

Psychiatric symptoms in patients with Parkinson's disease and caregivers

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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. The study aimed to examine the prevalence of psychiatric symptoms among PD and caregivers, demographic risk factors, and the influence of severity and manifestations of the PD on psychiatric distress.

Methods: In a descriptive cross-sectional study, 125 PD patients and 125 their primary caregivers were included. The severity of PD was evaluated according to the Hoehn and Yahr severity (H&Y) from the Movement Disorder Society-Sponsored Revision of the Unified Parkinson's Disease Rating Scale (MDS-UPDRS). PD patients and their caregivers filled Symptom Checklist-25 (SCL-25) to the presence of psychiatric distress were detected by SCL-

25. Also, demographic factors including age, high level of education, occupation, place of 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 gender, residency in city, and medical disease were risk factors for more psychiatric symptoms in PD patients. Also, the female gender, single status, residency in village, and having medical disease were risk factors for greater psychiatric symptoms in Parkinson's disease caregivers. PD patients in more advanced stages of disease suffered significantly from psychiatric distress, somatization, anxiety, interpersonal sensitivity, Obsessive-Compulsive Disorder, and phobia as 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. Higher stage of PD is associated with higher scores of psychiatric distress, phobia, and somatization in the patients and their caregivers.

Keywords: Parkinson, Psychiatric distress, Caregiver, Depression, Anxiety

INTRODUCTION

Parkinson's Disease (PD) is the second most common neurodegenerative disorder. The overall prevalence of PD is 1% in population over 60 years of age.¹ A study on the demography of PD in Iran revealed that the most frequent age of onset of PD was between 51 and 60 years. Also, 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 as 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 Parkinson's patients.⁷

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

Evidence suggests that the identification and treatment of psychiatric disorders in patients with PD and PDC have remained neglected.^{14,15} To the best of our knowledge, this study is the first to simultaneously provide data on the psychiatric symptoms of both patients /PDC and associations with severity of the Parkinson's disease. The aim of the study was to determine the prevalence of psychiatric symptoms among Parkinson patients and Parkinson's disease caregivers. The second purpose of the study was to examine the possible association between psychiatric symptoms and the socio-demographic plus clinical risk factors. The study also intended to assess the influence of severity of PD on psychiatric distress in patients and caregivers. Finally, the association between severity of PD and psychiatric distress in patients and caregivers was inspected.

METHODS

This is a descriptive cross-sectional study in a group of PD patients, 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 city (North of Iran) from May to November 2019. A total of 125 PD patients and 125 their primary caregivers were included in the study.

Sample size calculation

The sample size was determined as 150 PD patients and their caregivers assuming that 65% of caregivers have psychiatric disorders¹⁶ 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 with Parkinson Disease

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 the following criteria were excluded from the study; secondary causes of a Parkinsonian syndrome including history of repeated strokes or head injury, Parkinson's syndrome caused by taking neuroleptics, significant cognitive impairment preventing the patient from filling the questionnaire or providing informed consent. Also, PD patients who did not have capacity to self-report reliable information were excluded from the study to prevent possible alterations in data collection.

At the time of their recruitment, one member of the research team (a medical student) explained the study for PD and their caregivers and invited them to enter the study. She explained the goals and the questionnaires of the research. Then, she assessed the inclusion/exclusion criteria for the PD. After 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.¹⁷ He evaluated and managed the PD course, obtained the clinical records of the patients as well as disease information. Also, the severity of PD was evaluated according to the Hoehn and Yahr severity (H&Y)¹⁸ from the Movement Disorder Society-Sponsored Revision of the Unified Parkinson's Disease Rating Scale (MDS-UPDRS).¹⁹ Further, 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).

Parkinson's Disease Caregivers

The medical student assessed the inclusion/exclusion criteria for the primary caregiver of the PD. In this study, 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 education level higher than primary school were invited the study. However, the PDCs who did not have the capacity to self-report reliable information were excluded from the study to prevent possible alterations in data collection. A total of 125 eligible Parkinson's disease caregivers completed two questionnaires including demographic questionnaire and Symptom Checklist-25 (SCL-25).

Ethical Consideration

This research was approved by the ethics committee of Babol university of Medical Sciences (IR.MUBABOLHRI.REC.1398.121). Also, all PD patients and PDCs provided written informed consent to participating in the study.

Outcome Measures

Severity of PD

We assessed the severity of PD with Hoehn and Yahr (H&Y) severity and MDS-UPDRS.

Hoehn and Yahr (H&Y) severity: It 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 including: 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

Movement Disorder Society-Sponsored Revision of the Unified Parkinson's Disease Rating Scale (MDS-UPDRS): It 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.

Assessment of psychiatric distress

Symptom Checklist-25 (SCL-25): It is a brief form of SCL-90 with 25 questions in a Likert 0-4 scale including never (0), a few (1), somewhat (2), great (3) and very great or severe (4). The scale covers eight subscales including somatization, obsessive-compulsive, interpersonal sensitivity, phobia, depression, anxiety, paranoid ideation, and psychoticism. Raw scores were calculated through 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, via dividing the sum of scores of all questions by the number of questions. We used the Iranian version of SCL-25 whose suitable validity (Cronbach's 0.97) and reliability (re-test coefficients 0.78) had already been approved.²⁰ The current study would use a cutoff GSI ≥ 1.75 to define psychiatric distress.²¹

Statistical analysis

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 (PDC), as well as in categorical demographic variables such as age, education, and occupation. Also, Spearman test was applied to assess the correlation between variables. To examine the relationship between demographic characteristics of PD patients/PDC, Chi square tests was used. 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 (version 25.0, IBM, Chicago, IL, USA) software. The Statistical significance was determined as a $P < 0.05$, where all P values were two-tailed.

RESULTS

Baseline demographics of PD patients and Parkinson's disease caregivers

Table 1 describes the demographic characteristics of the participants. The mean age of the PD patients was 67.86 ± 10.13 years. A total of 52.8% of patients were men and 73% of them lived with their spouse. A large proportion of the patients had primary school education (81.6%), 18.4% were employed, and more than 50% lived in city.

The severity of PD cases with H&Y scale was stage 1 (n = 0), stage 2 (n = 21, 16.8%), stage 2.5 (n = 25, %20), stage 3 (n = 20, 16%), stage 4 (n = 8, 6.4%), and stage 5 (n = 0). Thus, nearly

52.8% were in stages 2 to 3. The duration of PD illness was 3.8 (SD=3.10.) years within a range of 1 to 20 years. The frequency of major cardinal manifestations of PD was tremor 65.6%, hypokinesia 22.4%, postural instability 9.6%, and rigidity 2.4%.

The mean age of Parkinson's disease caregivers was 50.54±14.86 ranging from 21 to 86 years. Most caregivers were women (58.4%); 91.2% of PDC were married; and 54% lived in city. About half of the PDCs had primary school education (51%) and 54% were employed. The relationship between caregivers and PD patients was as follows: 32% spouse, 66% daughter/son, and 2% sister/brother.

Prevalence of psychiatric distress in PD patients and caregivers

Table 2 reports the prevalence of psychiatric distress in PD patients and caregivers. The mean score of GSI was 1.05±0.58 for PD patients. The prevalence of overall rate of psychiatric distress ($GSI \geq 1$) for PD patients was 47.2%. Also, the total rate of psychiatric distress ($GSI \geq 1$) for caregivers of PD patients was 18.4%.

The results of this study showed (based on the mean score each subscale of SCL-25 ≥ 1) that the rate of psychiatric symptoms for PD patients was as follows; somatization 91.1%, OCD 67.2%, interpersonal sensitivity 71.2%, phobia 48%, depression 61.6%, anxiety 88.8%, paranoid ideation 58.4%, and psychoticism 19.2%.

The mean score of GSI was 0.61±0.41 for caregivers. The rates of psychiatric symptoms for caregivers (based on the mean score each subscale SCL-25 ≥ 1) were as follows: somatization 48.4%, OCD 39.2%, interpersonal sensitivity 38.4%, phobia 15.2%, depression 22.4%, anxiety 56.8%, paranoid ideation 29.%, and psychoticism 7.2%.

Association between psychiatric symptoms and the demographic factors

Table 3 reports the results of the t-tests on comparison of psychiatric symptoms according to the demographics of patients and caregivers. Women with PD had more psychotic symptoms than men ($P=0.04$). Also, PD patients who lived in city had more psychotic symptoms than those living in village ($p=0.04$). The mean scores of somatization and interpersonal sensitivity in PD patients who had medical disease were greater than those of individuals without medical disease ($P<0.05$).

Female Parkinson disease caregivers had higher scores in somatization, anxiety, and interpersonal sensitivity than male PDCs ($P<0.05$). The depressive symptoms had larger scores in the divorced PDCs as compared to married counterparts ($p=0.01$). PDCs who lived in village had larger somatization scores than those living in city ($p=<0.001$). The somatization score in smoker PDCs was higher than among non-smokers ($p=<0.001$). The mean scores of somatization and interpersonal sensitivity in PDCs who had medical disease were higher than those of subjects without medical disease ($P<0.05$).

The influence of severity of PD on psychiatric symptoms in patients and caregivers

Table 4 provides the results of ANOVA tests and on post-hoc Tukey's multiple comparison of mean psychiatric symptoms and of 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 that in stage 1.5 (2.06 ± 0.63 vs 0.97 , $p=0.002$) and in stage 2.5 (2.06 ± 0.63 vs 1.74 ± 0.86 , $p=0.001$). The PD patients in stage 2.5 significantly suffered from anxiety symptoms more than patients in stage 1.5 (1.45 ± 0.65 vs 0.92 ± 0.53 , $p=0.005$) and in stage 3 (0.92 ± 0.53 vs 2.05 ± 1.02 , $p=<0.001$) did. The mean OCD symptoms of PD patients in stage 4 were significantly higher than in stage 1.5 (2.33 ± 0.73 vs 0.66 ± 0.81 , $p=<0.001$). The PD patients in stage 4 significantly suffered from

phobia symptoms more than those in stage 1.5 (3.08 ± 0.68 vs 0.26 ± 0.46 , $p < 0.001$) and in stage 2 (3.08 ± 0.68 vs 0.43 ± 0.68 $p < 0.001$) did. Also, the mean interpersonal sensitivity in patients with stage 4 was significantly higher than the mean in stage 1.5 (1.78 ± 0.56 vs 0.48 ± 0.42 , $p < 0.001$) and in stage 2 (1.78 ± 0.56 vs 0.65 ± 0.54 $p = 0.003$).

According to Table 3, 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 those of patients with stage 1.5 (0.91 ± 0.50 vs 0.56 ± 0.60 , $p = 0.03$).

The caregivers of patients in stage 4 suffered from phobia symptoms more significantly than those of patients in stage 1.5 (0.62 ± 0.37 vs 0.33 ± 0.69 , $p = 0.04$) and in stage 3 (0.62 ± 0.37 vs 0.13 ± 0.31 , $p = 0.01$) did.

Association between four major cardinal manifestations of PD and psychiatric distress

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

DISCUSSION

This study investigated the prevalence of psychiatric symptoms in 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 both PD patients (47.2%) and their caregivers. (18.4%). Similar to this finding, a study assessing the depression and anxiety reported 50% psychological distress in 513 patients with PD annually for up to 4 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 2.1% to 71.4%, with a weighted mean of 34.9%, 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, residency in city, and having medical disease were risk factors for more serious psychiatric symptoms in PD patients. In line with this study, Leentjens et al. (2013) reported that female sex was a risk factor for depression in PD.²³ Another study reported that physical disease was a risk factor for mental disorders in PD.²⁴ In contrast to our results, some research 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 as compared to those with a lower severity of disease. As prior studies emphasized the influence of biological factors on the stage of PD²⁶, and this was the first study of its kind examining psychiatric symptoms with a comprehensive tool for problems in caregivers of PD patients, 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 elderly population with other illnesses^{28,29}, psychiatric disorders

are more frequent in PD patients than in other illness patients, especially in progression of PD patients.³⁰

The findings emphasized that Parkinson disease influenced the psychiatric symptoms of caregivers. Higher stage of Parkinson disease 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 Parkinson's disease caregivers, evaluations of some symptoms have been reported. In line with our results, a recent study indicated that stress level among caregivers of PD was correlated with the duration and severity of PD in patients.³¹ Another study reported that caregivers of PD patients had more severe depression, greater tiredness, and less satisfaction with life compared with healthy elderly population.³²

Our findings revealed that female gender, lower education level, single status, residency in village, and having medical disease were risk factors for more serious psychiatric symptoms in caregivers of PD patients. A study reported that severity of stress in caregivers of PD patients was correlated with their gender.³¹ Similar to this result, a study reported that Parkinson's disease caregivers 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 as 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 severity and prognosis of Parkinson disease.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 severity of PD. As an explanation, we postulate that postural instability, regardless of other factors, may cause or exacerbate psychiatric disorders in Parkinson's patients. Some evidence supports our hypothesis. Initially, postural instability increases the risk of psychotic symptoms (OR 3.02, 95%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 as social stigma, may cause PD patients to worry about being embarrassed because of falling in public.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 few 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 at all could not be included. Thus, this study cannot be generalized to high stages of the PD (stage 5). Secondly, we did not assess the influence of use of levodopa or the use of a dopamine agonist 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 future, a cohort study should be conducted to assess the influence of PD-specific risk factors (increased disease duration, more severe motor symptoms, 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 which should be confirmed in a large longitudinal design examining the influence of more factors affecting the psychiatric symptoms of PD patients.

Our findings have important conceptual implications for clinical settings. The study suggested that neurologists should pay more attention to the relationship between severity of

PD and psychiatric distress in both Parkinson 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 may 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 initiation and progression of Parkinson disease. Based on these results, a broader approach should be followed in future studies into the etiology of psychiatric factors in the progression of Parkinson disease.

CONCLUSION

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 both PD patients and their caregivers, especially in higher stages of PD with manifestation of postural instability, which requires adjuvant psychological supportive therapy for PD patients and their caregivers.

Abbreviations

PD: Parkinson's Disease; PDC: Parkinson's Disease; MDS-UPDRS: Movement Disorder Society-Sponsored Revision of the Unified Parkinson's Disease Rating Scale; GSI: Global Severity Index, SCL-25: Symptom Checklist-25; OCD: Obsession-Compulsion Disorder

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Authors Contributions

PS was the principal investigator of this study. MF and PS contributed the development, handling, monitoring of the project, and writing the manuscript. FS contributed to gathering the data and the development of the project and of the study. SK performed the statistical analyses. All authors contributed to the drafting of this paper and approved the final manuscript

Ethics approval and consent to participate

This study was approved by Ethics Committee of Babol University of Medical Sciences (IR.MUBABOLHRI.REC.1398.121). Anonymity and confidentiality for participants were guaranteed. All students wrote the informed consent at the beginning of the study.

Declaration of Conflict of Interests

The authors declare no conflict of interest.

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Table 1. Demographic characteristics of the patients with Parkinson 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)	37(29.6)
	University	13(10.4)	24(19.2)
Job	Employed	34(18.4)	67(53.6)
	Unemployed	91(72.8)	58(46.4)
Place Of Living	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, Diabetes and...

Table 2. The prevalence of psychiatric distress in patients with Parkinson disease and caregivers

Psychiatric symptoms	patients/ Caregivers	Patients with Parkinson disease N=125 n (%)	Parkinson's Disease Caregivers N=125 n (%)
	Somatization		77 (61.6)
Depression		111 (88.8)	71 (56.8)
Anxiety		114 (91.2)	61 (48.4)
Obsession Compulsion		89 (71.2)	48 (38.4)

Interpersonal Sensitivity	84 (67.2)	49 (39.2)
Phobia	60 (48.0)	19 (15.2)
Paranoid ideation	73 (38.4)	37 (29.6)
Psychoticism	24 (19.2)	9.0 (7.2)
*GSI \geq 1	59 (47.2)	23 (18.4)

*GSI: Global Severity Index

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

Symptoms	Somatization Mean \pm SD	
	patient	Care givers
Demographic variables		
Gender male female P Value	1.36 \pm 0.78 1.36 \pm 0.79 0.98	0.60 \pm 0.53 0.94 \pm 0.63 <0.001
Education Primary School High School University P Value	1.35 \pm 0.79 1.35 \pm 0.50 1.46 \pm 0.91 0.85	0.88 \pm 0.59 0.66 \pm 0.60 0.78 \pm 0.68 0.05
Job Employed Unemployed P value	1.39 \pm 0.67 1.35 \pm 0.82 0.68	0.90 \pm 0.66 0.68 \pm 0.53 0.06
Place Of Living Urban Rural P value	1.30 \pm 0.82 1.41 \pm 0.74 0.29	0.66 \pm 0.54 0.97 \pm 0.66 <0.001
Smoking Yes No P value	0.90 \pm 0.70 1.41 \pm 0.78 0.20	0.48 \pm 0.41 0.87 \pm 0.63 <0.001
Chronic Disease Yes No P value	1.49 \pm 0.80 1.12 \pm 0.71 0.03	1.30 \pm 0.60 0.63 \pm 0.52 <0.001
Symptoms of Parkinson Tremor Brady Kinesiya Rigidity Impaired Balance P value	1.22 \pm 0.81 1.62 \pm 0.58 1.00 \pm 0.73 1.75 \pm 0.80 <0.001	0.77 \pm 0.63 0.80 \pm 0.54 0.94 \pm 0.48 0.97 \pm 0.63 0.65

Depression		Anxiety		OCD		Interpernal Sensivity		Phobia		Paranoid ideation		Psychoticism	
Mean±SD		Mean±SD		Mean±SD		Mean±SD		Mean±SD		Mean±SD		Mean±SD	
patient	Care givers	patient	Care givers	patient	Care givers	patient	Care givers	patient	Care givers	patient	Care givers	patient	Care givers
0.70±0.75	0.51±0.64	1.19±0.67	0.25±0.47	1.31±1.11	0.77±0.74	0.90±0.71	0.65±0.75	0.90±1.20	0.26±0.55	1.03±1.14	0.98±1.04	0.16±0.28	0.18±0.58
0.93±0.93	0.42±0.70	1.38±0.89	0.63±0.58	1.11±0.96	0.81±0.76	0.92±0.69	0.92±0.82	0.81±1.00	0.37±0.55	1.30±1.40	0.98±1.07	0.31±0.44	0.20±0.46
0.21	0.25	0.36	<0.001	0.31	0.76	0.92	0.03	0.94	0.05	0.43	0.96	0.04	0.07
0.74±0.84	0.45±0.64	1.30±0.80	0.51±0.58	1.18±1.04	0.82±0.76	0.87±0.70	0.81±0.80	0.81±1.06	0.33±0.56	1.07±1.28	0.91±1.00	0.22±0.35	0.19±0.50
1.20±0.82	0.50±0.80	0.77±0.57	0.47±0.61	1.37±0.99	0.85±0.73	1.10±0.69	0.74±0.81	0.97±1.62	0.36±0.63	1.90±1.29	0.81±1.08	0.23±0.52	0.19±0.61
1.04±0.80	0.42±0.60	1.49±0.62	0.38±0.48	1.38±1.14	0.64±0.74	1.10±0.67	0.90±0.80	1.18±1.08	0.25±0.38	1.31±1.03	1.46±1.06	0.31±0.44	0.18±0.37
0.05	0.80	0.04	0.57	0.54	0.76	0.26	0.67	0.81	0.99	0.70	0.45	0.70	0.51
0.87±0.83	0.51±0.78	1.32±0.87	0.46±0.54	1.25±1.06	0.75±0.76	0.92±0.73	0.81±0.73	0.95±1.25	0.26±0.46	1.26±1.29	1.03±1.07	0.24±0.35	0.13±0.26
0.79±0.85	0.40±0.60	1.26±0.75	0.50±0.60	1.20±1.04	0.84±0.74	0.91±0.69	0.82±0.88	0.82±1.06	0.39±0.64	1.12±1.27	0.93±1.04	0.23±0.38	0.26±0.67
0.41	0.45	0.60	0.98	0.59	0.48	1.00	0.53	0.57	0.21	0.55	0.49	0.66	0.32
0.84±0.84	0.49±0.81	1.30±0.86	0.50±0.60	1.28±1.04	0.88±0.81	0.88±0.63	0.77±0.72	0.73±0.98	0.31±0.52	0.98±1.23	0.94±1.06	0.27±0.37	0.18±0.50
0.78±0.86	0.42±0.49	1.26±0.71	0.44±0.53	1.14±1.05	0.68±0.66	0.94±0.76	0.85±0.89	0.99±1.22	0.34±0.59	1.23±1.29	1.03±1.05	0.19±0.37	0.21±0.53
0.55	0.50	0.86	0.84	0.45	0.22	0.84	0.97	0.28	0.99	0.09	0.54	0.04	0.49
0.86±0.86	0.73±0.83	0.69±1.07	0.40±0.65	1.23±1.15	0.71±0.82	0.61±0.45	0.80±0.93	0.33±0.52	0.33±0.74	1.15±1.07	1.04±1.09	.26±0.45	0.35±0.81
0.70±0.82	0.40±0.63	0.82±0.82	0.49±0.55	1.21±1.03	0.84±0.75	0.95±0.71	0.81±0.77	0.92±1.15	0.33±0.51	1.16±1.30	0.97±1.05	0.23±0.36	0.26±0.42
0.40	0.07	0.28	0.36	0.15	0.34	0.15	0.67	0.09	0.17	0.75	0.76	0.89	0.80
1.26±0.80	0.48±0.61	1.00±0.56	0.60±0.56	1.22±1.03	0.840.79	1.00±0.68	1.09±0.79	1.00±1.18	0.35±0.52	1.21±1.32	1.13±1.15	0.20±0.33	0.21±0.59
1.30±0.76	0.45±0.70	1.31±0.80	0.43±0.56	1.20±1.06	0.78±0.74	0.76±0.72	0.720.79	0.59±0.89	0.31±0.56	1.07±1.19	0.94±1.02	0.29±0.43	0.17±0.54
0.66	0.49	0.19	0.07	0.98	0.73	0.06	<0.001	0.08	0.40	0.71	0.44	0.39	0.05
0.75±0.85	0.52±0.78	1.25±0.77	0.48±0.59	1.05±0.96	0.73±0.70	0.23±0.38	0.79±0.86	0.65±0.96	0.33±0.61	0.19±0.37	0.83±0.97	0.19±0.37	0.20±0.59
0.90±0.80	0.27±0.35	1.29±0.73	0.57±0.56	1.42±1.2	0.87±0.79	0.30±0.42	0.84±0.70	0.90±1.03	0.33±0.44	0.25±0.33	1.11±1.10	0.25±0.33	0.24±0.38
0.33±0.58	0.33±0.58	1.44±0.38	0.08±0.14	0.89±0.77	0.44±0.19	0.18±0.26	0.56±0.60	1.00±1.20	0=0	0.33±0.58	1.67±1.53	0.33±0.58	0=0
1.13±0.93	0.54±0.50	1.39±1.09	0.35±0.48	1.13±0.93	1.11±1.02	<0.001	0.92±0.64	2.19±1.42	0.45	0.42±0.38	1.58±1.24	0.42±0.38	0.06±0.19
0.30	0.45	0.81	0.47	0.07	0.59	<0.001	0.57	<0.001	0.45	<0.001	0.11	0.08	0.11

GSI Mean±SD		patient	Care givers
0.94±0.56 1.19±0.51 0.93±0.38 1.54±0.65 <0.001	0.60±0.44 0.64±0.37 0.44±0.18 0.68±0.35 0.60	1.11±0.59 0.94±0.57 0.15	0.81±0.35 0.55±0.41 <0.001
0.78±0.44 1.09±0.59 0.90	0.57±0.52 0.62±0.30 0.21	1.03±0.58 1.07±0.58 0.70	0.59±0.43 0.64±0.39 0.28
1.10±0.60 1.04±0.58 0.58	0.60±0.41 0.60±0.42 0.59	1.02±0.59 1.13±0.59 1.23±0.51 0.59	0.64±0.39 0.59±0.46 0.57±0.42 0.51
1.03±0.58 1.08±0.59 0.59	0.51±0.40 0.69±0.41 <0.001		

Table 4. Relationship between Parkinsons Stage and psychiatric symptoms in patients and caregivers

Parkinson's stage Symptoms	1.5 Mean±SD	2 Mean±SD	2.5 Mean±SD	3 Mean±SD	4 Mean±SD	P Value	Overall population
Somatization Patients Caregivers	0.97±0.71 ^a 0.56±0.60 ^a	1.25±0.56 ^{ab} 0.94±0.57 ^{ab}	1.74±0.86 ^b 0.91±0.50 ^{ab}	1.69±0.57 ^b 1.05±0.74 ^b	2.06±0.63 ^b 0.94±0.38 ^{ab}	<0.001 <0.001	
Depression Patients Caregivers	0.45±0.68 ^a 0.26±0.49	0.79±0.78 ^a 0.86±1.17	1.08±0.77 ^b 0.54±0.54	1.03±0.92 ^{ab} 0.42±0.46	1.75±0.92 ^{ab} 0.50±0.37	<0.001 0.03	
Anxiety Patients Caregivers	0.92±0.53 ^a 0.36±0.55	1.13±0.64 ^{ac} 0.58±0.64	1.45±0.65 ^b 0.62±0.58	2.05±1.02 ^b 0.42±0.43	1.50±0.71 ^{ab} 0.36±0.70	<0.001 0.18	

OC Patients Caregivers	0.66±0.81 ^a 0.52±0.53 ^a	1.14±0.90 ^{ab} 0.87±0.55 ^{ab}	1.81±0.93 ^b 1.05±0.94 ^{ab}	1.50±1.13 ^b 0.75±0.77 ^{ab}	2.33±0.73 ^b 1.62±0.93 ^b	<0.001 <0.001	
Interpersonal Sensitivity Patients Caregivers	0.48±0.42 ^a 0.75±0.99	0.65±0.54 ^a 0.82±0.57	1.33±0.6 ^b 1.00±0.75	1.41±0.66 ^b 0.72±0.57	1.78±0.56 ^b 0.79±0.56	<0.001 0.19	
Phobia Patients Caregivers	0.26±0.46 ^{ab} 0.33±0.69 ^a	0.43±0.68 ^{acd} 0.21±0.41 ^{abc}	1.11±1.23 ^{bd} 0.47±0.47 ^b	1.63±0.97 ^{bd} 0.13±0.31 ^{ac}	3.08±0.68 ^b 0.62±0.37 ^{ab}	<0.001 <0.001	
Paranoid ideation Patients Caregivers	0.94±1.22 0.78±1.06	1.62±1.17 1.19±0.98	1.08±1.08 0.88±0.93	1.30±1.59 1.20±1.06	1.25±1.58 1.50±1.41	0.33 0.22	
Psychoticism Patients Caregivers	0.11±0.28 ^{ac} 0.22±0.68	0.17±0.41 ^{ac} 0.14±0.40	0.31±0.41 ^{abc} 0.29±0.44	0.43±0.38 ^b 0.08±0.18	0.38±0.37 ^{abc} 0.12±0.24	<0.001 0.12	
*GSI Patients Caregivers	0.62±0.36 0.47±0.47	0.93±0.35 0.69±0.42	1.41±0.43 0.77±0.30	1.49±0.50 0.61±0.34	1.93±0.33 0.82±0.23	<0.001 <0.001	

*GSI: Global Severity Index