

## Original Research Article

# Prevalence of non-motor symptoms in Parkinson's disease

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### ABSTRACT

**Background:** Parkinson's disease is a common neurodegenerative movement disorder characterised by motor symptoms of rest tremor, bradykinesia, rigidity and postural instability and non-motor symptoms (NMS) which include neuropsychiatric symptoms, sleep disturbances, autonomic symptoms, sensory symptoms and symptoms of mixed aetiology. Parkinson's Disease Non Motor Group (PD-NMG) devised a comprehensive clinic-based self-completed NMS questionnaire that allows easy identification of NMS by the physician. Most NMS have a poor response to dopaminergic therapy as it is due to dysfunction of the serotonergic and noradrenergic pathways. Treatment of these nonmotor symptoms help in improving the quality of life in patients with Parkinson's disease.

**Methods:** There were 100 patients with Parkinson's disease who had presented to our neuromedicine movement clinic were included in the study. Patients were diagnosed as PD based on UK Parkinson's disease brain bank criteria. The inclusion criteria were diagnosis as PD, age >18 yrs, inclusion of both males and females and consent for the study. Patients with atypical parkinsonism and secondary parkinsonism, stroke, intake of antipsychotics were excluded from the study. Non motor symptom questionnaire was given to the study group and frequency of occurrence of each non motor symptoms and their predominance in both males and females were studied. The frequency of each NMS was calculated by computing the number of yes response and calculating the percentage related to the number of patients in the sample. Analysis was done to calculate the frequency of all NMS among the enrolled patient.

**Results:** Nocturnal sleep disturbances (43%) were most common followed by constipation (29%). The most common non motor symptoms in males were constipation (20%), urinary urgency (18%) and nocturia (11%). The most common non motor symptoms in females were nocturnal sleep disturbance (25%), feeling sad (19%), unexplained pains (17%) and being anxious (13%).

**Conclusions:** Non motor symptom questionnaire helps in screening patients with Parkinson's disease of non-motor symptoms and aims at providing holistic treatment improving the quality of life.

**Keywords:** Nonmotor symptoms questionnaire, Parkinson's disease

### INTRODUCTION

Parkinson's disease is one of the common neurodegenerative movement disorder. The hallmark manifestations of Parkinson's disease such as bradykinesia, rest tremor, rigidity and postural instability were described by James Parkinson in his 'essay on shaking palsy' in 1817. He also described certain non

motor manifestations such as sleep disturbances, constipation, dysphagia, dysarthria, sialorrhoea and urinary incontinence.<sup>1</sup> Among subjects with parkinsonism about 80-85% have Parkinson's disease and the rest are atypical parkinsonism and secondary parkinsonism.<sup>2</sup> Parkinson disease has a prevalence of 360/100,000 and incidence of 18/100,000.<sup>3</sup> In India, with an estimated population of over one billion, approximately 700 million people will

be above the age of 65 years, of which about 7 million will suffer from PD.<sup>4</sup> The cardinal manifestations of PD are bradykinesia, asymmetric tremor, rigidity due to dopamine deficiency as a result of nigrostriatal degeneration. The non motor symptoms of parkinsonism can occur both during early and late stage and are due to non dopaminergic cell dysfunction such as serotonin.

The non motor symptoms have been divided into many domains: neuropsychiatric, sleep, sensory, autonomic, gastrointestinal. The non motor symptoms have a greater impact on the quality of life and several questionnaires have been developed to identify non motor symptoms early. Several non motor symptoms olfactory problems, constipation, depression and erectile dysfunction may precede the motor symptoms of PD early and their presence by questionnaire helps in diagnosing early PD and aims at providing holistic approach towards treatment of both motor and non motor symptoms.<sup>5,6</sup> Braak staging 1 and 2 corresponds with degeneration of olfactory neurons and lower brainstem mediating sleep homeostasis, pedunculopontine nuclei, locus ceruleus, serotonergic neurons, dorsal vagus nucleus explaining visual hallucinations, REM sleep disorder, constipation. Stage 3, 4 corresponds to motor symptoms of PD and 5,6 with involvement of cortex.<sup>7</sup>

Stacy et al, reported that non motor symptoms were presented in early PD and could be identified with use of questionnaires: NMS questionnaire, NMS scale, both of which have been extensively used and validated in patients with PD. Most commonly used is the non-motor symptoms questionnaire (NMSQ) which identifies 30 different non motor symptoms and helps in early management and prevents general deterioration.<sup>8</sup>

**METHODS**

This was a cross sectional, observational and descriptive study. Patients with Parkinsons disease both new and already diagnosed cases presenting to Neuromedicine department of Government Rajaji Hospital, Madurai medical college, were included in the study conducted from 1<sup>st</sup> April 2016 to 31<sup>st</sup> March 2017. Patients were diagnosed as PD based on UK Parkinson’s disease brain bank criteria. The inclusion criteria were diagnosis as PD, age >18 yrs, inclusion of both males and females and consent for the study. Patients with atypical parkinsonism and secondary parkinsonism, stroke, intake of antipsychotics were excluded from the study. Informed consent was obtained. The participants were asked to fill up NMS Q (Annexure 1) by himself or with the help of examiner/family member which comprises of 30 questions representative of all non motor domains of sleep, autonomic, gastrointestinal, genitourinary, sensory. The participants would respond as yes if he/she had experienced the said symptom in the past 1 month. Routine demographic details and clinical examination were done.

An aggregate of 100 samples were selected for our study. After the questionnaires were filled in by all of the patients, data were entered and analysed using Statistical Package for Social Sciences (SPSS) V.25. The mean and SD were calculated for numerical variables. Categorical data were expressed as frequency and percentage. The frequency of each NMS was calculated by computing the number of yes response and calculating the percentage related to the number of patients in the sample. Analysis was done to calculate the frequency of all NMS among the enrolled patient.

**RESULTS**

The study was conducted for a period of one year from 1<sup>st</sup> April 2016 to 31<sup>st</sup> March 2017 and 100 patients were included in the study based on inclusion and exclusion criteria. The mean age was 59.39±8.97 with minimum age of presentation 33 and maximum age of 80 years.

**Table 1: Prevalence of individual non motor symptoms.**

Non motor symptoms	Percentage (Frequency)
Difficulty in sleeping at night	43
Constipation	29
Unexplained pains	27
Falling	25
Urinary urgency	24
Memory disturbance	24
Feeling sad	23
Dribbling of saliva	19
anxious	18
Loss of interest	17
Nocturia	16
Difficulty in concentrating	14
Dizziness while getting up from sitting position	13
Nausea/vomiting	13
Unexplained change in weight	11
Daytime sleepiness	11
Unpleasant sensation in legs	10
Incomplete bowel emptying	8
Disinterested in sex	8
Difficulty in swallowing	7
Change in ability to smell or taste	6
Excessive sweating	6
Bowel incontinence	4
Hallucinations	3
Swelling of legs	3
Frightening dreams	2
delusion	2
Acting out dream	1
Double vision	1

Among total of 100 patients 2% were in the age group of 31-40yrs, 7% in age group 41-50yrs, 46% in age group 51-60yrs, 36% in age group 61-70 yrs, 9% between 71-80

years, none were below 30 years and above 80 years. Females were more common 51% and 49% were males in our study. Majority of them had presented with motor symptoms of bradykinesia, rigidity, resting tremor of 98%, 98%, 94% and micrographia, hypophonia, dysphagia was present in 20%, 15% and 6% respectively. The most common symptom was sleep disturbance in the form of difficulty in sleeping in the night n=43(43%), however daytime sleepiness was present in 11 patients, frightening dreams were present in two patients and only one had complained of acting out a dream.

Gastrointestinal symptoms were next predominant of which constipation were present in n=29 (29%) of patients, nausea and vomiting in 13 patients, difficulty in swallowing which was mild in 7 patients. Nearly one fifth of the patients had neuropsychiatric manifestations in the form of loss of interest, becoming anxious, difficulty in concentrating in activities of daily living and their routine

job. Hallucinations and delusions were less common being present in only 3% and 2% of patients. Urinary urgency and nocturia were present in 24% and 16% of patients respectively. Unexplained pains and unexplained change in weight were common. Change in ability to smell or taste were present in only 6% of patients. The frequency of NMS symptoms are listed in Table 1.

The most common symptom in males were constipation, urinary urgency and nocturia. In females sleep disturbances and neuropsychiatric symptoms were common like nocturnal sleep disturbance, feeling low, being anxious. Delusions and hallucinations (100%) were found only in female patients. The comparison of nonmotor symptoms in male and female patients with Parkinson's disease is shown in Figure 1.

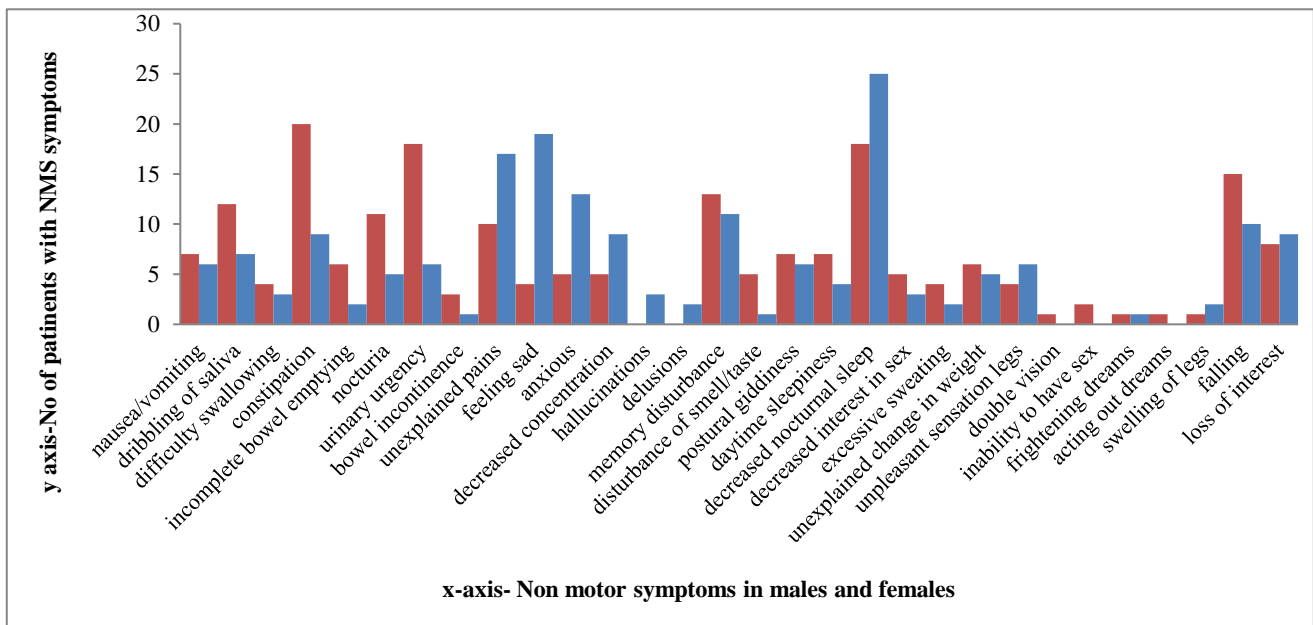


Figure 1: Comparison of non-motor symptoms in males and females with Parkinson's disease.

**DISCUSSION**

The presence of non-motor symptoms like sleep disorders, cognitive disturbances and gastrointestinal manifestations have been described with Parkinson's disease and its association with the impairment in quality of living is being increasingly recognised in recent studies.<sup>8</sup> About 62.5% of nonmotor symptoms in Parkinson's disease are not revealed to clinician because they attribute it due to some other reason which can be picked up NMS Questionnaire.<sup>9</sup> Non motor symptoms in Parkinson's disease is universally encountered and the NMS-Q is validated by many clinical studies.<sup>10</sup> A large

multicenter study comprising 545 patients using the NMSQ data done in the UK, USA, Germany, Israel, Japan and Italy, reported that the mean total NMS (NMSQ-T) was 10.3±5.4 (SD), with nocturia (61.9%) being reported as the most frequent symptom while incontinence of faeces was the least prevalent (8.21%). Only eight (1.6%) patients in this study declared that they had no NMS at all. There were no significant differences in NMS scores by gender, with the exception that depression/anxiety, sexual dysfunction, and cardiovascular and miscellaneous NMS were more prevalent in women.<sup>11</sup> The study from India and among the few from Asia by Krishnan et al compared 174 patients and 128 normal controls to assess the prevalence

of NMS and its relation to disease progression measured by the Hoehn and Yahr scale, reported a higher frequency of NMS in patients with PD compared with controls. All patients had at least one NMS. Women with PD had higher scores in the cardiovascular, sleep/fatigue, mood/cognition and urinary domains, whereas men had higher scores for the sexual domain.<sup>12</sup>

A multicenter survey, the PRIAMO study, using a semi structured interview in 1072 consecutive patients with PD from Italian centers to assess the prevalence of NMS found that 98.6% of the patients with PD reported the presence of NMS. The most common symptoms were fatigue (58%), anxiety (56%), leg pain (38%), insomnia (37%), urgency and nocturia (35%), drooling of saliva and difficulties in maintaining concentration (31%).<sup>13</sup> Li et al, reported a cross-sectional study of 82 Chinese patients with PD and found that NMS were very common in Chinese patients with PD, with a prevalence of the whole spectrum of NMS being 100%, and the NMSS significantly correlated with disease duration. Another study from India done by Ravan et al studied the prevalence of non-motor symptoms in PD patients and its correlation with motor worsening. A total of 81 patients were studied. The most common symptom reported was nocturia (74 patients, 91%), followed by constipation in 48 patients and fatigue in 41 patients.<sup>14</sup>

A study done in Pakistan compared the prevalence of various non motor symptoms in male and female patients. The most common NMS in men included constipation (54%), getting up regularly to pass urine at night (50%) and problems with short-term memory (48%). The most common NMS in women included feeling sad or blue (80%), unexplained pain (67%), feeling light-headed or dizzy (73%), feeling anxious or panicky (61%), and feeling unpleasant sensations in the legs while at rest.<sup>15</sup> In our study, out of the total of 100 patients studied, sleep disturbances were most common. Our study population had predominant females 51% compared to males 49%. Most common sleep disturbances were nocturnal sleep problems (43%) difficulty in falling asleep, 10% had awakenings due to unpleasant sensation in the legs and acting out a dream was present in only 1 patient. Sleep disturbance are among the most common non motor symptom commonly encountered, these include difficulty falling asleep, fragmentation of sleep, nocturnal awakenings, hallucinations, restless leg syndrome. Sleep disturbances are caused by abnormalities in the sleep-wake cycle-related pathway mediating thalamocortical arousal while the pedunculopontine nucleus, locus coeruleus, and serotonergic raphe nuclei are thought to be key areas related to the origin of visual hallucinations and RBD. They were more common in females (25%) than males (18%) in our study. Among males nocturia (11%), constipation (20%) and urinary urgency (18%) were common. The increase in predominance of urinary urgency in our population can be explained by male predominant older population which could be due to benign prostrate hypertrophy in old age. Several case

control studies have reported increased prevalence of constipation in PD of between 28% and 61% compared to control cases (6%-33%). Constipation has been reported as a prominent complaint prior to the onset of motor symptoms of PD in about 50% of patients in one series. Lewy body pathology in the peripheral autonomic nervous system involving the myenteric plexus with subsequent colonic sympathetic denervation contributes to constipation in PD.<sup>16</sup> Constipation was present in 29% of our patients which was well within the documented prevalence in PD patients.

Neuropsychiatric manifestations were present in almost one fifth of our study population. The prevalence of major depression in PD is estimated to be 40%, with reported prevalence rates ranging from 4% to 70%.<sup>17</sup> Many of the female patients (19%) were feeling low than males (4%) and showed other symptoms of depression like loss of pleasure in daily activities, less interested in self care, insomnia. Females were also anxious regarding the disease and about their daily living. Hallucinations and delusions were also present in female patients only. Psychiatric manifestations in PD can be attributed to disease progression, medication use and psychological reaction to illness. The effect of the psychological reaction could explain the predominance in females compared to males in our study.

The most common NM symptoms in males were constipation (20%), urinary urgency (18%) and nocturia (11%). The most common non motor symptoms in females were nocturnal sleep disturbance (25%), feeling sad (19%), unexplained pains (17%) and being anxious (13%).

## CONCLUSION

Non motor symptom questionnaire helps in screening patients with Parkinson's disease of non-motor symptoms and aims at providing holistic treatment improving the quality of life. There is a need for large and well-designed prospective, adequately powered, large community-based study on the prevalence, the symptom stratification based on NMSS, the efficacy of treatment, and the progression over time, of NMS in PD. This will provide a basis for improving the quality of care of these patients by clinicians.

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**Annexure 1: Non motor symptom questionnaire-30 item scale.**

A range of problems is listed below. Tick the box 'yes' if the problem had been experienced during the past month. Answer 'no' if the problem had not been experienced in the past month and also even if it had been experienced in the past but not in the past month. Have you experienced any of the following in the last month?		
1. Dribbling of saliva during the daytime	Yes	No
2. Loss or change in your ability to taste or smell	Yes	No
3. Difficulty swallowing food or drink or problems with choking	Yes	No
4. Vomiting or feeling of sickness (nausea)	Yes	No
5. Constipation (less than 3 bowel movements a week) or having to strain to pass a stool (faeces)	Yes	No
6. Bowel (faecal) incontinence	Yes	No
7. Feeling that your bowel emptying is incomplete after having been to the toilet	Yes	No
8. A sense of urgency to pass urine makes you rush to the toilet	Yes	No
9. Getting up regularly in the night to pass urine	Yes	No
10. Unexplained pains (not due to known conditions such as arthritis)	Yes	No
11. Unexplained change in weight (not due to change in diet)	Yes	No
12. Problems remembering things that have happened recently or forgetting to do things	Yes	No
13. Loss of interest in what is happening around you or doing things	Yes	No
14. Seeing or hearing things that you know or are told are not there	Yes	No
15. Difficulty in concentrating or staying focused	Yes	No
16. Feeling sad, low or blue	Yes	No
17. Feeling anxious, frightened or panicky	Yes	No
18. Feeling less interested in sex or more interested in sex	Yes	No
19. Feeling difficult to have sex when you try	Yes	No
20. Feeling light headed, dizzy or weak standing from sitting or lying	Yes	No
21. Falling	Yes	No
22. Finding it difficult to stay awake during activities such as working, driving or eating	Yes	No
23. Difficulty getting to sleep at night or staying asleep at night	Yes	No
24. Intense vivid dreams or frightening dreams	Yes	No
25. Talking or moving about in your sleep as if you are acting out a dream	Yes	No
26. Unpleasant sensations in your legs at night or while resting and a feeling that you need to move	Yes	No
27. Swelling of legs	Yes	No