

Neuropsychiatric Symptoms and Caregiver Burden in Parkinson's Disease

Abhishek Juneja, Kuljeet Anand, Mina Chandra¹, Smita Deshpande¹, Rajinder Dhamija², Parul Kathuria¹, Rahul Mahajan

Department of Neurology and ¹Psychiatry, Dr. RML Hospital, Delhi, ²Department of Neurology, LHMC and Sucheta Kriplani Hospital, Delhi, India

Abstract

Objective: Parkinson's disease (PD) is a neurodegenerative disorder. It has a significant impact on the quality of life of patients and their caregivers. The present study aims to study the phenomena of neuropsychiatric symptoms and their association with caregiver burden in PD. **Methods:** The study was conducted in 100 patients of Parkinson's disease and their primary caregivers. The patients of PD were diagnosed on the basis of UK Brain Bank criteria; severity/staging of Parkinson's disease was done by Movement Disorder Society - Unified Parkinson's disease rating scale (MDS-UPDRS-III). Patients who fulfilled inclusion and exclusion criteria were recruited for the study. The neuropsychiatric evaluation was based on Neuropsychiatric Inventory-Questionnaire (NPI-Q). Caregiver burden was assessed with the Zarit Caregiver Burden Inventory (ZCBI). **Results:** Mean age of PD patients was 61.48 ± 6.71 years, majority of them were males (68%). Mean total NPI score of patients was 44.46 ± 5.38 . Mean age of caregivers was 52.26 ± 6.80 years, majority of them were females (72%) and spouse (76%) in relation to the patient. Caregiver burden was significantly related to age of the patient, duration of illness, severity of illness, and total NPI score. **Conclusion:** Neuropsychiatric symptoms significantly contribute to the caregiver burden in Parkinson's disease.

Keywords: Caregiver burden, neuropsychiatric symptoms, Parkinson's disease

INTRODUCTION

Parkinson's disease (PD) is a neurodegenerative disorder. It has a significant impact on the quality of life of patients and their caregivers. With disease progression, the patients require increasing assistance to carry out the activities of daily living. Caring for a PD patient in family is an extremely stressful process. It not only requires physical commitment, but also involves emotional and financial resources.^[1] Caregiver burden refers to physical, mental, social and financial problems encountered by the caregivers of patients with chronic disease.^[2] Factors affecting caregiver burden are related to both caregiver and patient characteristics, including clinical disease manifestations and complications.^[2] Neuropsychiatric symptoms (NPS), such as anxiety, depression, apathy, mental fatigue, and impulse control disorders (ICDs) affect up to 60%–80% of PD patients.^[3] Depression and anxiety can precede motor manifestations by several years. They are classified as nonmotor features that may be the early symptoms of PD.^[3] Presence of NPS is associated with increased caregiver burden in PD. This study aimed to study the phenomena of NPS and their association with caregiver burden in PD.

MATERIALS AND METHODS

This observational study commenced after taking approval from institutional ethical committee. The study was conducted in 100 patients of PD and their primary caregivers presenting to the Department of Neurology, ABVIMS and Dr. RML Hospital, New Delhi between January 2018 and April 2019. The patients of PD were diagnosed on the basis of UK Brain Bank criteria; severity/staging of PD was done by

Movement Disorder Society-Unified Parkinson's disease rating scale (MDS-UPDRS-III). All patients on levodopa therapy were assessed in the "on phase." Patients who fulfilled inclusion and exclusion criteria were recruited for the study. Written informed consent was taken from all the patients and their caregivers before enrolment in the study. Sociodemographic data and illness variables including duration of illness and treatment duration were collected and detailed clinical history and examination including neurological assessment was conducted. Participants of PD were included irrespective of treatment duration, age and sex, and duration of illness. Moderate to severe dementia was excluded using Clinical Dementia Rating Scale (CDR). The neuropsychiatric evaluation was based on Neuropsychiatric Inventory-Questionnaire (NPI-Q). Primary caregiver was defined as "person who, without being a professional or belonging to a social support network, usually lives with the patient and, in some way, is directly implicated in the

Address for correspondence: Dr. Abhishek Juneja,
A-15, Old Quarters, Ramesh Nagar, New Delhi 110 015, India.
E-mail: drabhishekjuneja@gmail.com

Submitted: 12-Feb-2020 **Revised:** 09-Apr-2020 **Accepted:** 20-Apr-2020

Published: 08-Jul-2020

This is an open access journal, and articles are distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 4.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as appropriate credit is given and the new creations are licensed under the identical terms.

For reprints contact: reprints@medknow.com

DOI: 10.4103/aian.AIAN_91_20

patient's care or is directly affected by the patient's health problem." The caregivers were asked to provide the following sociodemographic data: sex, age, level of education, nature of relationship with the patient, and the number of years caring for the patient. Caregiver burden was assessed with the Zarit Caregiver Burden Inventory (ZCBI).

Sample size calculation

NPS and caregiver's burden in PD was observed by Martinez-Martin *et al.*^[4] The study observed that out of 584 patients, 523 patients had NPS. Taking this value as reference, the minimum required sample size with 5% level of significance is 71 patients. Formula used is $N \geq ((p(1-p))/(ME/z_{\alpha})^2)$, Z_{α} = value of Z at two sided alpha error of 5%, ME = margin of error, and P = prevalence rate. We recruited 100 dyads of participants with PD and their primary caregivers in the study.

Sampling method

Consecutive sampling of registered patients of PD in Movement Disorder Speciality Clinic in Department of Neurology was done. Patients were assessed for the Study Criteria. All patients and primary caregivers providing written

informed consent were enrolled in the study till the desired sample size was reached.

Statistical analysis

Inferential statistics were used. Normality of data was tested by Kolmogorov–Smirnov test. Quantitative variables were correlated using Independent T test/Mann–Whitney test (when the data sets were not normally distributed) between NPS and Non NPS participants of PD. Qualitative variables were correlated by Chi-square test/Fisher exact test. A value of $P < 0.05$ was considered statistically significant. The data were analyzed using Statistical Package for Social Sciences (SPSS) software program, version 21.0.

RESULTS

The study was conducted in 100 dyads of PD patients and their primary caregivers. Mean age of patients was 61.48 ± 6.71 years. Most of the patients were male (68%). Patients were also studied for the duration and severity of their illness, along with the treatment regimen [Table 1]. NPS were recorded using Neuropsychiatric Inventory (NPI-Q). Mean total NPI score of patients was 44.46 ± 5.38 . Severity of NPS was recorded as mild, moderate and severe [Table 2].

Mean age of caregivers was 52.26 ± 6.80 years. Sociodemographic profile of caregivers is depicted in Table 3. Mean total ZBI score was 47.41 ± 4.58 . It was correlated with various clinical variables [Table 4]. Also, presence of various NPS was correlated with caregiver burden [Table 5].

DISCUSSION

In PD, motor symptoms and complications are well established factors that increase caregiver burden. Impact of nonmotor symptoms, including neuropsychiatric manifestations, on the caregiver burden needed to be evaluated further. Earlier, PD was reported to have less NPS compared to other synucleopathies.^[5] But, in recent years, many studies reported high prevalence of these symptoms

Table 1: Patient profile

Variable	Category	Frequency (%)
Gender	Male	68 (68)
	Female	32 (32)
Severity of PD (H & Y stage)	2	78 (78)
	3	22 (22)
Duration of Illness (years)	<5	12 (12)
	10-May	78 (78)
	>10	10 (10)
Treatment regime	Levodopa	8 (8)
	Levodopa + THP	86 (86)
	Dopamine agonists (PPX)	6 (6)
Comorbidity	Diabetes mellitus	14 (14)
	Hypertension	18 (18)

Table 2: Neuropsychiatric manifestations as per NPI Scores

NPI Domain	Severity			Frequency (%)
	Mild <i>n</i> (%)	Moderate <i>n</i> (%)	Severe <i>n</i> (%)	
Delusions	31 (31)	2 (2)	0 (0)	33 (33)
Hallucinations	17 (17)	1 (1)	0 (0)	18 (18)
Agitation/aggression	27 (27)	11 (11)	4 (4)	42 (42)
Depression	22 (22)	14 (14)	1 (1)	37 (37)
Anxiety	37 (37)	14 (14)	5 (5)	56 (56)
Elation/euphoria	13 (13)	2 (2)	0 (0)	15 (15)
Apathy/indifference	29 (29)	19 (19)	3 (3)	51 (51)
Disinhibition	13 (13)	3 (3)	0 (0)	16 (16)
Irritability	26 (26)	23 (23)	4 (4)	53 (53)
Aberrant motor Behavior	26 (26)	7 (7)	1 (1)	34 (34)
Sleep&Night time Behavior disorders	23 (23)	14 (14)	7 (7)	44 (44)
Appetite & eating disorders	28 (28)	5 (5)	0 (0)	33 (33)

Table 3: Caregiver profile

Variable	Category	Frequency (%)
Gender	Male	28 (28)
	Female	72 (72)
Relationship with patient	Spouse	76 (76)
	Adult child	24 (24)
No. of years caring	<5	12 (12)
	10-May	78 (78)
	>10	10 (10)

Table 4: Association between clinical variables of PD and caregiver burden

Correlation variables	Pearson's correlation coefficient	P
Total ZBI score Age of patient	0.352	0.001*
Total ZBI score Duration of illness	0.300	0.007*
Total ZBI score H & Y stage	0.536	0.000*
Total ZBI score Total NPI score	0.804	0.000*
Total ZBI score Education level of caregiver	0.022	0.850
Total ZBI score Type of relationship with patient	0.154	0.174
Total ZBI score No. of years caring	0.300	0.007*

*P value<0.05

Table 5: Correlation between neuropsychiatric symptoms and caregiver burden

Correlation variables	Pearson's correlation coefficient	P
Total ZBI score Delusion	0.175	0.120
Total ZBI score Hallucination	0.034	0.764
Total ZBI score Agitation	0.281	0.012*
Total ZBI score Depression	0.101	0.374
Total ZBI score Anxiety	0.338	0.002*
Total ZBI score Elation	0.142	0.211
Total ZBI score Apathy	0.329	0.003*
Total ZBI score Disinhibition	0.185	0.100
Total ZBI score Irritability	0.288	0.010*
Total ZBI score Aberrant motor behavior	0.208	0.064
Total ZBI score Sleep disorder	0.220	0.050*
Total ZBI score Eating disorder	0.210	0.061

* P value<0.05

in PD patients.^[6] Depression occurs in more than a half of geriatric PD patients impairing the quality of life.^[7] Also, psychosis is a frequent complication of PD, and it is characterized mainly by visual hallucinations and delusions. It affects up to 40 percent of PD patients, particularly those with dementia.^[8,9] Panic disorder, generalized anxiety disorder and social phobia are prevalent anxiety disorders in PD.^[10] Multiple previous studies have shown significant impact of patient's mood/apathy, psychotic symptoms, and disease duration on caregiver burden.^[11-14] In addition to screening for these factors, we specifically looked at patient's

NPS and their impact on caregiver burden so that appropriate intervention strategies could be devised.

The aim of this study was to assess the impact of NPS on caregivers' burden. In our study, caregivers were mostly middle-aged women who took care of a male patient/spouse, a profile coincident with most studies on PD caregivers.^[15,16] In this study, ZBI scores were significantly related to total NPI scores. Also, and in agreement with a previous study, other PD aspects such as motor impairment and disease severity were also related to caregiver burden.^[16] Different profiles of NPS were observed in this study using NPI scale. Caregivers reported significantly more burden when patients experienced NPS. ZBI scores were found to have significant correlation with different NPI domains including apathy, agitation, anxiety, irritability and sleep disorder. These results are in line with previous studies and highlight the need for carrying out complete neuropsychiatric assessments of PD patients in clinical practice.^[17]

Martinez *et al.*^[4] studied a sample of 584 pairs of PD patients and their primary caregivers. Patients' NPS were measured with the Scale for Evaluation of Neuropsychiatric Disorders in PD (SEND-PD), and the Zarit Caregiver Burden Inventory was used to quantify caregiver burden. The most frequent NPS were depression (in 66% of the sample), anxiety (65%) and mental fatigue (57%). The main determinants of caregiver burden were NPS including mood/apathy and psychosis, PD-related disability and disease duration.^[4] Similarly, in our study the most frequent NPS were anxiety (56%), irritability (53%) and apathy (51%) as per NPI scores. Also, in our study ZBI scores had significant correlation with H and Y stage of PD and duration of illness. Yoon-Sang *et al.*^[17] also studied 48 PD patients at two hospitals. Neuropsychiatric inventory (NPI) was applied to assess the frequency and severity of patient's mental and behavioral problems. Burden interview and caregiver burden inventory were used for evaluating caregiver burden. They found that all except one patient had at least one or more NPS. The most frequent three NPS were apathy and anxiety (70.8%), followed by depression (68.7%). Similar to our results, total NPI score had a significant correlation with both burden interview and caregiver burden inventory scores.^[17] Grun *et al.*^[18] assessed, in 59 patient-caregiver pairs, various motor, nonmotor, and cognitive symptoms as well as quality of life by standardized tests and questionnaires. Repercussions on the caregiver were evaluated by Zarit Burden Interview, Health-related Quality of Life (HrQoL), Generalized Anxiety Disorder Assessment-7, Patient Health Questionnaire-9, and the Montreal Cognitive Assessment. They found that sleep problems and autonomic dysfunction of the patient strongly impact caregiver burden and Health-related Quality of Life (HrQoL) of the caregiver. Higher CB is less strongly linked with patient's motor impairment.^[18] They concluded that in PD, the CB is primarily dependent on patients' nonmotor symptoms. Patient care requires considerable time investment and can trigger depression in the caregiver.^[18] These results were similar to

Table 6: Overview of major previous studies on neuropsychiatric symptoms and caregiver burden in Parkinson's disease

Study	Number of patients	Scales used	Main determinants of CB
Schrag <i>et al.</i> ^[19]	123	BDI, CBI	NPS (depression, hallucination), PD related disability
Martinez <i>et al.</i> ^[4]	584	SEND-PD, ZCBI	NPS (apathy, psychosis), PD related disability, Disease duration
Yoon-Sang <i>et al.</i> ^[17]	48	NPI-Q, CBI	NPS (delusion, hallucination, agitation, anxiety, irritability), H & Y stage
Álvarez-Avellón <i>et al.</i> ^[20]	100	NPI-Q, NPI-D	NPS (depression, apathy, anxiety)
Grun <i>et al.</i> ^[18]	59	GAD A-7, ZCBI	Nonmotor symptoms (sleep problems, autonomic dysfunction)

BDI=Beck Depression Inventory, CB=Caregiver burden, CBI=Caregiver Burden Inventory, CG=Caregivers, GAD Assessment-7=Generalized Anxiety Disorder Assessment-7, NPI-D=Neuropsychiatric Inventory Caregiver Distress Scale, NPI-Q=Neuropsychiatric Inventory-Questionnaire, NPS=Neuropsychiatric Symptoms, ZCBI=Zarit Caregiver Burden Inventory

our study where patients' NPS (nonmotor symptoms) had a significant relation to the caregiver burden.

Schrag *et al.*^[19] conducted a postal survey in 123 caregivers of patients with PD to assess caregiver-burden and factors associated with it. Over 40% of caregivers indicated that their health had suffered as a result of caregiving, almost half had increased depression scores, and two-thirds reported that their social life had suffered. After adjustment of disease duration, there was no difference in caregiver-burden between younger and older caregivers, or between male and female caregivers. This is in agreement to our study, where caregiver burden was not related to age or education level of caregiver. Nor was it related to the type of relationship between caregiver and patient. Álvarez-Avellón *et al.*^[20] studied 100 patients with PD using Neuropsychiatric Inventory-questionnaire (NPI-Q). They found that at least one NPS was present in more than 80% of participants. The most frequent symptom was depression, followed by apathy, anxiety, depression and hallucinations. In our study, frequent NPS were anxiety, irritability, apathy and sleep related disorder. They reported that nearly 60% of caregivers reported suffering a moderate to severe level of stress due to these symptoms [Table 6].

Hence, our study findings are in consonance with existing scientific literature from developed countries or high income settings. This is the first study exploring Caregiver burden in PD in low and middle income countries (LMIC). One of the limitations of this study was its cross-sectional observational nature. Longitudinal prospective studies are required to study the trend of caregiver burden in PD patients with NPS. Also, the study was carried out at a tertiary care center. The data thus acquired may not be generalizable to community settings. Based on the results, we concluded that NPS significantly contribute to the caregiver burden in PD.

Acknowledgment

Thanks to all patients and caregivers who participated in the study.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients

understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

REFERENCES

- McRae C, Sherry P, Roper K. Stress and family functioning among caregivers of persons with Parkinson's disease. *Parkinsonism Relat Disord* 1999;5:69-75.
- Martínez-Martín P, Forjaz MJ, Frades-Payo B, Rusiñol AB, Fernández-García JM, Benito-León J, *et al.* Caregiver burden in Parkinson's disease. *Mov Disord* 2007;22:924-31.
- Aarsland D, Marsh L, Schrag A. Neuropsychiatric symptoms in Parkinson's disease. *Mov Disord* 2009;24:2175-86.
- Martínez-Martín P, Rodríguez-Blázquez C, Forjaz MJ, Frades-Payo B, Agüera-Ortiz L, Weintraub D, *et al.* Neuropsychiatric symptoms and caregiver's burden in Parkinson's disease. *Parkinsonism Relat Disord* 2015;21:629-34.
- Kao AW, Racine CA, Quitania LC, Kramer JH, Christine CW, Miller BL. Cognitive and neuropsychiatric profile of the synucleinopathies: Parkinson disease, dementia with Lewy bodies, and multiple system atrophy. *Alzheimer Dis Assoc Disord* 2009;23:365-70.
- Aarsland D, Larsen JP, Tandberg E, Laake K. Predictors of nursing home placement in Parkinson's disease: A population-based, prospective study. *J Am Geriatr Soc* 2000;48:938-42.
- Dissanayaka NNW, Sellbach A, Silburn PA, O'Sullivan JD, Marsh R, Mellick GD. Factors associated with depression in Parkinson's disease. *J Affect Disord*. 2011 Jul; 132:82-8.
- Wint DP, Okun MS, Fernandez HH. Psychosis in Parkinson's disease. *J Geriatr Psychiatry Neurol* 2004;17:127-36.
- Forsaa EB, Larsen JP, Wentzel-Larsen T, Goetz CG, Stebbins GT, Aarsland D, *et al.* A 12-year population-based study of psychosis in Parkinson disease. *Arch Neurol* 2010;67:996-1001.
- Brown RG, Landau S, Hindle JV, Playfer J, Samuel M, Wilson KC, *et al.* Depression and anxiety related subtypes in Parkinson's disease. *J Neurol Neurosurg Psychiatry* 2011;82:803-9.
- O'Reilly F, Finnan F, Allwright S, Smith GD, Shlomo YB. The effects of caring for a spouse with Parkinson's disease on social, psychological and physical well-being. *Br J Gen Pract* 1996;46:507-12.
- Leroi I, Harbeshettar V, Andrews M, McDonald K, Byrne EJ, Burns A. Carer burden in apathy and impulse control disorders in Parkinson's disease. *Int J Geriatr Psychiatry* 2012;27:160-6.
- Viwattanakulvanid P, Kaewwilai L, Jitkritsadakul O, Brenden NR, Setthawatcharawanich S, Boonrod N, *et al.* The impact of the nocturnal disabilities of Parkinson's disease on caregivers' burden: Implications for interventions. *J Neural Transm* 2014;121(Suppl 1):S15e24.

14. Martinez-Martin P, Rodriguez-Blazquez C, Forjaz MJ. Quality of life and burden in caregivers for patients with Parkinson's disease: Concepts, assessment and related factors. *Expert Rev Pharmacoecon Outcomes Res* 2012;12:221-30.
15. Drutyte G, Forjaz MJ, Rodriguez-Blazquez C, Martinez-Martin P, Breen KC. What impacts on the stress symptoms of Parkinson's carers? Results from the Parkinson's UK Members' Survey. *Disabil Rehabil* 2014;36:199-204.
16. Lee AH, Weintraub D. Psychosis in Parkinson's disease without dementia: Common and comorbid with other non-motor symptoms. *Mov Disord* 2012;27:858-63.
17. Oh Y-S, Lee JE, Lee PH, Kim J-S. Neuropsychiatric symptoms in Parkinson's disease dementia are associated with increased caregiver burden. *J Mov Disord* 2015;8:26-32.
18. Grün D, Pieri V, Vaillant M, Diederich NJ. Contributory factors to caregiver burden in Parkinson disease. *J Am Med Dir Assoc* 2016;17:626-32.
19. Schrag A, Hovris A, Morley D, Quinn N, Jahanshahi M. Caregiver-burden in parkinson's disease is closely associated with psychiatric symptoms, falls, and disability. *Parkinsonism Relat Disord* 2006;12:35-41.
20. Álvarez-Avellón T, Arias-Carrión Ó, Menéndez M. Neuropsychiatric symptoms and associated caregiver stress in geriatric patients with Parkinson's disease. *Neurol Neurosci* 201521;. doi: <http://dx.doi.org/10.3823/352>.