

FREQUENCY OF NON MOTOR SYMPTOMS AMONG PATIENTS OF PARKINSON'S DISEASE IN PAKISTAN

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ABSTRACT

OBJECTIVE

To screen the patients of Parkinson disease for presence of non motor symptoms.

STUDY DESIGN

Cross sectional study.

PLACE AND DURATION OF STUDY

Three months duration observational study was carried out at Military Hospital Rawalpindi from October 2015 to December 2015.

SUBJECTS AND METHODS

All the patients of Parkinson's disease (PD) presenting in neurology department filled a self administered Non Motor System questionnaire (NMS Quest) comprising of 30-itmes. Patients had to respond as "yes," or "no," to each item. Frequency of each symptom was calculated to look for the common NMS experienced by patients.

RESULTS

A total of 62 patients were screened through NMS questionnaire. Mean age of patients was 64.5 (range 34–91 years). 93.5% were male. The mean of total symptoms positive on NMS Quest was 11.8. Most commonly experienced NMS included nocturia (80.61%) and unexplained pains (80.61%) followed by urgency (70.9%) and constipation (67.7%). NMS least reported were difficulty during sex (1.61%) and change in sex drive (8.06%) followed by diplopia (12.9%) and incomplete bowel emptying (16.1%).

CONCLUSION

The study concluded that prevalence of NMS among patients of PD was high so these symptoms should be assessed carefully by physicians at the time of consultation so that overall quality of life of patients is improved.

KEY WORDS

Parkinson disease, Non motor symptoms, Neurodegenerative disorder.

INTRODUCTION

In 1817 James Parkinson described Parkinson disease (PD) for the first time in his famous essay¹. It is a common, idiopathic disorder associated with inadequate dopamine in brainstem due do degeneration of neurons in the substantia nigra.

Traditionally only motor symptomatology was associated with PD, now it is considered as a broad spectrum disorder with multiple features including psychiatric and non-motor manifestations (NMS)². These include cognitive dysfunction, anhedonia, hallucinosis and other disorders related to mood and behavior. Hyposmia, pain, bad sleep quality and other sensory disturbances like numbness, coldness, burning and parasthesias are also common. Majority of PD patients have complains related to autonomic system as well including constipation, postural hypotension and urogenital problems^{2,3}.

NMS may be related to neurodegenerative changes affecting several neural systems and/or caused by drugs employed in treatment of PD. The clinical picture of PD may be considered as iceberg. The visible part presents the motor symptoms and the larger non visible part represents the several NMS. Martinez-Martin et al. performed a multicentric, international, cross-sectional study using the NMS Questionnaire and reported that NMS were present in 98.4% of the patients³. The PRIAMO study showed similar results that NMS were present in the vast majority of PD patients⁴.

Previously only late or advanced PD was associated with presence of NMS but a study done in recent past clarified this myth. It revealed that non-motor manifestations may occur earlier than motor disturbances and cause more disability than motor symptoms⁵. Patients of PD experience more NMS as the disease progresses⁴. Various studies done in the past showed that non motor symptoms at the time of diagnosis were not much alarming⁶ but after few years of disease progression they increased to an extent that disturbs the patient more than motor symptoms⁷.

Study done in our neighboring country on a similar set of population revealed that disease burden and pattern is not very different in our part of the world. Around 91.8% patients presented with NMS in a study done in India on patients of PD⁸. The impact of NMS is also sometimes greater than motor signs, especially in the late stages of PD and they significantly impair quality of life and may precipitate hospitalization⁹⁻¹¹.

Normally it is believed that NMS are hard to treat, but reality is different. They should be given importance and assessed in detail because they can be

treated by dopamine analogues and other forms of treatment, thus contributing positively to the daily life of the patient.

It is unfortunate that very little data is available regarding NMS in patients of PD in Pakistan. Previously a study was done to look for depression in PD patients¹³ but NMS has not been addressed so far so this study was designed to look for the prevalence of NMS in patients of Parkinson disease in Pakistani setting.

SUBJECTS AND METHODS

Participants

All the patients of PD of either gender aged \geq 18 who gave written consent were included in the study regardless of the duration of disease. Pediatric patients, patients' already on psychiatric treatment and those who did not give consent or were unable to understand or complete the questionnaire were excluded from the study. UK Brain Bank criterion was used to diagnose the patients of PD i-e Patients presenting with tremor, bradykinesia with or without rigidity and postural instability were included in the analysis 14 .

Instruments

Non motor Symptoms Questionnaire (The NMSQuest) is a 30 item screening tool used to look for non motor manifestations of PD. It is a self reporting instrument comprising of 12 NMS domains which include GIT, urinary, CVS, respiratory, neuropsychiatric, cutaneous and sensory symptoms. Disorders of sleep, apathy, fatigue and attention are also part of these domains. Each domain includes 2 to 8 specific questions featuring answers as yes or no.

Procedure

After ethical approval from ethical committee Military Hospital Rawalpindi, this cross sectional study was carried from October 2015 to December 2015. The patients were provided with a detailed description of the study. Inclusion was strictly based on informed written consent. All consenting PD patients completed the NMS Questionnaire in outpatient department (OPD) while waiting for their turn to meet the treating physician. Help of caregivers was acquired where necessary. Routine history including information about drugs and the demographic profile were entered in a structured form. The NMSQuest used in the study (see annexure A). Frequency of the individual non motor symptoms was obtained by adding all the "yes" responses. Percentage was calculated by transforming the frequencies related to the number of patients in the sample. Prevalence of each domain was obtained by transforming the sum of item positive responses on the maximum possible number of positive responses in the domain. All statistical analysis was performed using Statistics Package for Social Sciences version 20.0.

RESULTS

After the application of inclusion and exclusion criteria total 62 patients were included in the analysis. Mean age of patients was 64.5 (range 34–91 years), 93.5% were male. Table 1 and 2 showed the frequency and percentage of individual symptoms and domains respectively. The mean of total symptoms positive on NMS Quest was

11.8. Most commonly experienced NMS included nocturia (80.61%) and unexplained pains (80.61%) followed by urgency (70.9%) and constipation (67.7%). NMS least reported were difficulty during sex (1.61%) and change in sex drive (8.06%) followed by diplopia (12.9%) and incomplete bowel emptying (16.1%). Domain most commonly affected is urinary (75.75% of the individuals reported) followed by depression and anxiety (as reported by 66.05% of individuals).

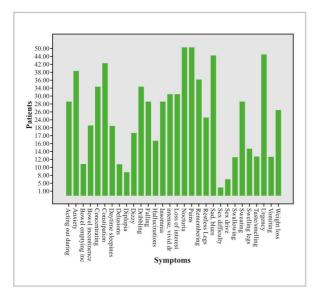
Table 1Frequency and percentage of positive responses

	Symptoms	N	%
1	Dribbling	34	54.8
2	Taste/smelling	12	19.3
3	Swallowing	12	19.3
4	Vomiting	12	19.3
5	Constipaton	42	67.7
6	Bowel incontinence	18	29.03
7	Bowel emptying incomplete	10	16.1
8	Urgency	44	70.9
9	Nocturia	50	80.61
10	Pains	50	80.61
11	Weight loss	26	41.9
12	Remembering	36	58.06
13	Loss of interest	30	48.3
14	Hallucinations	16	25.8
15	Concentrating	34	54.8
16	Sad, blues	44	70.9
17	Anxiety	38	61.2
18	Sex drive	05	8.06
19	Sex difficulty	01	1.61
20	Dizzy	17	27.4
21	Falling	28	45.1
22	Daytime sleepiness	18	29.03
23	Insomnia	28	45.1
24	Intense, vivid dreams	30	48.3
25	Acting out during dreams	28	45.1
26	Restless legs	24	38.7
27	Swelling legs	14	22.5
28	Sweating	28	45.1
29	Diplopia	08	12.9
30	Delusions	10	16.1

TABLE 2Positive symptoms analyzed according to NMS Quest domains

NMS Questionnaire – domains	Mean Percentage of positive individuals
Gastrointestinal	30.2
Urinary	75.75
Sexual function	4.8s
Cardiovascular	36.05
Apathy/attention/memory	53.7
Hallucinations/delusions	20.95
Depression/anxiety	66.05
Sleep disorder	41.2
Miscellaneous	39.5

Figure 1
Spectrum of NMS presented by the patients in our study.



DISCUSSION

Results of our study show that a wide spectrum of NMS exists among all the patients suffering from Parkinsonism. Similar results were reported in a study done on more than 1000 patients that NMS were present among all the patients of PD regardless of stage of disease⁶. Ranging from urinary problems to neuropsychiatric symptoms, variety of NMS may be present in one patient so this demands the requirement for a detailed assessment at the time of patient presentation in OPD.

Urinary problems were the commonest among most of the patients. Nocturia was present in 80.6% patients and urgency in 70.9%. In an international study done by K. Ray Chaudhuri et al these symptoms were 65% and 60 % respectively¹⁵. Hyperactivity of detrusor due to dysfunction of dopamine basal ganglia circuit may be responsible for urinary problems. As the disease advances and there is rise in motor symptoms, lower urinary tract problems also increase. Degeneration of neurons producing dopamine may be the cause. Use of anticholinergic agents to reduce detrusor hyperactivity must be very vigilant¹⁶.

Unexplained pains not related to arthritis or other systemic problem were reported in 80.6% of the cases which is in accordance with the results of review article that pain is the most frequent complaint with which patients of PD present. It is often neglected and treated inadequately due to more focus on motor symptomatology¹⁷ and its prevalence increases with the duration of disease ^{18,19}.

Gastrointestinal symptoms were also present in considerable number of patients especially constipation was reported in 67.7% cases. Similar results were shown in a study done in Malaysia that disabling constipation was the commonest NMS experienced by 61.9% of the patients²⁰.

Sexual symptoms were very rarely reported in our study as compared with other studies which showed high frequency of Sexual dysfunction among patients of PD²¹. Previous research showed that men suffering from PD are also at increased risk of developing erectile dysfunction²². Under reporting in our study may be due to the social barrier that patients hesitate in telling these symptoms to physician in our set up or usually people here think that sexual activity concerns only of young age group.

Neuropsychiatric symptoms also make major bulk of NMS in PD patients. Chronic diseases involving lifelong medication cause significant psychiatric morbidity. In case of PD abnormal neuronal pathways and neurotransmitter imbalances may add to the situation. 66.05% of our patients showed anxiety and depression like features. A study done in the same hospital by psychiatry department in the past showed that depression and anxiety were present in 38% of the patients¹³. Majority of PD patients present with sleep disorders. Our data showed 41.2% patients complaining of sleep disturbances out of which intense vivid dreams was commonest followed by insomnia and acting out of dreams similar to results of The PRIAMO Study showing insomnia and RBD as chief sleep disorders present in PD patient⁴.

Postural hypotension is a common symptom in many patients with parkinsonism²³. Failure of autonomic system in these patients is main cause of drop in blood pressure on changing the posture. 27.4% of the patients in our study complained of dizziness on change of posture which is very much in accordance with the available data.

Our study has few limitations. NMSQuest is subjective and it does not cover certain areas such as speech, gait and dopamine dysregulation syndrome. The sample size and use of self administered questionnaires pose methodological issues as well. The findings cannot be generalized as our study population was not selected from randomized patients of PD from all neurology units of Pakistan. We suggest further studies on a broader based and a more representative sample size preferably case control studies that would be helpful in giving true prevalence of some of the commoner NMS.

CONCLUSION

The study concluded that prevalence of NMS among patients of PD was high so these symptoms should be assessed carefully by the physicians at the time of consultation so that overall quality of life of patients may be improved.

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Non motor Symptoms Questionnaire for patients of Parkinson disease (NMSQuest)

Non motor symptoms in Parkinsonism

Name	Sex	Age
Duration of Parkinsonism		
Contact No	Location	

Have you experienced any one of the following in last month?

Sr.	Question	Yes	No
1	Day time dribbling of saliva		
2	Smell and taste ability lost or changed		
3	Choking or Swallowing difficulties during eating or drinking		
4	Vomiting or feeling of sickness (nausea)		
5	Constipation (weekly bowel movements are less than 3) or straining for stools		
6	Bowel incontinence		
7	Incomplete bowel emptying even after passing the stool		
8	A sense of urgency to pass urine that makes you rush to toilet		
9	Frequent awakenings at night for passing the urine		
10	Pains which can be explained by any inflammatory disease or trauma (not due to known condition as arthrits)		
11	Weight loss (which cant be attributable to dietary change)		
12	Forgetfulness in doing routine things or difficulty in remembering recent affairs		
13	Loss of interest in doing things and events happening around you		
14	Seeing or hearing things that you know but others say or not there		
15	Problems in focusing and concentration issues		
16	Feeling low, blue or sad		
17	Feeling of fear anxiety or irritability		
18	Increase or decrease in sexual desire		
19	Difficulty in having sex		
20	Feeling weak, dizzy and light headed when standing from sitting or lying position		
21	Falling		
22	Difficulty in keeping yourself awake while doing activites like eating, working or driving		
23	Finding it difficult to sleep at night and maintain the sleep		
24	Experience dreams at night which are very frightening or vivid24		
25	Moving out or talking in your dreams as you are acting out your dreams		
26	Unpleasent desire to move legs at night or during resting periods		
27	Legs are swollen		
28	Excessive sweating		
29	Double vision		
30	Believing expriances you are having that others think are incorrect		

Sr. #	Author Name	Affiliation of Author	Contribution	Signature
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2	Usama Bin Zubair	Medical officer, MH RWP	Data analysis and writing the final manuscript	A