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ORIGINAL ARTICLE

Non-Motor Symptoms and Their Associated Factors in Parkinson's Disease

Wajeeha Qayyum[1], Sohail Khan[2], Muhammad Shahid Iqbal[3], Muhammad Fozan Khan[4], Zaland Ahmed Yousafzai[5], Fawad Jan[6]

[1]Senor Registrar, Department of Medicine and Allied, Rehman Medical Institute, Khyber Pakhtunkhwa
[2,3]Assistant Professor, Department of Neurology, Rehman Medical Institute, Khyber Pakhtunkhwa
[4]Consultant, physician and store Medicine, Rehman Medical Institute, Khyber Pakhtunkhwa
[5]Medical Officer, Department of Medicine and Allied, Rehman Medical Institute, Khyber Pakhtunkhwa
[6]Assistant Professor, Department of Neurology, Gajju Khan Medical College, Swabi, Khyber Pakhtunkhwa

ABSTRACT

Background: Parkinson's disease is a common neurologic ailment that causes tremor and bradykinesia. The prevalence of Parkinson's disease is estimated to be 1–2 in 1000, affecting about 1% of the population over the age of 60 years. The objective of this study was to find the frequency of Non-Motor Symptoms in patients with Parkinson's Disease (PD) and its association with various factors.

Methodology: A cross-sectional study was carried out in Rehman Medical Institute, Peshawar for 1 year from 1st Oct 2019- 30th Sep 2020. A total of 68 patients with idiopathic Parkinson's disease (PD) were included by consecutive nonprobability sampling. Non-motor symptoms (NMS) were evaluated and noted in a predesigned proforma. Data was entered and analyzed by SPSS 21.

Results: The age of the participants was 62.10±10.01 years. 58.82%(n=40) were males, 47.05%(n=32) belonged to urban residence. Mean duration of illness was 4.52±3.82 years. NMS were found in 100% (n=68) patients. Among NMS, sleep disturbance was the most common symptom found in 77.9% (n=53) followed by constipation that was present in 75% (n=51) of patients. Among associated factors with NMS, hallucinations were significantly associated with advanced age (P = 0.004). Orthostatic hypotension was associated with longer duration of disease (P = 0.03). Depression was significantly associated with other comorbid states.

Conclusion: Non-Motor Symptoms were seen in all the patients presenting to Neurology OPD of Rehman Medical Institute. The most common NMS was sleep disturbance followed by constipation and depression. Hallucinations were observed significantly more in elderly patients.

Key Words: Depression, Orthostatic hypotension, Parkinson disease

Authors' Contribution:	Correspondence:	Article info:
[1]Conception; Literature research; manuscript design and drafting; [2,] Critical analysis and manuscript review; [3] Data analysis; Manuscript Editing.	*Wajeeha Qayyum* *Email: drwajeeha13@yahoo.com*	*Received: February 18, 2021* *Accepted: December 23, 2021*

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Introduction

Parkinson's disease (PD) is a progressive neurodegenerative disorder characterized by the presence of a resting tremor, rigidity, bradykinesia and postural instability[1]. The prevalence and Incidence for PD varies according to different studies and regions, but reported prevalence is 1 – 2 per 1000, affecting nearly 1% of all the population aged above 60 years.[2] The overall incidence of PD in Men

and Women aged 40 Years and above was found to be 61.21/100,000 and 37.55/100,000 respectively.[3] The overall prevalence of PD in Khyber Pakhtunkhwa, Pakistan was estimated to be 1.7/100.[4]

Although Parkinson's Disease is recognized as a motor disorder, over the past two decades, the non-Motor symptoms associated with Parkinson's disease have been given extensive consideration as they are usually under treated and overlooked. Non-motor symptoms (NMS) are known to affect the quality of life of Parkinson's disease patients significantly.[5,6] Some of the most frequent and well-studied non motor symptoms associated with Parkinson's Disease include disturbances of the autonomic nervous system (ANS) including Orthostatic Hypotension, Decreased Gastrointestinal Motility, Urinary Urgency, Hesitancy, Nocturia and Neuropsychiatric symptoms like depression, impaired cognition, and REM Rapid Eye Movement sleep behavior disorders.[7]

A case series by Gulunay et al, concluded that 100% of the patients had non-motor symptoms with fatigue (58%) and anxiety (56%) being the commonest symptoms.[8] Another study revealed that each of the subjects had almost 13 different non motor symptoms related to PD, with autonomic disturbances like nocturia, urgency and constipation being present in 60 to 77% of the subjects, followed by dementia in 58% of the subjects.[9]

A Study from Islamabad, Pakistan determining the frequency of Non motor symptoms in Parkinson's disease patients found out that urinary urgency and dizziness were the most common NMS of Parkinson's Disease.[10] Another study from Lahore revealed that 56% patients of Parkinson's disease had Constipation and 49% had Nocturia.[11]

PD is a disabling disease and NMS may worsen the course of disease. Non-Motor Symptoms greatly impair the functional status of patients, their timely identification and management cannot be underestimated. Treatment of PD patients is mostly focused on their motor symptoms hence NMS remains unaddressed. The purpose of our study is to emphasize the importance of elaborating history regarding NMS hence treating this aspect also to bring improvement in patient's quality of life. Our study will identify, the magnitude of Non-Motor Symptoms in PD and the factors associated with its high incidence.

Methodology:

It was a cross-sectional study carried out over a period of one year from 1st Oct 2019- 30th Sep 2020. Ethical approval was obtained from Research Ethics Committee, Rehman Medical Institute. All patients of idiopathic Parkinson's disease (PD) presenting to OPD were included. Patients were diagnosed according to the United Kingdom Parkinson's Disease Society Brain Bank (UK PDS Brain Bank diagnostic criteria). Sample size was calculated by taking the prevalence of nonmotor symptoms in PD as 50%. With confidence interval and absolute precision of 10% each, sample size was 68. Patients were recruited by consecutive nonprobability sampling techniques. Written informed consent was taken from the participants. A detailed history regarding NMS was taken and entered in a predesigned proforma by neurologist. The following symptoms were assessed: Neuropsychiatric symptoms (depression, anxiety, hallucinations, cognitive impairment, dementia), Autonomic dysfunction symptoms (constipation, urinary symptoms (incontinence, retention, nocturia), perspiration, orthostatic hypotension), sleep disturbance, hyposmia, fatigue and pain.

Different tools were used to evaluate the symptoms. Depression and anxiety were evaluated on the basis of Patients Health Questionnaire (PHQ) and Hamilton Anxiety Rating Scale (HAM-A) respectively.[12,13] Memory and concentration were evaluated using the Montreal Cognitive Assessment (MoCA). Gastrointestinal, urinary symptoms and perspiration were evaluated using the SCOPA-AUT questionnaire.[13]

Orthostatic hypotension was evaluated by the SCOPA-AUT and assessed by taking blood pressure in lying and then in a standing position (a cutoff of > 10 mmHg in Systolic blood pressure was considered as indicating orthostatic hypotension).[14]

Sleep disturbance was evaluated by the Pittsburgh Sleep Quality Index (PSQI).[15]

The fatigue was assessed using the Parkinson's fatigue scale, and pain was evaluated by the Douleur neuropathique-4 (DN4) questionnaire.[15] Argentina Hyposmia Rating Scale (AHRS) was used to assess hyposmia.

Data was entered and analyzed by SPSS 21 software. Quantitative variables were expressed as mean ± SD and qualitative variables were expressed in frequency and percentages.

Frequency of NMS was noted in PD. Statistical significance in association of NMS with gender, age and duration of illness was noted by chi square and t test and P value <0.05 was taken as significant.

Results

Mean Age of the participants was 62.10±10.01 years. 58.82%(n=40) were males and 47.05%(n=32) belonged to urban residence. Mean duration of illness was 4.52±3.82 years.

94.1%(n=64) were taking treatment for PD for their motor symptoms while rest were not on any treatment. 67.64%(n=46) had co morbidities; Hypertension being most common 35.29%(n=24) followed by Ischemic Heart disease 22.05% (n=15) and Diabetes mellitus 10.29% (n=7).

NMS were found in 100% (n=68) patients. Among NMS, sleep disturbance was the most common symptom found in 77.9% (n=53) followed by constipation that was present in 75%(n=51) of patients. Table 1 represents the frequency of different NMS.

Table 1: Frequency of Non-Motor Symptoms in Parkinson's disease.

NMS		% (n=68)
Autonomic dysfunction	Urinary Symptoms	47(32)
	Gastrointestinal Symptoms	75(51)
	Orthostatic Hypotension	40(27)
	Thermo regulatory dysfunction	29(20)
Sleep disturbance		78(53)
Neuropsychiatric Dysfunction	Cognitive Impairment	32(22)
	Depression	70(48)
	Anxiety	28(19)
	Hallucination	22(15)
	Dementia	29(20)
Misc	hyposmia	22(15)
	Pain	37(25)
	Fatigue	57(39)

To find out the association of NMS with age, we stratified the age into 3 groups. Among associated factors with NMS, hallucinations were significantly associated with advanced age (P = 0.004).

Duration of illness was also divided into less than 5years, 6-10years and above 10years. Orthostatic hypotension was associated with longer duration of disease i.e., >10 years (P = 0.03).

Depression was significantly associated with other comorbid states.

Table 2 elaborates the association of each NMS with age groups, duration of illness. Table 3 describes the relation of NMS with gender and comorbidities.

Table 2: Association of each NMS with Age groups and Duration of illness.									
NMS		Age				Duration of illness			
		≤50 %(n) N=10	51-60 %(n) N=21	>60 %(n) N=37	P value	<5 n(%)	6-10 n(%)	>10 n(%)	P value
Autonomic dysfunction	Urinary Symptoms	40(4)	60(12)	46(17)	0.58	41(19)	67(10)	43(3)	0.4
	Gastrointestinal Symptoms	70(7)	65(13)	81(30)	0.98	78(36)	80(12)	43(3)	0.47
	Orthostatic Hypotension	50(5)	40(8)	35(13)	0.82	17(8)	67(10)	71(5)	0.03
	Thermo regulatory dysfunction	50(5)	40(8)	19(7)	0.18	22(10)	47(7)	43(3)	0.29
Sleep disturbance		0(0)	15(3)	5(2)	0.33	80(37)	67(10)	100(7)	0.36
Neuropsychiatric Dysfunction	Cognitive Impairment	0(0)	15(3)	32(12)	0.21	37(17)	33(5)	0(0)	0.33
	Depression	70(7)	80(16)	81(30)	0.67	74(34)	67(10)	43(3)	0.60
	Anxiety	20(2)	25(5)	40(15)	0.42	17(8)	20(3)	43(3)	0.55
	Hallucination	20(2)	65(13)	86(32)	0.004	22(10)	33(5)	0(0)	0.41
	Dementia	20(2)	25(5)	35(13)	0.58	33(15)	33(5)	0(0)	0.38
Misc	hyposmia	0(0)	25(5)	27(10)	0.35	17(8)	13(2)	28(2)	0.64
	Pain	20(2)	50(10)	35(13)	0.38	37(17)	33(5)	43(2)	0.84
	Fatigue	40(4)	25(5)	27(10)	0.93	52(24)	67(10)	71(5)	0.55

Table 3: Association of NMS with Gender and Comorbidities.							
NMS		Gender			Comorbidities		
		Male (n=40)	Females (n=28)	P value	Yes(n=46)	No(n=22)	P value
Autonomic dysfunction	Urinary Symptoms	46(18)	50(14)	0.79	52(24)	36(8)	0.42
	Gastrointestinal Symptoms	79(32)	69(19)	0.45	80(37)	59(13)	0.17
	Orthostatic Hypotension	37(15)	44(12)	0.69	37(17)	45(10)	0.58
	Thermo regulatory dysfunction	21(8)	44(12)	0.12	30(14)	32(7)	0.94
Sleep disturbance		71(28)	94(26)	0.07	85(39)	68(15)	0.23
Neuropsychiatric Dysfunction	Cognitive Impairment	33(13)	25(7)	0.58	30(14)	36(8)	0.57
	Depression	71(28)	69(19)	0.88	80(37)	45(10)	0.02
	Anxiety	29(12)	25(7)	0.77	30(14)	23(5)	0.66
	Hallucination	25(10)	19(5)	0.64	26(12)	14(3)	0.45
	Dementia	33(13)	25(7)	0.57	22(10)	45(10)	0.12
Misc	hyposmia	21(8)	25(7)	0.75	30(14)	9(2)	0.12
	Pain	29(12)	50(14)	0.18	43(20)	23(5)	0.19
	Fatigue	50(20)	69(19)	0.24	52(24)	68(15)	0.29

Discussion

The mean age of our population was 62.10±10.01 years. The age range between 55 -65 years has been described in multiple studies conducted on Parkinson's disease.[11,13-18] It is in accordance with disease natural history that, it affects elderly.

Male gender slightly predominated in our study making 58.8% of study population. The finding is similar to the study conducted by Shalash et al, which has described 59.8 % males in their study on NMS in PD.[19] Other studies described equal number of males and females in their studies.[4,16,17] It stands true for PD as it affects males more than females.

Mean duration of disease was 4.52±3.82 years in our study. Different research work on NMS in PD has described variable duration of disease i.e 2.7 ± 2.08 years, 7 ± 6 years and 5.3± 4.1 years (17-19). The wide range of disease duration at presentation can be due to the unpredictable and slow coarse of disease, difference in availability of health facilities and population's behavior towards seeking medical attention.

NMS are common in PD, ranging from 14% to 80%.[19,20] It can occur at any stage of disease, may aggravate as the disease progresses and may present before onset of motor symptoms.[19-21]

All our patients (100%) had at least one NMS. Two other studies in literature also described 100% prevalence of NMS in PD.[18,19] The reason for the high frequency of NMS in our population can be multifactorial. It can be related to progressive disease, late presentation and can be due to racial or ethnic difference which needs further clarification.

On further description of NMS, we found that sleep disturbance followed by constipation and depression was found as common NMS. Sleep and mood disorders were found in 88.3% and 80.6% of the patients studied by Berganzo K et al. [22]

Regarding NMS, the most common were urinary dysfunctions (82.6%), sleep (80.6%), and gastrointestinal (80%) disorders in a study carried out in Morocco.[18]

A study conducted in Pakistan from Islamabad region described urinary symptoms as the most frequent NMS followed by constipation. This study recorded significant number of patients suffering from neuropsychiatric symptoms.[9]

Osama et al, in Tanta University Hospital, while studying 41 patients of PD observed that gastrointestinal symptoms especially constipation, depressive symptoms, and sleep disturbance were common in newly diagnosed PD.[20]

A study by Mukhtar et al, stated constipation in 54% patients, nocturia in 50% and dementia in 48% of patients with PD. Depression, pain and paresthesia were more common in female gender.[11] The variation in different studies may be attributed to multiple tools used in studies, social and cultural factors or under reporting of symptoms by patients. We didn't find association of any NMS with gender. However, depression was significantly more in patients having other comorbidities whereas orthostatic hypotension was related to advanced disease. Hallucinations were observed significantly in elderly. These relationships have not been described earlier in literature.

It is one of the few studies published from Pakistan throwing light on NMS in PD. However, we have tried to cover almost all important NMS in it and described their association with age, gender, comorbidities and disease duration. Moreover, we didn't rely on simple questionnaire filled by patients, rather we tried to evaluate every NMS by well-established tool.

There are some limitations to the study. It is single centered study, we kept absolute precision 10% and CI 90% in order to get less sample size because as the disease is rare, limited number of patients were expected in a single institution; studies in multiple centers can be carried out with optimal precision and CI to elaborate the findings. We didn't describe the disease stage neither we elaborated NMS according to it.

Conclusion

NMS were seen in all the patients presenting to Neurology OPD in our study. The most common NMS was sleep disturbance followed by constipation and depression. Orthostatic hypotension was associated with longer disease duration while depression was associated with comorbid states. Hallucinations were observed significantly more in elderly patients.

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