

A Study on the Non-Motor Symptoms of Idiopathic Parkinson's Disease in Correlation with the Severity and Duration of Disease in a Tertiary Referral Hospital

Karnakaran K.¹, Kalpana R.²

Abstract

Aim: To determine the non-motor symptoms and to assess the stage and duration of the disease in patients above 50 years, with idiopathic Parkinson's disease.

To analyse the correlation of non-motor symptoms of Parkinson's disease with the severity and duration of disease.

Materials and Methods: Following the institutional ethical committee approval 105 patients who attended the Neurology department between July 2013 and July 2014 with Idiopathic Parkinson's Disease as outpatient and inpatient were studied in a tertiary care referral medical college hospital in Chennai. Motor symptoms were assessed by the Unified Parkinson's Disease Rating Scale (UPDRS) and stage of the disease with the Hoehn and Yahr staging. Non-motor Symptoms Questionnaire (NMS QUEST) which contains 30 items was used to determine the non-motor features and to correlate with the severity and duration of the illness was studied.

Observation and Results: Among 105 patients studied, sixty seven belonged to the age group between 50 - 60 years, thirty patients belonged to age group between 61-70 years and eight patients were aged more than 70 years. Seventy five patients had the disease duration between 0 - 5 years, eighteen had duration of 5 - 10 yrs and twelve had the disease for more than 10 years. Upon observation 22.9% of the study population belonged to Hoehn and Yahr stage 1 and 1.5, 37.1% of the patients belonged to stage 2 and 2.5. Amid the rest, 32.2% had Stage 3 and stage 4 consisted of 7.6% of the study group respectively. The number of Non-motor Symptoms in Stages 1 and 1.5 were in the range of 2 to 5, Stages 2 and 2.5 were in the range of 3 to 9, Stages 3 were 6 to 11 and in stage 4 between 11 and 12. This study also revealed a higher occurrence of NMS like Nocturia (60%), urgency (44.8%) and constipation (52.4%), dizziness (43.8%), anxiety (34.3%), depression (34%), memory (37.1%), dreams (24.8%), sleepiness (22.9%) and hallucinations (24.8%).

Conclusion: The most prevalent Non-motor symptoms are Autonomic dysfunction like Constipation, Nocturia, urgency and sweating, followed by insomnia, depression and memory disturbances followed by dizziness, drooling, falls and unexplained pains. NMS also shows an increase during the progression of the disease as the highest incidence was in the stages 3 and stage 4 (Hoehn and Yahr).

Keywords: Parkinson's Disease; Non-Motor Symptoms; Hoehn and Yahr Staging; Unified Parkinson's Disease Rating Scale (UPDRS); Autonomic Symptoms; Cognitive Symptoms and Behavioural Symptoms.

Author's Affiliation: ¹Neurologist, Karpaga Vinayaga Institute of Medical Sciences and Research Centre, Madurantagam, Kancheepuram District, Tamil Nadu - 603308, India. ²Assistant Professor of Neurology, SRM Medical College Hospital and Research Centre, SRM Nagar, Kattankulathur, Kancheepuram District, Tamil Nadu 603203, India.

Corresponding Author Kalpana R., Assistant Professor of Neurology, SRM Medical College Hospital and Research Centre, SRM Nagar, Kattankulathur, Kancheepuram District, Tamil Nadu 603203, India.

E-mail: dr.kalpanasenthilkumar@gmail.com

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Introduction

Idiopathic Parkinson's disease (PD) the Shaking Palsy' is a very old common disease [1]. It is well known for its classical motor signs. They are akinesia, rigidity, tremor and postural instability. Besides the typical parkinsonian motor syndrome, patients with PD can present with a wide array of non-motor symptoms, mainly neuropsychiatric manifestations (as depression and cognitive

impairment), sleep disorders (as rapid eye movement behaviour disorder), autonomic dysfunctions (as constipation, postural hypotension and urinary disorders) and others like fatigue and pain. In their various combinations, non-motor symptoms (NMS) may eventually become the main manifestation of patients with PD. Early recognition and treatment of non-motor symptoms will improve the quality of life of the patients.

Aims and Objectives

To determine the non-motor symptoms prevailing among patients above 50 years with idiopathic Parkinson's disease.

To assess stages and severity of idiopathic Parkinson's disease.

To analyse the correlation of non-motor symptoms of Parkinson's disease with the severity and duration of disease.

Materials and Methods

Patients with Idiopathic Parkinson's Disease who attended the Neurology department as outpatient and inpatient in a tertiary care referral medical college hospital, Government Stanley Medical College Hospital in Chennai during the period July 2013 and July 2014 were studied. A total of 105 patients were studied. A detailed and complete neurological examination was done. Imaging (CT and MRI brain) was done to exclude atypical Parkinsonism. The patients were in the age group of more than 50 years and the disease duration varied between less than 5 years, 5 to 10 years and more than 10 years. The motor symptoms were assessed through the Unified Parkinson's Disease Rating Scale (UPDRS) and the disease staged according to the Hoehn and Yahr staging from stage 0 to stage 5. A total number of 105 Parkinson's disease patients who were above 50 years attending neurology department as outpatient and in-patient have been interviewed and clinically examined with a predesigned, pretested proforma. The non-motor features were assessed through the non-motor Symptoms Questionnaire (NMS QUEST) which contains 30 items.

This included cognitive dysfunction, sleep disorders, autonomic abnormalities, fatigue and depression. The prevalence of these non-motor symptoms across the various stages of the disease was studied and its correlation with the disease severity and duration assessed.

Study Type: Descriptive study.

Inclusion Criteria

1. Idiopathic Parkinson's disease patients with the age of onset of the disease at 50 years and above.
2. Patients willing to participate in the study.

Exclusion Criteria

1. Young onset Parkinson's disease (YOPD) with the age of onset below 50 years.
2. Parkinson's Plus Syndromes like Progressive Supranuclear Palsy (PSP), Multi System Atrophy (MSA), and Corticobasal Degeneration (CBD).
3. Patients with Vascular Parkinsonism.

Review of Literature

Idiopathic Parkinson disease is observed in all countries, all ethnic groups, and all socioeconomic classes. The incidence in African Americans is only one quarter than that in whites. There may be an increased incidence in rural compared to urban areas. In Asians, the incidence is one-third to one-half that in whites. The disease is frequent in North America, where there are approximately 1 million affected patients, constituting about 1 per cent of the population over the age of 65 years. The incidence in European countries is also the same.

Epidemiology of Parkinson's Disease (PD) in India

It differs from other countries populations and varies in different areas of India. Study done in Mumbai-Western by Bharucha et al. [2], in 1988 shows age-specific prevalence (>50 years) of 148/100,000. Study done in Kashmir-Northern by Razdan et al [3], in 1994 shows age-specific prevalence (>50 years) of 134/100,000, Crude prevalence of 14.2/100,000. Similarly another study by Gourie-Devi et al [4] 2004 in Karnataka-Southern shows Crude prevalence and age-specific prevalence of 33/100,000 and 76/100,000 respectively. In Das et al. [5], 2006 study in Kolkata-Eastern shows crude prevalence 45.82/100,000

Clinical Features

The motor features of Parkinson disease are, bradykinesia, resting tremor, rigidity, postural instability, stooped posture and festinating gait.

In addition the non-motor symptoms are also

common such as the sensory Symptoms (Olfactory dysfunction, abnormal sensations, Pain), Autonomic Dysfunction (Orthostatic hypotension, Urogenital dysfunction, Constipation), Neuropsychiatric manifestations-Mood disorders, Apathy, Frontal

executive dysfunction, Dementia and psychosis, Sleep Disorders, Sleep fragmentation, insomnia, REM sleep behaviour disorder (RBD), Periodic limb movements in sleep (PLMS) / Restless legs syndrome (RLS), Excessive daytime somnolence.

Symptom	Frequency (%)	Associated with Off Periods (%)
Tightening sensation	42	76
Tingling sensation	38	95
Diffuse pain	36	89
Neuralgic pain	18	78
Burning sensation	8	75

N = 50

From Witjas et al [6]

Diagnosis of Parkinson's Disease

The pathophysiology of NMS is suspected to involve neurotransmitters like dopamine, noradrenaline, and serotonin. The diagnosis is made by clinical examination which include history and neurological examination. By using Unified Parkinson's Disease Rating Scale patient was interviewed and observed.

The UPDRS is a scale that was developed as an effort to incorporate elements from existing scales to provide a comprehensive but efficient and flexible means to monitor PD-related disability and impairment. The scale itself has four components, largely derived from pre-existing scales that were reviewed and modified by a consortium of movement disorders specialists (Part I, Mentation, Behaviour and Mood; Part II, Activities of Daily Living; Part III, Motor; Part IV, complications). The UPDRS is often accompanied by and reported with such scales as the Schwab and England and Hoehn and Yahr scales [7], these latter scales are not part of the UPDRS per se. The strengths of the UPDRS are many, and the scale provides a relatively comprehensive assessment of motor aspects of PD. Extensive clinometric analyses have already been conducted on the UPDRS, providing it both scientific and clinical credibility. The UPDRS is less comprehensive in its assessment of non-motor features of the disease.

Hoehn and Yahr Stage

STAGE

- 0- No signs of disease
- 1- Unilateral disease
- 1.5- Unilateral plus axial involvement
- 2.0- Bilateral disease, without impairment of balance
- 2.5- Mild bilateral disease, with recovery on pull test
- 3.0- Mild to moderate bilateral disease, some postural instability, physically independent
- 4.0- Severe disability, still able to walk or stand unassisted
- 5.0- Wheelchair bound or bedridden unless aided

After G. Goetz et al - Rating Scales for Parkinson's disease [8].

Observation & Results

Age Distribution

The number of patients in the age group between 50 -60 years is 67. About 30 patients belonged to age group between 61-70 years and 8 of them were more than 70 years of age. Table 1 illustrates the age distribution of the study population.

Table 1:

S. No.	Age distribution	Frequency N=105
1	50-60	67
2	61-70	30
3	>70	8

Table 2:

S. No	Duration of disease in yrs	Frequency N=105	%
1	0-5	75	71.4
2	5-10	18	17.1
3	>10	12	11.5

Sex Distribution

There were 70 males and 35 females in the study population.

Duration of the Disease

The number of patients with the duration of the disease from 0-5 years were 75, 5-10 years were 18 and more than 10 years were 12. Table 2 illustrates the duration of the disease among the study population.

Stage of Disease

Table 3 illustrates the modified Hoehn and Yahr staging among the study population [8].

A prevalence of 22.9% of the study population belonged to stage 1 and 1.5. About 37.1% of them belonged to stage 2 and 2.5. Stage 3 consisted of 32.2% and stage 4 consisted of 7.6% of the study group.

Frequency of NMS among the Study Population

This study showed a higher prevalence of NMS like Nocturia (60%), urgency (44.8%) and constipation (52.4%). The next prevalent NMS were dizziness

(43.8%), anxiety (34.3%), depression (34%), memory (37.1%), dreams (24.8%), sleepiness (22.9%) and hallucinations (24.8%). Table 4 illustrates NMS among the study population.

Frequency of NMS among the Different Stages of Parkinsonian Disease.

The number of NMS in Stages 1 and 1.5 were in the range of 2 to 5 and mean 3.32.

The number of NMS in Stages 2 and 2.5 were in the range of 3 to 9 and mean 5.89.

The numbers of NMS in Stages 3 were 6 to 11 with mean as 7.67.

The number in stage 4 between 11 and 12 with mean 11.25.

In stage 1 no patient had dreams, insomnia, day time sleepiness, memory disturbances and falls. They also had very low prevalence of depression (12.5%), hallucination (16.7%), sexual dysfunction (12.5%) and sweating (8.3%). As the stage advances from stage 1 to stage 2 the NMS like dreams, insomnia, day time sleepiness, memory disturbances, RLS and falls increased in the range of 8% to 50%. As the stage advances from stage 2 to stage 3 there is significant increase in the prevalence of urgency (from 38.5% to 70.6%), dizziness (25% to 58.8%), day time sleepiness

Table 3: NMS based on the Hoehn and Yahr Staging

S. No	Stage	Frequency N=105	%
1	1 & 1.5	24	22.9
2	2 & 2.5	39	37.1
3	3	34	32.2
4	4	8	7.6

Table 4: Frequency of NMS among the study population

S. No	Symptoms	N=105	%
1	Drooling	22	21
2	Taste/Smell disturbance	20	19
3	Swallow	24	22.9
4	Constipation	55	52.4
5	Urgency	47	44.8
6	Nocturia	63	60
7	Dizziness	46	43.8
8	Pain	20	19
9	Dreams	26	24.8
10	Insomnia	36	33.3
11	Sleep	24	22.9
12	Memory	39	37.1
13	Anxiety	36	34.3
14	Depression	36	34.3
15	Hallucination	26	24.8
16	Sexual dysfunction	27	25.7
17	Fall	27	25.7
18	RLS	23	21.9
19	Sweating	32	30.5
20	Weight loss	23	21.9

(from 15.4% to 41.2%), falls (from 7.7% to 47.1%). As the stage advances from stage 3 to stage 4 there is increase in prevalence of NMS like Nocturia(from 64.7% to 100 %), depression (from 41.2% to 75%), hallucination (from 23.5 % to 50%), taste and smell disturbances from (23.5% to 62.5%).

Statistical Analysis

Data was obtained by clinical examination and by administering the questionnaire to the study population by interview method. Microsoft office excel 2010 was used to make the data entry and the data was entered was analysed using IBM SPSS 16.0 software.

Table 5: Frequency of NMS among the different stages of Parkinsonian disease

	Symptoms	Stage 1&1.5		Stage 2		Stage 3		Stage 4	
		N=24	%	N=39	%	N=34	%	N=8	%
1	Drooling	5	20.8	7	17.9	2	5.9	8	100
2	Taste/Smell disturbance	4	16.6	3	7.7	8	23.5	5	62.5
3	Swallow	5	20.8	7	17.9	4	11.8	8	100
4	Constipation	5	20.8	21	53.8	21	61.8	8	100
5	Urgency	4	16.6	15	38.5	24	70.6	4	50
6	Nocturia	6	25	27	69.2	22	64.7	8	100
7	Dizziness	12	50	10	25.6	20	58.8	4	50
8	Pain	11	45.8	5	12.8	4	11.8	8	100
9	Dreams	0	0	6	15.7	16	47.7	4	50
10	Insomnia	0	0	22	56.4	10	29.4	4	50
11	Sleepiness	0	0	6	15.4	14	41.2	4	50
12	Memory	0	0	12	30.8	23	67.6	4	50
13	Anxiety	7	29.2	13	33.3	12	35.3	4	50
14	Depression	3	12.5	13	33.3	14	41.2	6	75
15	Hallucination	4	16.7	10	25.6	8	23.5	4	50
16	Sexual dysfunction	3	12.5	17	43.6	7	20.6	8	100
17	Fall	24	22.9	3	7.7	16	47.1	8	100
18	RLS	1	4.2	12	30.8	10	29.4	8	100
19	Sweating	2	8.3	9	23.1	13	38.2	8	100
20	Weight loss	1	4.2	12	30.8	20	29.4	8	100

Discussion

Parkinson's disease was first described by James Parkinson in the year 1817. The natural history of the disease occurred between 45 to 70 years of age with the peak age of onset in the sixth decade. It was infrequent before 30 years and is more common in men than women.

Non-motor signs and symptoms in PD, although common, have been studied only recently in a comprehensive manner. It needs more attention for early recognition, quantitative assessment, and treatment. Patients usually under-report NMS. Health care professionals inadequately assess these symptoms and hence they are frequently missed. It is now accepted that many NMS will appear after beginning of classical motor signs while some NMS may even precede them. The Non-Motor Symptoms Questionnaire (NMS Quest) was used to measure NMS in PD. This questionnaire was developed by Chaudhuri et al [9] to address the need for a quantitative and validated instrument to measure NMS in PD. The NMS Quest is a self-completed

screening tool designed to assess the presence of NMS in PD patients [10]. It comprises of 30 items grouped according to nine domains, and it takes only a few minutes to complete assessment. This questionnaire was used in this study.

Prevalence of NMS among the Study Population:

Our study showed a higher prevalence of NMS like Nocturia (60%), urgency (44.8%) and constipation (52.4%) among the study population. This is comparable to a study done by Chaudhuri et al [9,10] who also reported a higher prevalence of Nocturia (60%), urgency (53%) and constipation (50%).

The next prevalent NMS were Dizziness (43.8%) Anxiety (34.3%), depression (34.3%) insomnia (33.3) memory (37.1%), dreams (24.8%), hallucinations (24.8%) and sleepiness (22.9%) These were less compared to Chaudhuri et al [9,10].

Which has documented a higher prevalence of the same, namely Insomnia(43%), memory (43%), Depression (45%) dreams (34%), anxiety (42%), sleepiness (29%), and hallucinations (20%).

A study done by PD Hinduja National hospital Mumbai by Amrita Ravenshows prevalence of constipation 56%, urgency 48%, weight loss 24.6% but other symptoms show higher percentage when compared to our study [11].

A study done in Peru by Carlos Cosentino et al shows a prevalence of constipation 55.7%, Dizziness 47.7%, swallowing difficulty 22.3% which is similar to our study [12].

Urinary Symptoms

In the Current study the prevalence of nocturia is 60% and urgency 44.85%. This goes hand in hand with a study done by Choudhari et al with prevalence of Nocturia 60%, Urgency 53% [10]. In the study by Amrita Raven et al, nocturia was reported in 91% & urgency in 48% [11], In an international study in Peru by Carlos Cosentino reported Nocturia 77.3%, Urgency 66.3%, Constipation 55.7% [13].

Constipation

Current study reveals constipation 52.4% which is similar to studies by Choudhari [9,10] which disclosed a prevalence of 50%. Amrita Raven et al showed 59% [11] and Carlos Cosentino et al showed a prevalence of 55.7% [12].

Dizziness

In the Current study 43.8% of the study population had dizziness. This is similar to a study done by Choudhari et al [9,10], with a prevalence of 35%. Another study done by Amrita Raven et al [11] showed a prevalence of 23% and Carlos Cosentino et al [12] reported with prevalence of 47.7%.

Mood Disturbances

The Current study showed a prevalence of Anxiety 34.3% and Depression 34.3%. This is similar to a study done by Choudhari et al with anxiety 42% [10] and depression 45%, Choudhari et al [11] showed a prevalence of anxiety 55% and depression 48% [11]. Carlos Cosentino et al [12] also showed a prevalence of anxiety 61.3% and depression 80.7%. Cummings et al [13] showed a mean of 40%. This also goes hand in hand with a study done by Shulman et al [14] which showed a prevalence of 36-50% and Arun et al [15] showing a prevalence of 54.3%.

Sleep Disorders

This study shows a prevalence of insomnia 33.3% and 22.9% day time sleepiness. This goes hand in

hand with a study done by Choudhari et al [11] in PD Hinduja National hospital Mumbai with a prevalence of day time sleepiness and insomnia 35.8% and 43.2% respectively.

Another study done by Suresh Kumar et al [16] in All India Institute of Medical Sciences, New Delhi reported insomnia in 32%, nightmares in 32%, and excessive day time sleepiness in 15%. Choudhari et al [10] reported insomnia in 43% and day time sleepiness in 29%.

Memory Disturbance

The Current study shows a prevalence of memory disturbances in 37.1% which is similar to a study done by Aarsland D et al [17] with 31% and Choudhari et al [9,10] with 43%.

Hallucination

The current study showed a prevalence of hallucination in 24.8%. In a study done by Fenelon et al [18] the prevalence was 40%, Choudhari et al 20% [9,10], Meena Gupta et al [19] 34.9% and et al [11] showed 13%.

Taste and Smell Disturbance

In the current study the study population had a prevalence of 19% taste and smell disturbances. However this is similar with a study done by et al [11] with 20% and Choudhari et al [9,10] with 29%.

Pain

The prevalence of pain in the current study is 19%. In a study done by L. Nègre-Pagès et al [20] and C.G. Goetz, et al [8] showed the prevalence of pain is 30% to 85% respectively. The most prevalent NMS in the current study is the autonomic symptoms namely nocturia urgency, constipation, sweating, dizziness and drooling. This was followed by neuropsychiatric symptoms like memory disturbances, depression, anxiety and hallucinations and sleep disturbances which include insomnia, sleepiness and dreams. Pain and weight loss were also Prevalent. Diplopia, delusions, bowel and bladder incontinence were reported in a small percentage of patients. A study done by Aaron de Souza et al [21] the NMS range is 0 to 8 with the median 3. In his study the most common symptoms were autonomic symptoms (urinary urgency, constipation), cognitive and behavioural symptoms. The sexual dysfunction and sleep disturbance were seen in a lesser number of patients. NMS was significantly related to H & Y stage

[7].

Correlation with Severity and Duration

The current study shows an increase in the prevalence of NMS as the severity and duration of the disease advances. The number of NMS ranged between 2 to 5 in stages 1 and 1.5, increased to 3 to 9 in stages 2 and 2.5 and ranged between 6 to 11 in stages 3 and ranged between 11 to 12 in stages 4. The number of NMS were 5.1 when the duration of the disease was less than 5 years and increased to more than 9 with the duration of the disease more than 5 years. It was reported maximum when the duration of the disease was more than 10 years.

The current study shows that in stage 1, none of the patient had dreams, insomnia, day time sleepiness, memory disturbances and falls. Very low prevalence of depression (12.5%), hallucination (16.7%), sexual dysfunction (12.5%) and sweating (8.3%) was reported. As the stage advances from stage 1 to stage 2 the NMS like dreams, insomnia, day time sleepiness, memory disturbances, RLS and falls increased in the range of 8% to 50%. As the stage advances from stage 2 to stage 3 there is significant increase in the prevalence of urgency (from 38.5% to 70.6%), dizziness (25% to 58.8%), day time sleepiness (from 15.4% to 41.2%), falls (from 7.7% to 47.1%). As the stage advances from stage 3 to stage 4 there is increase in prevalence of NMS like nocturia (from 64.7% to 100%), depression (from 41.2% to 75%), hallucination (from 23.5% to 50%), taste and smell disturbances from (23.5% to 62.5%). Thus this study goes hand in hand with a study done by Aaron de Souza et al in Goa [21].

Our study has highlighted the fact that NMS occur quite early in the clinical course of Parkinson disease (H & Y stage 1). Hence the evaluation of any patient presenting with Parkinson disease should necessarily include assessment of non-motor symptoms along with motor symptoms since early treatment of these NMS will improve the overall physical quality of life in these patients.

Further research is needed to unravel the exact aetiopathophysiological mechanisms of these NMS in Parkinson disease, which will pave way for better and more effective therapeutic options in future.

Conclusion

Non-motor symptoms are prevalent across all stages of Parkinson's disease.

In our study, the most prevalent non-motor

symptoms were autonomic dysfunctions such as constipation, nocturia, urgency and sweating, followed by insomnia, depression and memory disturbances. Dizziness, drooling, falls and unexplained pains were also reported commonly.

As the disease severity progresses, the number of NMSs also showed an increase in their prevalence. The number of NMS in stages 1 and 1.5 were the least. It increased through stages 2 and 2.5 and was highest reported in stages 3 and 4. The number of NMSs also correlated with the duration of the disease. The number of NMSs was least when the duration of Parkinson's disease was less than 2 years, increasing as the duration increased and maximum reported when duration of the illness was more than 5 years.

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