consent to participate in the study. We assessed the severity of PD using the H&Y severity scale and MDS-UPDRS. The H&Y severity scale is a widely used clinical rating scale of motor function in PD. This scale evaluates the extent of patients' clinical disability from 1 to 5: stage 1 (unilateral involvement only), stage 1.5 (unilateral and axial involvement), stage 2 (bilateral involvement without impairment of balance), stage 2.5 (mild bilateral disease with recovery on pull test), stage 3 (mild to moderate bilateral disease; some postural instability; physically

independent), stage 4 (severe disability; still able to walk or stand unassisted), and stage 5 (wheelchair-bound or bedridden unless aided).[18]

The MDS-UPDRS is a comprehensive 50-question assessment of both motor and non-motor Parkinson's symptoms. The MDS-UPDRS is comprised of four sections including non-motor experiences of daily living, motor experiences of daily living, motor examination, and motor complications.[19] In this study, we used part 3 (motor examination) and 4 (motor complication) to assess four major cardinal manifestations of PD, including tremor, hypokinesia, rigidity, and postural instability.

The SCL-25 is a brief form of SCL-90 with 25 questions on a Likert 0–4 scale including never (0), a few (1), somewhat (2), great (3), and very great or severe (4) to assess psychiatric distress. The scale covers eight subscales, including somatization, obsessive-compulsive disorder (OCD), interpersonal sensitivity, phobia, depression, anxiety, paranoid ideation, and psychoticism. Raw scores were calculated by dividing the sum of scores for each subscale by the number of items. Also, the global severity index (GSI) was used to measure the extent or depth of the individual's mental health problems by dividing the sum of scores of all questions by the number of questions. We used the Iranian version of the SCL-25 whose suitable validity (Cronbach's 0.97) and reliability (re-test coefficients 0.78) had already been approved.[20] The current study used a cutoff GSI ≥ 1.75 to define psychiatric distress.[21]

Categorical variables such as education and job were reported as percentages. Continuous variables, all subscales of SCL-25, and GSI were normally distributed. Thus, we conducted a test to compare the mean scores of subscales of SCL-25 in PD patients and their caregivers and categorical demographic variables such as age, education, and occupation. Also, Spearman's test was applied to assess the correlation between variables. We used the chi-square tests to examine the relationship between demographic characteristics of PD patients/PDCs. Further, ANOVA tests were employed to compare the score subscales of SCL-25 and GSI in different stages of PD. All data were analyzed using SPSS software (IBM Corp. Released 2017. IBM SPSS Statistics for Windows, Version 25.0. Armonk, NY: IBM Corp.). Statistical significance was determined as a p-value < 0.050, where all p-values were two-tailed.

Table 1: Demographic characteristics of the patients with Parkinson's disease and their caregivers.

Variables	Patients, n (%)	Caregivers, n (%)
Gender		
Male	66 (52.8)	52 (41.6)
Female	59 (47.2)	73 (58.4)
Education		
Primary school	102 (81.6)	64 (51.2)
High school	10 (8.0)	37 (29.6)
University	13 (10.4)	24 (19.2)
Job		
Employed	34 (27.2)	67 (53.6)
Unemployed	91 (72.8)	58 (46.4)
Residence		
Urban	62 (49.6)	68 (54.4)
Rural	63 (50.4)	57 (45.6)
Smoking		
Yes	13 (10.4)	52 (41.6)
No	112 (89.6)	73 (58.4)
Chronic disease*		
Yes	81 (64.8)	11 (8.8)
No	44 (35.2)	114 (91.2)

**Hypertension, ischemic heart disease, and diabetes.*

RESULTS

Table 1 describes the demographic characteristics of the participants. The mean age of the PD patients was 67.8±10.1 years. A total of 52.8% of patients were men, and 73.0% lived with their spouses. The majority (81.6%) of patients had primary school education, 27.2% were employed, and < 50.0 % lived in the city.

The number of PD cases with H&Y scale stage 1 was 0 (0.0%), stage 2 was 21 (16.8%), stage 2.5 was 25 (20.0%), stage 3 was 20 (16.0%), stage 4 was 8 (6.4%), and stage 5 was 0 (0.0%). Thus, nearly 52.8% were in stages 2 to 3. The duration of PD illness was 3.8±3.1 years (range = 1–20 years). The frequency tremor was 65.6%, hypokinesia was 22.4%, postural instability was 9.6%, and rigidity was 2.4%.

The mean age of PDCs was 50.5±14.8 ranging from 21 to 86 years. Most (58.4%) caregivers were women, 91.2% of PDC were married, and 54.4% lived in a city. About half (51.2%) of the PDCs had primary school education and 53.6% were employed. The relationship between caregivers and PD patients was as follows: 32.0% spouse, 66.0% daughter/son, and 2.0% sister/brother.

Table 2 reports the prevalence of psychiatric distress in PD patients and caregivers. The mean

Table 2: The prevalence of psychiatric distress in patients with Parkinson's disease (PD) and their caregivers (PDCs).

Psychiatric symptoms	PD patients n = 125	PDCs n = 125
	n (%)	n (%)
Somatization	77 (61.6)	28 (22.4)
Depression	111 (88.8)	71 (56.8)
Anxiety	114 (91.2)	61 (48.8)
Obsessive-compulsive	89 (71.2)	48 (38.4)
Interpersonal sensitivity	84 (67.2)	49 (39.2)
Phobia	60 (48.0)	19 (15.2)
Paranoid ideation	73 (58.4)	37 (29.6)
Psychoticism	24 (19.2)	9 (7.2)
GSI ≥ 1	59 (47.2)	23 (18.4)

GSI: global severity index.

score of GSI was 1.0±0.5 for PD patients. The overall rate of psychiatric distress (GSI ≥ 1) for PD patients was 47.2%. Also, the total rate of psychiatric distress (GSI ≥ 1) for PDCs was 18.4%.

The results of this study showed (based on the mean score of each subscale of SCL-25 ≥ 1) that the rate of psychiatric symptoms for PD patients was as follows: somatization 61.6%, OCD 71.2%, interpersonal sensitivity 67.2%, phobia 48.0%, depression 88.8%, anxiety 91.2%, paranoid ideation 58.4%, and psychoticism 19.2%.

The mean score of GSI was 0.6±0.4 for caregivers. The rates of psychiatric symptoms for caregivers (based on the mean score of each subscale of SCL-25 ≥ 1) were as follows: somatization 22.4%, OCD 38.4%, interpersonal sensitivity 39.2%, phobia 15.2%, depression 56.8 %, anxiety 48.8%, paranoid ideation 29.6%, and psychoticism 7.2%.

Table 3 reports the results of the *t*-tests on comparison of psychiatric symptoms according to demographics. Women with PD had more psychotic symptoms than men ($p = 0.040$). PD patients who lived in the city had more psychotic symptoms than those living in villages ($p = 0.040$). The mean scores of somatization and interpersonal sensitivity in PD patients who had chronic disease were greater than those without chronic disease ($p < 0.050$).

Female PDCs had higher scores in somatization and anxiety than male PDCs ($p < 0.050$). The depressive symptoms had larger scores in the divorced PDCs than their married counterparts ($p = 0.010$). PDCs who lived in a village had larger somatization scores than those living in the city ($p < 0.001$). The somatization score in smoker PDCs was lower than among non-smokers ($p < 0.001$). The mean scores of somatization and interpersonal sensitivity in PDCs who had chronic disease were higher than those without chronic disease ($p < 0.001$).

Table 4 provides the results of ANOVA tests and post-hoc Tukey's multiple comparisons of mean psychiatric symptoms and PD status among PD patients and caregivers. The comparison of mean GSI of patients in different stages of PD revealed that higher stages of PD were associated with higher scores of psychiatric distress in patients ($p < 0.001$). The mean somatization symptom of PD patients in stage 4 was significantly higher than those in stage 1.5 (2.0±0.6 vs. 0.9±0.7, $p = 0.002$) and stage 2.5 (2.0±0.6 vs. 1.7±0.8, $p = 0.001$). The PD patients in stage 2.5 significantly suffered from anxiety symptoms more than patients in stage 1.5 (1.4±0.6 vs. 0.9±0.5, $p = 0.005$) and in stage 2 (1.4±0.6 vs. 1.1±0.6, $p < 0.001$) did. The mean OCD symptoms of PD patients in stage 4 were significantly higher than in stage 1.5 (2.3±0.7 vs. 0.6±0.8, $p < 0.001$). The PD patients in stage 4 suffered from phobia symptoms significantly more than those in stage 1.5 (3.0±0.6 vs. 0.6±0.4, $p < 0.001$) and in stage 2 (3.0±0.6 vs. 0.4±0.6, $p < 0.001$) did. Also, the mean interpersonal sensitivity in patients with stage 4 was significantly higher than the mean in stage 1.5 (1.7±0.5 vs. 0.4±0.4, $p < 0.001$) and in stage 2 (1.7±0.5 vs. 0.6±0.5, $p = 0.003$).

According to Table 4, the comparison of mean GSI of caregivers in different stages of PD patients revealed that among higher stage PD patients, higher scores of psychiatric distress were observed in caregivers ($p < 0.001$). The mean somatization symptom was significantly higher in caregivers of patients in stage 3 than stage 1.5 patients (1.0±0.7 vs. 0.5±0.6, $p = 0.030$).

The caregivers of patients in stage 4 suffered from phobia symptoms more significantly than those of patients in stage 1.5 (0.6±0.3 vs. 0.3±0.6, $p = 0.040$) and stage 3 (0.6±0.3 vs. 0.1±0.3, $p = 0.010$).

The PD patients with postural instability suffered from psychiatric distress (higher GSI) significantly more than patients with manifestations of tremor, hypokinesia, and rigidity. Also, the mean somatization and phobia symptoms were significantly higher in PD patients with postural

Table 3: Relationship between psychiatric symptoms and demographic characteristics in Parkinson's disease patients and their caregivers.

Demographic variables	Somatization		Depression		Anxiety		OCD		Interpersonal sensitivity		Phobia		Paranoid ideation		Psychoticism		GSI	
	Patient	Caregivers	Patient	Caregivers	Patient	Caregivers	Patient	Caregivers	Patient	Caregivers	Patient	Caregivers	Patient	Caregivers	Patient	Caregivers	Patient	Caregivers
Gender																		
Male	1.3 ± 0.7	0.6 ± 0.5	0.7 ± 0.7	0.5 ± 0.60	1.1 ± 0.6	0.2 ± 0.4	1.3 ± 1.1	0.7 ± 0.7	0.9 ± 0.7	0.6 ± 0.7	0.9 ± 1.2	0.2 ± 0.5	1.0 ± 1.1	0.9 ± 1.0	0.1 ± 0.2	0.1 ± 0.5	1.0 ± 0.5	0.5 ± 0.4
Female	1.3 ± 0.7	0.9 ± 0.6	0.9 ± 0.9	0.4 ± 0.7	1.3 ± 0.8	0.6 ± 0.5	1.1 ± 0.9	0.8 ± 0.7	0.9 ± 0.6	0.9 ± 0.8	0.8 ± 1.0	0.3 ± 1.4	1.3 ± 1.4	0.9 ± 1.0	0.3 ± 0.4	0.2 ± 0.4	1.0 ± 0.5	0.6 ± 0.4
p-value	0.980	< 0.001	0.210	0.250	0.360	< 0.001	0.310	0.760	0.920	0.030	0.940	0.430	0.430	0.0960	0.040	0.070	0.590	< 0.001
Education																		
Primary school	1.3 ± 0.7	0.8 ± 0.5	0.7 ± 0.8	0.4 ± 0.6	1.3 ± 0.8	0.5 ± 0.5	1.1 ± 1.0	0.8 ± 0.7	0.8 ± 0.7	0.8 ± 0.8	0.8 ± 1.0	0.3 ± 0.5	1.0 ± 1.2	0.9 ± 1.0	0.2 ± 0.3	0.1 ± 0.5	1.0 ± 0.5	0.6 ± 0.3
High school	1.3 ± 0.5	0.6 ± 0.6	1.2 ± 0.8	0.5 ± 0.8	0.7 ± 0.5	0.4 ± 0.6	1.3 ± 0.9	0.8 ± 0.7	1.1 ± 0.6	0.7 ± 0.8	0.9 ± 1.6	0.3 ± 0.6	1.9 ± 1.2	0.8 ± 1.0	0.2 ± 0.5	0.1 ± 0.6	1.1 ± 0.5	0.5 ± 0.4
University	1.4 ± 0.9	0.7 ± 0.6	1.0 ± 0.8	0.4 ± 0.6	1.4 ± 0.6	0.3 ± 0.4	1.3 ± 1.1	0.6 ± 0.7	1.1 ± 0.6	0.9 ± 0.8	1.1 ± 1.0	0.2 ± 0.3	1.3 ± 1.0	1.4 ± 1.0	0.3 ± 0.4	0.1 ± 0.3	1.2 ± 0.5	0.5 ± 0.4
p-value	0.850	0.050	0.050	0.800	0.040	0.570	0.540	0.760	0.260	0.670	0.810	0.990	0.700	0.450	0.700	0.510	0.590	0.510
Job																		
Employed	1.3 ± 0.6	0.9 ± 0.6	0.8 ± 0.8	0.5 ± 0.7	1.3 ± 0.8	0.4 ± 0.5	1.2 ± 1.0	0.7 ± 0.7	0.9 ± 0.7	0.8 ± 0.7	0.9 ± 1.2	0.2 ± 0.4	1.2 ± 1.2	1.0 ± 1.0	0.2 ± 0.3	0.1 ± 0.2	1.1 ± 0.6	0.6 ± 0.4
Unemployed	1.3 ± 0.8	0.6 ± 0.5	0.7 ± 0.8	0.4 ± 0.6	1.2 ± 0.7	0.5 ± 0.6	1.2 ± 1.0	0.8 ± 0.7	0.9 ± 0.6	0.8 ± 0.8	0.8 ± 1.0	0.3 ± 0.6	1.1 ± 1.2	0.9 ± 1.0	0.2 ± 0.3	0.26 ± 0.6	1.0 ± 0.5	0.6 ± 0.4
p-value	0.680	0.060	0.410	0.450	0.600	0.980	0.590	0.480	1.000	0.530	0.570	0.210	0.550	0.490	0.660	0.320	0.580	0.590
Place of living																		
Urban	1.3 ± 0.8	0.6 ± 0.5	0.8 ± 0.8	0.4 ± 0.8	1.3 ± 0.8	0.5 ± 0.6	1.2 ± 1.0	0.8 ± 0.8	0.8 ± 0.6	0.7 ± 0.7	0.7 ± 0.9	0.3 ± 0.5	0.9 ± 1.2	0.9 ± 1.0	0.2 ± 0.3	0.8 ± 0.5	1.0 ± 0.5	0.5 ± 0.4
Rural	1.4 ± 0.7	0.9 ± 0.6	0.7 ± 0.8	0.4 ± 0.4	1.2 ± 0.7	0.4 ± 0.5	1.1 ± 1.0	0.6 ± 0.6	0.9 ± 0.7	0.8 ± 0.8	0.9 ± 1.2	0.3 ± 0.5	1.2 ± 1.2	1.0 ± 1.0	0.1 ± 0.3	0.2 ± 0.5	1.0 ± 0.5	0.6 ± 0.3
p-value	0.290	< 0.001	0.550	0.500	0.860	0.840	0.450	0.220	0.840	0.970	0.280	0.990	0.090	0.540	0.040	0.490	0.700	0.280
Smoking																		
Yes	0.9 ± 0.7	0.4 ± 0.4	0.8 ± 0.8	0.7 ± 0.8	0.6 ± 1.0	0.4 ± 0.6	1.2 ± 1.1	0.7 ± 0.8	0.6 ± 0.4	0.8 ± 0.9	0.3 ± 0.5	0.3 ± 0.7	1.1 ± 1.0	1.0 ± 1.0	0.2 ± 0.4	0.3 ± 0.8	0.7 ± 0.4	0.57 ± 0.5
No	1.4 ± 0.7	0.87 ± 0.6	0.7 ± 0.8	0.4 ± 0.6	0.8 ± 0.8	0.4 ± 0.5	1.2 ± 1.0	0.8 ± 0.7	0.9 ± 0.7	0.8 ± 0.7	0.8 ± 1.1	0.3 ± 0.5	1.1 ± 1.3	0.9 ± 1.0	0.2 ± 0.3	0.2 ± 0.4	1.0 ± 0.5	0.6 ± 0.3
p-value	0.200	< 0.001	0.400	0.070	0.280	0.360	0.150	0.340	0.150	0.670	0.090	0.170	0.750	0.760	0.890	0.800	0.900	0.210
Chronic disease																		
Yes	1.4 ± 0.8	1.3 ± 0.6	1.2 ± 0.8	0.4 ± 0.6	1.0 ± 0.5	0.6 ± 0.5	1.2 ± 1.0	0.8 ± 0.7	1.0 ± 0.6	1.0 ± 0.7	1.0 ± 1.1	0.3 ± 0.5	1.2 ± 1.3	1.1 ± 1.1	0.2 ± 0.3	0.2 ± 0.5	1.1 ± 0.5	0.8 ± 0.3
No	1.1 ± 0.7	0.6 ± 0.5	1.3 ± 0.7	0.4 ± 0.7	1.3 ± 0.8	0.4 ± 0.5	1.2 ± 1.0	0.7 ± 0.7	0.7 ± 0.7	0.7 ± 0.7	0.5 ± 0.8	0.3 ± 0.5	1.0 ± 1.1	0.9 ± 1.0	0.2 ± 0.4	0.1 ± 0.5	0.9 ± 0.5	0.5 ± 0.4
p-value	0.030	< 0.001	0.660	0.490	0.190	0.070	0.980	0.730	0.060	< 0.001	0.080	0.400	0.710	0.440	0.390	0.050	0.150	< 0.001
Symptoms of Parkinson																		
Tremor	1.2 ± 0.8	0.7 ± 0.6	0.7 ± 0.8	0.5 ± 0.7	1.25 ± 0.7	0.4 ± 0.5	1.0 ± 0.9	0.7 ± 0.7	0.2 ± 0.3	0.7 ± 0.8	0.6 ± 0.9	0.3 ± 0.6	0.1 ± 0.3	0.8 ± 0.9	0.1 ± 0.3	0.2 ± 0.5	0.9 ± 0.5	0.6 ± 0.4
Bradykinesia	1.6 ± 0.51	0.8 ± 0.5	0.9 ± 0.8	0.2 ± 0.3	1.2 ± 0.7	0.5 ± 0.5	1.4 ± 1.2	0.8 ± 0.7	0.3 ± 0.4	0.8 ± 0.7	0.9 ± 1.0	0.3 ± 0.4	0.2 ± 0.3	1.1 ± 1.1	0.2 ± 0.3	0.2 ± 0.3	1.1 ± 0.5	0.6 ± 0.3
Rigidity	1.0 ± 0.7	0.9 ± 0.4	0.3 ± 0.5	0.3 ± 0.5	1.4 ± 0.3	0.0 ± 0.1	0.8 ± 0.7	0.4 ± 0.1	0.7 ± 0.1	0.5 ± 0.6	1.0 ± 1.2	0.0 ± 0.0	0.3 ± 0.5	1.6 ± 1.5	0.3 ± 0.5	0.0 ± 0.0	0.9 ± 0.3	0.4 ± 0.1
Impaired balance	1.7 ± 0.8	0.9 ± 0.6	1.1 ± 0.9	0.5 ± 0.5	1.3 ± 1.0	0.3 ± 0.4	1.1 ± 0.9	1.1 ± 1.0	0.1 ± 0.2	0.9 ± 0.6	2.1 ± 1.4	0.3 ± 0.4	0.4 ± 0.3	1.5 ± 1.2	0.4 ± 0.3	0.0 ± 0.1	1.5 ± 0.6	0.6 ± 0.3
p-value	< 0.001	0.650	0.300	0.450	0.810	0.470	0.070	0.590	< 0.001	0.570	< 0.001	0.450	< 0.001	0.110	0.080	0.110	< 0.001	0.600

Data were given as mean±standard deviation. OCD: obsessive-compulsive disorder; GSI: global severity index.

Table 4: Relationship between Parkinson's disease stage and psychiatric symptoms in patients and caregivers.

Parkinson's stage	Symptoms					
	1.5	2	2.5	3	4	*p*-value
Somatization						
Patients	0.9 ± 0.7[a]	1.2 ± 0.5[ab]	1.7 ± 0.8[b]	1.6 ± 0.5[b]	2.0 ± 0.6[b]	< 0.001
Caregivers	0.5 ± 0.6[a]	0.9 ± 0.5[ab]	0.9 ± 0.5[ab]	1.0 ± 0.7[b]	0.9 ± 0.3[ab]	< 0.001
Depression						
Patients	0.4 ± 0.6[a]	0.7 ± 0.7[a]	1.0 ± 0.7[b]	1.0 ± 0.9[ab]	1.7 ± 0.9[ab]	< 0.001
Caregivers	0.2 ± 0.4	0.8 ± 1.1	0.5 ± 0.5	0.4 ± 0.4	0.5 ± 0.3	0.030
Anxiety						
Patients	0.9 ± 0.5[a]	1.1 ± 0.6[ac]	1.4 ± 0.6[b]	2.0 ± 1.0[b]	1.5 ± 0.7[ab]	< 0.001
Caregivers	0.3 ± 0.5	0.5 ± 0.6	0.6 ± 0.5	0.4 ± 0.4	0.3 ± 0.7	0.180
Obsessive-compulsive						
Patients	0.6 ± 0.8[a]	1.1 ± 0.9[ab]	1.8 ± 0.9[b]	1.5 ± 1.1[b]	2.3 ± 0.7[b]	< 0.001
Caregivers	0.5 ± 0.5[a]	0.8 ± 0.5[ab]	1.0 ± 0.9[ab]	0.7 ± 0.7[ab]	1.6 ±0.9[b]	< 0.001
Interpersonal sensitivity						
Patients	0.4 ± 0.4[a]	0.6 ± 0.5[a]	0.6[b]	0.6[b]	1.7 ± 0.5[b]	< 0.001
Caregivers	0.7 ± 0.9	0.8 ± 0.5	1.0 ± 0.7	0.7 ± 0.5	0.7 ± 0.5	0.190
Phobia						
Patients	0.2 ± 0.4[ab]	0.4 ± 0.6[acd]	1.1 ± 1.2[bd]	1.6 ± 0.9[bd]	3.0 ± 0.6[b]	< 0.001
Caregivers	0.3 ± 0.6[a]	0.2 ± 0.4[abc]	0.4 ± 0.4[b]	0.1 ± 0.3[ac]	0.6 ± 0.3[ab]	< 0.001
Paranoid ideation						
Patients	0. 9 ± 1.2	1.6 ± 1.1	1.0 ± 1.0	1.3 ± 1.5	1.2 ± 1.5	0.330
Caregivers	0.7 ± 1.0	1.1 ± 0.9	0.8 ± 0.9	1.2 ± 1.0	1.5 ± 1.4	0.220
Psychoticism						
Patients	0.1 ± 0.2[ac]	0.1 ± 0.4[ac]	0.3 ± 0.4[abc]	0.4 ± 0.3[b]	0.3 ± 0.3[abc]	< 0.001
Caregivers	0.2 ± 0.6	0.1 ± 0.4	0.2 ± 0.4	0.0 ± 0.1	0.1 ± 0.2	0.120
GSI						
Patients	0.6 ± 0.3	0.9 ± 0.3	1.4 ± 0.4	1.4 ± 0.5	1.93 ± 0.33	< 0.001
Caregivers	0.4 ± 0.4	0.6 ± 0.4	0.7 ± 0.3	0.6 ± 0.3	0.8 ± 0.2	< 0.001

GSI: global severity index. Data were given as mean±standard deviation..

instability than the patients whose manifestations of PD were tremor, hypokinesia, and rigidity.

DISCUSSION

We investigated the prevalence of psychiatric symptoms in patients with PD and their caregivers, the association between psychiatric symptoms and demographic characteristics, and the influence of severity and manifestations of the PD on psychiatric distress of patients and caregivers.

The findings revealed that the prevalence of psychiatric distress was high in PD patients (47.2%) and their caregivers (18.4%). Similar to this finding, a study assessing depression and anxiety reported 50% psychological distress in 513 patients with PD annually for up to four years.[22] Also, a systematic review of 10 studies of mood and anxiety fluctuations in PD patients with motor fluctuations reported that the frequency of psychiatric disorders was as follows: anxiety ranged from 3.1% to 67.7% with a weighted mean of 35.4%, depressive symptoms from 2.1% to 71.4% with a weighted mean of 34.9%, and panic symptoms ranged from 3.1% to 54.5% with a weighted mean of 37.1% 8. The differences of prevalence may be related to the type of study, the diversity of assessment tools, diversity of cutoff points of depression tools, and sociocultural heterogeneity of nations.

The results indicated that female sex, city residency, and having medical disease were risk factors for more serious psychiatric symptoms in PD patients. In line with this study, Leentjens et al,[23] reported that female sex was a risk factor for depression in PD. Another study reported that physical disease was a risk factor for mental disorders

in PD.[24] In contrast to our results, some researchers reported that older age, being single, a low level of education, and smoking were the risk factors of psychiatric disorders in PD patients.[24,25]

The findings emphasized that the greater the severity of PD, the larger the psychiatric distress (GSI scores) will be in PD patients. PD patients in higher stages of disease significantly suffered from somatization, anxiety, interpersonal sensitivity, OCD, and phobia compared to those with lower disease severity. As prior studies emphasized the influence of biological factors on the stage of PD,[26] and this was the first study of its kind examining psychiatric symptoms with a comprehensive tool for problems in PDCs, we could not find any study to compare their results against ours. Nevertheless, a study revealed that advanced PD stage was a risk factor for depressive symptoms in PD patients.[27] Although mental disorders often occur in the elderly with other illnesses,[28,29] psychiatric disorders are more frequent in PD patients, especially as the disease progresses.[30]

The findings emphasized that PD influenced the psychiatric symptoms of caregivers. A higher stage of PD was associated with higher scores of phobia, somatization, and psychiatric distress among caregivers. Although we did not find any published study to report all psychiatric symptoms in PD caregivers, evaluations of some symptoms have been reported. In line with our results, a recent study indicated that the stress level among PDCs was correlated with the duration and severity of PD in patients.[31] Another study reported that PDCs had more severe depression, greater tiredness, and less life satisfaction compared with the healthy elderly population.[32]

Our findings revealed that female sex, lower education level, single status, village residency, and having chronic disease were risk factors for more serious psychiatric symptoms in PDCs. A study reported that the severity of stress in caregivers was correlated with their gender.[31] Similar to this result, a study reported that PDCs had more anxiety and depressive symptoms than their male counterparts.[8]

Among four major cardinal manifestations of PD, only postural instability was associated with a higher score of somatization, phobia, and psychiatric distress compared to tremor, hypokinesia, and rigidity. A cohort study showed that higher scores of postural instability and gait difficulty were associated with more depression and anxiety in PD patients. Also, the postural instability score, rather than the tremor score, was associated with PD severity and prognosis.[33] Another study highlighted that presence of motor fluctuations increased the psychiatric symptoms in PD patients. Also, it reported that the presence of dyskinesias was a predictor for depression in PD.[23]

In contrast with previous research, we found that postural instability, rather than tremor, was associated with PD severity. We postulate that postural instability, regardless of other factors, may cause or exacerbate psychiatric disorders in PD. Some evidence supports our hypothesis. Initially, postural instability increases the risk of psychotic symptoms (odds ratio (OR) = 3.02, 95% confidence interval (CI): 1.41–6.49) and depression (OR = 1.08, 95% CI: 1.01–1.15).[34] PD patients with postural instability fear of falling and fractures. Also, balance dysfunction, considered a social stigma, may cause PD patients to worry about falling in public and becoming embarrassed.[35] Secondly, recent evidence suggests that postural instability may provide an evaluation of disease severity and progression in PD patients.[36] Finally, the severity of postural instability is a useful indicator of the status and prognosis in PD.[33]

This study had some limitations, which may limit its generalizability. First, it was performed in an outpatient clinic, so patients with severe motor disabilities who were unable to move could not be included. Thus, this study cannot be generalized to the high stages of the PD (stage 5). Secondly, we did not assess the influence of the use of levodopa or dopamine agonists on psychiatric symptoms. The psychiatric symptoms seen in PD patients may be primarily a psychiatric response to the disease or a side effect of levodopa therapy. In the future, a cohort study should be conducted to assess the influence of PD-specific risk factors (increased disease duration, more severe motor symptoms, and the use of levodopa), and non-PD-specific risk factors (demographic characteristics) on the prevalence and severity of psychiatric symptoms in PD patients. Finally, the results were obtained from a cross-sectional model and should be confirmed in a large longitudinal design examining the influence of more factors affecting PD patients' psychiatric symptoms.

Our findings have important conceptual implications for clinical settings. The study

suggested that neurologists should pay more attention to the relationship between the severity of PD and psychiatric distress in both patients and their caregivers. It seems that management of PD, especially in higher stages, requires adjuvant psychological supportive therapy for both patients and their caregivers. This study implied that the manifestation of postural instability might increase the risk of psychiatric symptoms in PD patients. Further studies with a cohort design are required to determine the role of postural instability in the initiation and progression of PD. Based on these results, a broader approach should be followed in future studies into the etiology of psychiatric factors in the progression of PD.

CONCLUSION

The prevalence of psychiatric distress was high in both PD patients and their caregivers. Neurologists must pay more attention to the relationship between severity of PD and psychiatric distress in PD patients and their caregivers, especially in higher stages of PD with the manifestation of postural instability, which requires adjuvant psychological supportive therapy for patients and their caregivers.

Disclosure

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