Paper

Non motor symptoms in patients with Parkinson disease: experience from a tertiary care center in Sri Lanka

S B Gunatilake[1], N D Perera[1], K M Bandara[1], A U Pathirana[1], A G S Asiri[2], M T M Riffsy[2]

Sri Lanka Journal of Neurology, 2014, **3**, 5-11

Abstract

Non motor symptoms (NMS) of Parkinson's disease (PD) lead to morbidity, impaired quality of life and frequent hospitalization. NMS are under-recognized and under-reported. NMSQuest is a validated screening tool adopted to identify these symptoms in patients with PD. We conducted a descriptive cross sectional study during March 2012 – September 2012 in a tertiary care hospital in Sri Lanka to describe the non-motor symptoms of PD and to determine the percentage of NMS that remain undeclared to the healthcare professionals. 103 patients, age 64.55 (SD 9.62, range 43-86) years, 58 (56.3%) males and 45 (43.7%) females completed the study. Mean duration of illness was 3.16 yrs. 98.1% of patients had at least one NMS. The mean total NMSQ-T was 9.08 +/- 5.087(SD). Memory loss was the commonest NMS. NMSQ-T increased with the severity of PD ($p<0.001$) but no association was found between NMSQ-T and age, sex or duration of illness. Loss of weight, difficulty in swallowing and falls were significantly commoner among males than females. ($p <0.05$) A significant proportion of NMS (Mean 76.1 +/- 17.7, range 36.7% to 100%) were undeclared to the health care personnel. Incomplete bowel evacuation, sweating, diplopia and anxiety were the least declared symptoms. In conclusion, NMS are present in the majority of patients with PD increasing with the severity of disease. A significant proportion of NMS are undeclared to the healthcare personnel highlighting the importance of using screening tools to identify these symptoms during health visits.

Index words: Parkinson's disease, non motor symptoms

Introduction

Parkinson's disease (PD) is the second commonest neurodegenerative disorder affecting people from all cultures and races around the world. Although the motor symptoms of Parkinson's disease are well defined, the non-motor features of this disorder are under-recognized and consequently, under treated. However, James Parkinson, who first described the disease in 1817, described the non-motor symptoms, sleep disturbance, constipation, dysarthria, dysphonia, dysphagia, sialorrhoea, urinary incontinence and 'constant sleepiness with slight delirium' in his essay titled "The Shaking Palsy"[1].

There has been growing interest in research on non-motor symptoms (NMS) of PD and recent studies reveal that these symptoms could manifest prior to the onset of motor symptoms (pre motor PD) inevitably merging with disease progression[2,3]. As disease advances, non-motor symptoms dominate the clinical picture causing additional morbidity, impaired quality of life and shortened life expectancy. National Institute for Clinical Excellence in England has found under-reporting and under-recognition of non-motor symptoms an important unmet need in PD[4]. Additionally, non-motor symptoms are a frequent cause of hospitalization and institutionalization, which increases the cost of care of patients with PD[4].

Some of these symptoms are undeclared to the health care providers, further delaying recognition. A recent international survey has shown that up to 62% of symptoms of Parkinson's disease remain undeclared to the health care professionals because they are unaware that the symptoms are linked to Parkinson's disease or are embarrassed to talk about them[10]. Early identification would result in better outcome for the patients by symptom directed therapy.

Because of the range of non-motor symptoms, questionnaires and tools have been developed to help identify NMS in PD patients. NMSQuest is a self-administered 30 item questionnaire, validated as a screening tool identifying nine NMS domains. (Appendix 1) Chaudhri and colleagues described the presence of approximately 10-12 NMS in PD patients with the use of NMSQuest[6].

There is paucity of studies on non-motor symptoms of PD from developing countries and no published data in Sri Lanka. We conducted a cross sectional study in a tertiary care institution in Sri Lanka to identify the presence of NMS in patients diagnosed with PD and to identify the proportion of patients with undeclared symptoms.

[1] *Department of Medicine, University of Jayewardenepura,* [2] *Colombo South Teaching Hospital, Sri Lanka.*

Objective

To describe the non-motor symptoms of Parkinson's disease and to determine the percentage of non-motor symptoms that remains undeclared to the healthcare professionals.

Methods

This was a descriptive cross sectional study conducted at Colombo South Teaching Hospital, a tertiary care center in the city of Colombo. Study was conducted during March 2012 – September 2012. We recruited 103 patients diagnosed as PD (according to diagnostic criteria of the United Kingdom Parkinson's Disease Society Brain Bank) attending neurology and medical clinics. Exclusion criteria were employed to exclude patients with an alternative explanation as the cause for Parkinsonism (Table 1).

Table 1. Exclusion criteria

Features considered as exclusion criteria in patients with parkinsonism
• History of repeated strokes with stepwise progression of parkinsonism features
• History of repeated head injury
• History of definite encephalitis
• Neuroleptic treatment at onset of symptoms
• >1 affected relatives
• Sustained remission
• Strictly unilateral features after 3 years
• Supranuclear gaze palsy
• Cerebellar signs
• Early severe autonomic involvement
• Early severe dementia with disturbances of memory, language and praxis
• Babinski's sign
• Presence of a cerebral tumour or communicating hydrocephalus on computed tomography scan

Patients included in the study were interviewed to obtain demographic data, duration of disease, presence of non-motor symptoms and to assess severity of PD. NMS were assessed using the NMSQuest and the severity of PD was assessed using the Hoehn and Yahr staging. 28 questions were used to identify non motor symptoms and the presence or absence was documented as a "Yes" or "No" response. Further clarification was sought on whether symptoms were "declared" or "undeclared". Questions on sexual problems were not assessed due to poor response from patients and cultural reasons.

Statistical analysis

Data (NMSQ-T) was scattered in a normal distribution when tested with Shapiro- Wilk test (p 0.087). Descriptive statistics such as percentage was used to determine the frequency of each NMS. NMSQ total score (NMSQ-T) was calculated by computing the number of positive responses in NMSQuest. Frequency of undeclared NMS was computed and expressed as a percentage of patients with each non motor symptom. Association between NMSQ-T and sex, HY stage was assessed using ANOVA test. Comparison of means was also used to assess the association between NMSQ-T and HY stage categories. Correlation was used to identify the association between NMSQ-T and age, duration of illness. Test results were interpreted as significant when $p<0.05$ with a 95% confidence interval. Analysis was performed using SPSS 19.0 version.

Ethical approval

Informed consent was obtained from all participants. Ethical approval was obtained from the Ethics Review Committee of Faculty of Medical Sciences, University of Sri Jayewardenepura.

Results

Hundred and three patients, age 64.55 (SD 9.62, range 43-86) years, 58 (56.3%) males and 45 (43.7%) females completed the study. Mean duration of illness was 3.16 years and ranged from 1 month to 15 years. Duration of illness was further categorized into four groups. (≤59, 60-119, 120-179 and 180 or more months)

One patient had a family history of Parkinson's disease. Co-morbidities such as diabetes mellitus, hypertension, ischemic heart disease, and stroke were seen in 57 (55.3%) patients. Resting tremor (102, 99%) and muscular rigidity (96, 93.2%) were the commonest motor symptoms, while bradykinesia and postural instability were reported in 53 (51.5%) and 41 (39.8%) patients respectively. Patient characteristics are summarized in table 2.

Table 2. Characteristics of the sample population

	Total (N= 103)
Males, N (%)	58 (56.3)
Age, Mean (SD)	64.55 (9.62)
Disease duration in months, N (%)	
Mean	38.63
≤59	81 (78.6)
60-119	13 (12.6)
120-179	8 (7.8)
180 or more	1 (1.0)
Smoking, N (%)	24 (23.3)
Co morbidities, N (%)	57 (55.3)
Diabetes mellitus	24 (23.3)
Hypertension	36 (38.9)
Dyslipidaemia	22 (21.4)
Ischaemic heart disease	13 (12.6)
Antiparkinsonian medication, N (%)	
Drug naive	2 (2)
Levodopa	100 (97.1)
Dopamine agonists	11 (10.7)
Hoehn and Yahr staging N (%)	
Stage 1	22 (21.4)
Stage 2	37 (35.9)
Stage 3	32 (31.1)
Stage 4	11 (10.7)
Stage 5	1 (1)

Presence of non-motor symptoms

Majority of patients (n= 101, 98.1%) had at least one or more non-motor symptoms. Two patients without any NMS were below the age of 50yrs (44yrs and 47yrs respectively). The mean total NMSQ-T was 9.08 (SD 5.09) ranging from 0 to 24 of a maximum of 28. Memory loss was the commonest non-motor symptom (n= 64, 62.1%) while vomiting was the least observed symptom (n=4, 3.9%). Difficulty in concentrating, daytime sleepiness, restless legs, constipation, weight loss and memory loss were seen in more than 50% of patients.

ANOVA test revealed a significant association between the HY stage and NMSQ-T ($p<0.001$). NMSQ-T gradually decreased in stages 4 and 5 compared to stage 3 but remained higher than mean NMSQ-T of stages 1 and 2. (Figure 1) We further categorized HY stages 1 and 2 as "Mild" and stages 3, 4, 5 as "Moderate-severe". Comparison of mean NMSQ-T by t-test between these 2 groups revealed a significant difference (7.08 and 12.14, $p<0.01$) suggesting that NMSQ-T was commoner among moderate-severe disease than mild disease.

No association was found between the NMSQ-T and age (r= 0.127, p 0.149) or duration of disease (r= 0.097, p 0.328). Duration of disease was further divided into four

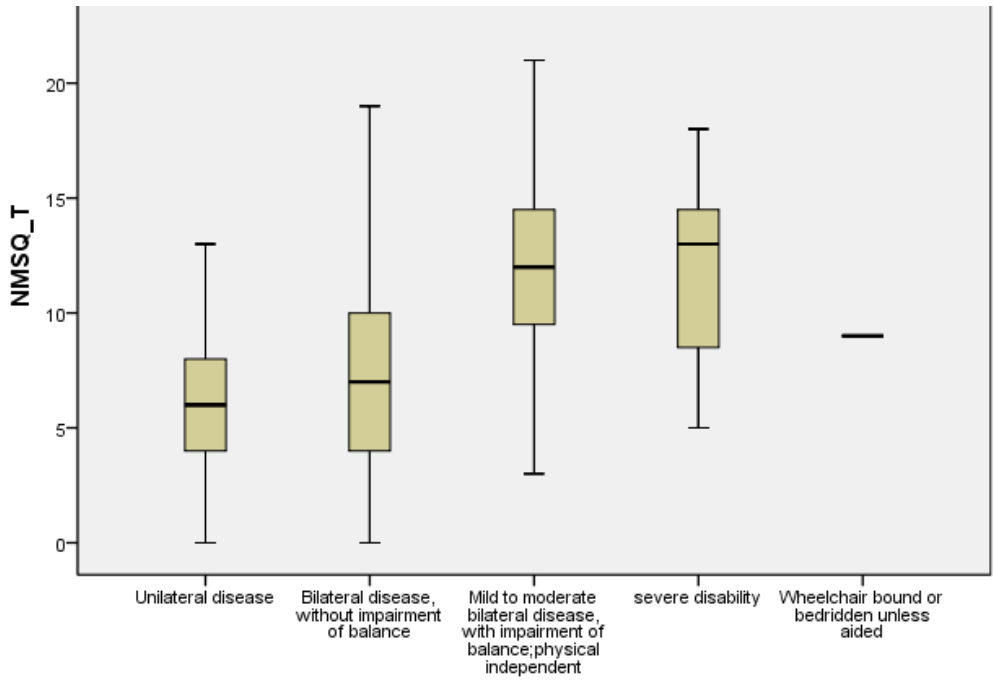

Figure1. Association between NMSQ-T and the HY stage of Parkinson disease.

groups (≤59, 60-119, 120-179 and 180 or more months) and the mean NMSQ-T of each group was compared, which did not reveal a significant difference between the groups. T-test did not reveal a significant association between NMSQ-T and sex. (P 0.095) Chi-square test was used to compare the presence of individual NMS in males and females. Loss of weight, difficulty in swallowing and falls were significantly commoner among males than females with p values of 0.037, 0.03 and 0.038 respectively.

Undeclared symptoms

A significant proportion of non-motor symptoms were undeclared to the health care personnel. Proportion of undeclared symptoms varied with the individual symptom ranging from 36.7% to 100%. Mean was 76.1 +/- 17.7 (SD) (Figure 2). Incomplete bowel evacuation, sweating, diplopia and anxiety were the least declared symptoms (Table 4).

Table 3. Individual NMS assessed by NMS Questionnaire

NMS	*Male, N (%)*	*Female, N (%)*	*Total, N (%)*
Nausea/ Vomiting	3 (2.9)	1 (1.0)	4 (3.9)
Incomplete bowel emptying	4 (3.9)	2 (1.9)	6 (5.8)
Faecal incontinence	6 (5.8)	3 (2.9)	9 (8.8)
Loss of taste/smell	6 (5.8)	3 (2.9)	9 (8.8)
Acting out during dreams	7 (6.8)	5 (4.8)	12 (11.6)
Leg swelling	6 (5.8)	9 (8.8)	15 (14.6)
Diplopia	11 (10.7)	9 (8.8)	20 (19.4)
Nocturia	13 (12.6)	7 (6.8)	20 (19.4)
Hallucinations	16 (15.5)	9 (8.8)	25 (24.2)
Delusions	15 (14.6)	10 (9.7)	25 (24.2)
Dribbling of saliva	20 (19.4)	9 (8.8)	29 (28.1)
Falls*	17 (16.5)	12 (11.6)	29 (28.1)
Insomnia	19 (18.4)	11 (10.7)	30 (29.1)
Fearful dreams	21 (20.4)	10 (9.7)	31 (30.1)
Anxiety	22 (21.4)	9 (8.8)	31 (30.1)
Swallowing difficulty*	37 (35.9)	13 (12.6)	40 (38.9)
Sweating	25 (24.3)	16 (15.5)	41 (39.8)
Urgency	24 (23.3)	18 (17.5)	42 (40.8)
Body pains	20 (19.4)	23 (22.3)	43 (41.8)
Postural dizziness	26 (25.2)	19 (18.4)	45 (43.7)
Sad/low mood	27 (26.2)	21 (20.4)	48 (46.6)
Loss of interest	32 (31.1)	19 (18.4)	51 (49.5)
Difficulty concentrating	32 (31.1)	21 (20.4)	53 (51.4)
Daytime sleepiness	35 (34.0)	19 (18.4)	54 (52.4)
Restless legs	35 (34.0)	20 (19.4)	55 (53.4)
Constipation	31 (30.1)	25 (24.3)	56 (54.3)
Weight loss*	36 (35.0)	21 (20.4)	57 (55.4)
Memory loss	37 (35.9)	27 (26.2)	64 (62.1)

* These symptoms were common among males than females with a p<0.05 when analyzed by chi-square test

Table 4. Percentage of undeclared non motor symptoms among the study population

Non motor symptom	*Total no of patients (n)*	*No with undeclared symptoms (n)*	*Percentage undeclared (%)*
Insomnia	30	11	36.7
Faecal Incontinence	09	04	44.4
Falls	29	13	44.8
Body aches	43	21	48.8
Leg swelling	15	08	53.3
Restless legs	55	33	60.0
Postural hypotension	45	28	62.2
Constipation	56	37	66.1
Drooling saliva	29	20	68.9
Vomiting	04	03	75.0
Acting out dreams	12	09	75.0
Hallucinations	25	19	76.0
Dementia	64	51	79.69
Difficulty in swallowing	40	32	80.0
Difficulty concentrating	53	43	81.1
Daytime somnolence	54	45	83.3
Low mood	48	41	85.4
Loss of interest	51	44	86.3
Urgency	42	37	88.1
Loss of taste or smell	09	08	88.9
Nocturia	20	18	90.0
Fearful dreams	31	28	90.3
Loss of weight	57	52	91.2
Delusions	25	23	92.0
Anxiety	31	29	93.6
Diplopia	20	19	95.0
Sweating	40	38	95.0
Incomplete bowel emptying	06	06	100.0

Discussion

Our study included 103 diagnosed PD patients in all stages of disease, representing a disease duration of 1 month to 15 years. Non motor symptoms were present in the majority of these patients with 98.1% reporting at least one NMS. Patients had an average of 9 non motor symptoms which is comparable to the published literature. Study conducted by Chaudri et al found that patients with PD had 10-12 NMS[6]. A multicenter study on 545 patients by Pablo Martinez-Martin et al revealed a prevalence of 9-12 NMS in patients with PD[7].

Commonest non motor symptoms were memory loss, weight loss and constipation. Memory loss was the commonest symptom in our group (62.1%) but ranged from 25.1% - 51.2% in other studies[6,7,8]. This wide range could be due to the different tools adopted to identify memory loss and cognitive function. However, studies using specific cognitive assessment methods have also found a similar prevalence of cognitive impairment to our study among patients with PD[9]. Studies further reveal that patients with memory impairment frequently complain of other NMS than patients without memory problems[9]. Therefore, memory loss should be identified in these patients for a better overall outcome. Gastro-intestinal symptoms such as vomiting, incomplete bowel emptying and faecal incontinence were the least reported NMS in our study population.

We found that non motor symptoms increased significantly with the severity of PD as judged by Hoehn and Yahr stage. A positive association was seen up to stage 3. This finding was consistent with the other international studies demonstrating an increase in NMS with the increasing severity of motor symptoms of PD[6,7,8]. Patients with severe motor symptoms (HY stage 4 and 5) had less NMS than moderate disease. It is possible that patients do not declare NMS in the presence of severe motor disability. However, patients with moderate-severe PD had significantly higher NMS scores than patients

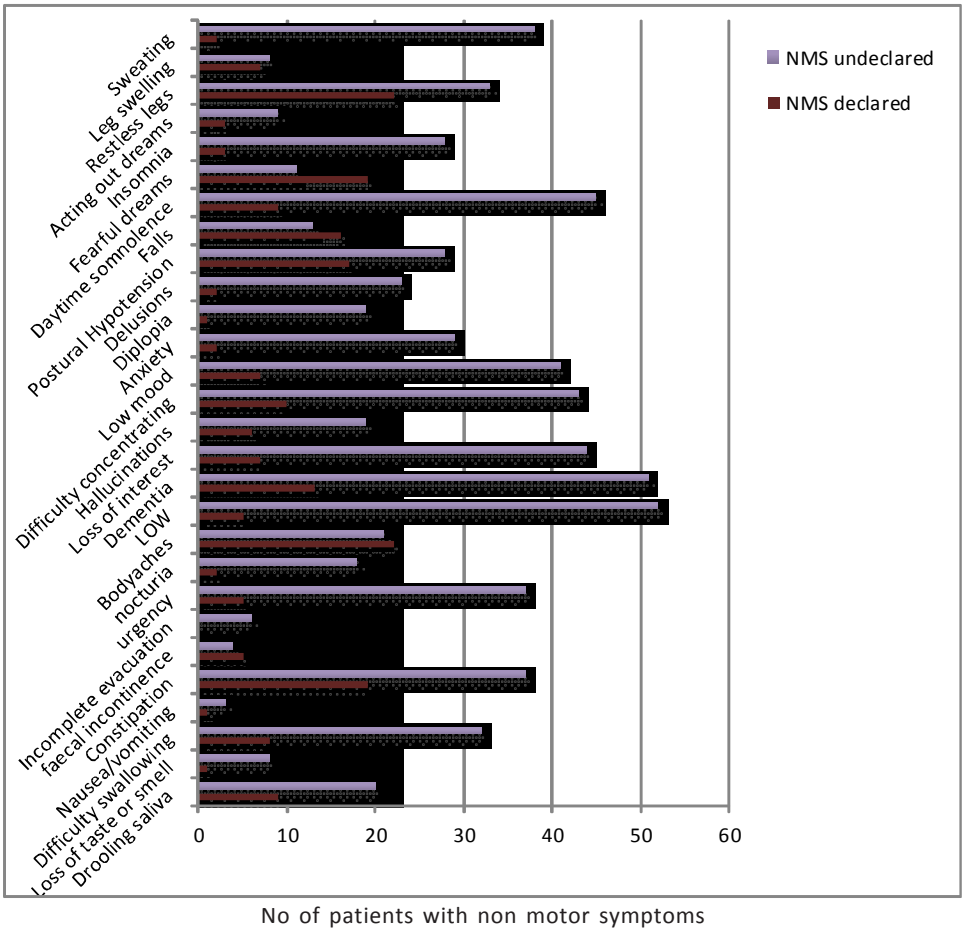

Figure 2. Individual declared and undeclared NMS.

This figure demonstrates the higher proportion of undeclared symptoms (light purple) compared to declared individual symptoms (red).

with mild disease. It is well known that NMS contribute to morbidity and impaired quality of life[8]. Therefore, NMS should be identified in patients with moderate-severe disease to minimize disability. Our study also highlights that NMS occur in mild PD patients as well (HY stage 1 and 2) and screening for NMS should not be limited to severe PD.

We did not find an association between NMSQ-T and sex or age but few individual symptoms (loss of weight, falls and difficulty in swallowing) were more common among males. There was no association between NMSQ-T and disease duration in our population which was in contrast to the available data demonstrating an increase in NMS with duration of disease[6,7]. Severity of disease (Mean and Median HY stage) in our study population was similar to published literature but with a lower duration of disease. Mean duration of illness was 3 yrs as compared to 5-9 yrs in other studies[7,8]. It is possible that our patients had a delayed presentation to healthcare providers resulting in failure to demonstrate an association between NMS and the disease duration on final analysis.

Most important finding in our study was the significant proportion of undeclared symptoms. 76% of symptoms were undeclared to the healthcare provider on average with symptoms such as incomplete bowel emptying, sweating, diplopia, anxiety and delusions being least declared despite their presence. This highlights the importance of inquiring about these symptoms and the use of screening tools during health visits for early identification of NMS in patients with PD.

Study limitations

Main limitation was the absence of an age matched control group to compare the NMS, as some of these

symptoms are common among the elderly. NMS are also subjective and could've influenced the results.

Conclusion

Non motor symptoms are present in the majority of patients with PD increasing with the severity of disease. Memory impairment, weight loss and constipation are frequently observed. A significant proportion of NMS are undeclared to the healthcare personnel highlighting the importance of using screening tools to identify these symptoms during health visits.

References

1. Alves G, Forsaa EB, Pedersen KF, Dreetz Gjerstad M, Larsen JP. Epidemiology of Parkinson's disease. *J Neurol* 2008; **255** (Suppl. 5): 18-32.
2. Chaudhuri KR, Schapira AHV. The non motor symptoms of Parkinson's disease: dopaminergic pathophysiology and treatment. *Lancet Neurol* 2009; **8**: 464-74.
3. Hawkes C, Del Tredici K, Braak H. Parkinson's disease: a dual hit hypothesis. *Neuropathol Appl Neurobiol* 2007; **33**: 599-614.
4. The National Institute for Clinical Excellence (NICE). Clinical guideline 35. Chapter 9. Parkinson's disease, June 2006 http://www.nice.org.uk/
5. Chaudhuri KR, Odin P, Antonini A, Martinez-Martin P. Parkinson's disease: The non-motor issues. *Parkinsonism and Related Disorders* 2011; **17**: 717-23.
6. Chaudhuri KR , Martinez-Martin P, Schapira AHV, et al. International Multicenter Pilot Study of the First Comprehensive Self-Completed Nonmotor Symptoms Questionnaire for Parkinson's Disease: The NMSQuest Study. *Movement Disorders* 2006; **21**: 916-23.
7. Martinez-Martin P, Schapira AHV, Stocchi F, et al. Prevalence of Nonmotor Symptoms in Parkinson's Disease in an International Setting; Study Using Nonmotor Symptoms Questionnaire in 545 Patients. *Movement Disorders* 2007; **22**: 1623-9.
8. Barone P, Antonini A, Colosimo C, et al. The Priamo Study: A Multicenter Assessment of Nonmotor Symptoms and Their Impact on Quality of Life in Parkinson's Disease. *Movement Disorders* 2009; **24**: 1641-9.
9. Naismith SL, Pereira M, Shine JM, Lewis SJG. How well do caregivers detect mild cognitive change in Parkinson's disease? *Movement Disorders* 2011; **26**: 161-4.
10. Chaudhuri KR, Healy DG, Schapira AH. Non motor symptoms of Parkinson's disease: diagnosis and management. *Lancet Neurol.* 2006; **5**(3): 235-45.