Original Article

Profile of Nonmotor Symptoms and the Association with the Quality of Life of Parkinson's Disease Patients in Nigeria

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Abstract

Context: Parkinson's disease (PD) is the second most common neurodegenerative disorder. Several nonmotor symptoms (NMS) are associated with the condition, affecting multiple body systems in addition to the nervous system. **Aims:** The aim of the study is to describe the profile of NMS and the factors related to their severity as well as their association with the quality of life (QoL) among patients with PD in a Nigerian neurology clinic. **Methods:** A total of 105 patients with PD and 105 healthy controls were assessed for various NMS using a validated NMS assessment scale. A validated PD-specific QoL assessment tool, the PD Questionnaire-39 was also administered to the study patients with PD. Analyses for correlation and difference were performed to determine the associated factors of NMS severity and their association with QoL. **Results:** The most common NMS in the PD patients were in the domains of sleep/fatigue and mood/cognition. The total NMS score were significantly higher in patients compared to controls (median [interquartile range] 42 [13–72] vs. 20 [14–29], $P < 0.001$). There was a significantly higher score in the advanced Hoehn and Yahr stages ($P < 0.001$). The duration of PD had a positive correlation with the NMS scores ($r_s = 0.207$, $P = 0.034$. The total NMS score had a strong positive correlation with the QoL ($r_s = 0.851$, $P < 0.001$). **Conclusion:** PD is associated with significant NMS and worsens with the progression of the disease and the duration of illness. These NMS have a significant association with the QoL, necessitating the need for detailed and prompt evaluation and management.

Keywords: Africa, Nigeria, nonmotor symptoms, Parkinson's disease, quality of life

Introduction

James Parkinson first cogently described Parkinson's disease (PD) in 1817 in his essay on the shaking palsy. Initially termed "paralysis agitans," the name was changed over time to PD or idiopathic PD.[1] Parkinsonism, including PD, is the most common movement disorder and PD is the second most common neurodegenerative disorder.[2-4]

It is clinically characterized by resting tremor, bradykinesia, rigidity, and postural instability, all of which are due to pathology in the nigrostriatal pathways with depigmentation of the dopaminergic neurons at the substantia nigra pars compacta and dystrophic putaminal projections.[3] However, it is also associated with significant nonmotor symptoms (NMS), which may precede or postdate the onset of motor symptoms with a substantial effect on a patient's quality of life (QoL).[5]

The motor symptoms in PD are usually more striking to the clinician, resulting in a tendency to relegate NMS to the background. However, to the patient, the NMS are equally if not more important. NMS in PD have not been extensively studied like the motor symptoms. The progression and impact of these symptoms on QoL are essential in the diagnosis and treatment of this illness but are not yet well researched.[3,6,7] NMS predicts disability and QoL and substantially increases the cost of care with increased hospitalization and need for treatment. However, assessment and management of NMS in PD have remained an unmet need.[5,8-11]

The relative paucity of data on the NMS among PD patients in Nigeria is the rationale for this study which aimed to describe the profile and factors related to NMS severity as well as the association between NMS severity and the PD-related QoL among patients with PD in Southwestern Nigeria.

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Methods

Study design

This was a hospital-based cross-sectional study.

Setting

The study was carried out at the Neurology Outpatient Clinic of Lagos State University Teaching Hospital (LASUTH), which is a tertiary hospital located in the Southwestern part of Nigeria and is a major referral center for medical cases.

Participants

The study population comprised 105 PD attending the Neurology Outpatient Clinic at LASUTH who were consecutively selected over a 6-month period. The diagnosis of PD was based on the 2015 Movement Disorders Society clinical diagnostic criteria.[12] Patients with a known history of stroke or other neurodegenerative diseases, secondary Parkinsonism (based on clinical and radiological features), diabetes mellitus, and frank psychosis or schizoaffective disorders were excluded from the study. Age- and sex-matched individuals without PD from the Medical Outpatient Clinic at LASUTH were selected as controls.

Study instrument

A structured questionnaire divided into three parts. The first part consist of the participant's biodata, comorbidities, disease duration, Hoehn and Yahr (H and Y) staging and drug treatment status.The second part is the standard NMS assessment scale for PD (NMSS) while the third part is the PD questionnaire (PDQ-39). The license for the PDQ-39 was provided by Clinical Outcomes at Oxford University Innovation Limited. The NMSS and PDQ-39 were translated to the local language (Yoruba) and back-translated to English.

Main outcome measures

Nonmotor symptoms assessment scale

The NMSS has thirty items grouped into nine domains: cardiovascular (2 items), sleep/fatigue (4 items), mood/cognition (6 items), perceptual problems/hallucinations (3 items), attention/memory (3 items), gastrointestinal tract (3 items), urinary function (3 items), sexual function (2 items), and miscellaneous (4 items). Each item is scored on severity (score range: 0–3) and frequency (score range: 1–4). A product of the severity and frequency score of each of the items is summed to determine the NMS burden (NMSB). NMSB ranges from 0 to 360.[8]

Parkinson's disease questionnaire summary index score

The PDQ-39 is a 39-item questionnaire that assesses the PD-related QoL in the preceding month. Eight discrete scales are examined, namely mobility (ten items, #1–10), activities of daily living (six items, #11–16), emotional well-being (six items, #17–22), stigma (four items, #23–26), social support (three items, #27–29), cognition (four items #30–33), communication (three items, #34–36), and bodily discomfort (three items, #37–39). A five-point ordinal scale is used to determine the frequency of assessed questions, with scores given as 0 – never, 1 – occasionally, 2 – sometimes, 3 – often, and 4 – always.[13] The PDQ summary index (PDQSI) is derived by summing up the scores of the eight discrete scales after they are converted into percentages. The summed-up scores are then divided by eight to give a single summary index value which is the PDQSI. The values of PDQSI range from 0 to 100.[13]

Data collection method

Each participant was interviewed using the questionnaires with each interview lasting between 30 and 45 min. The questionnaires were pretested in a 20-patient subset who were carried over into the main study. A unique identifier was tagged to the patient's record to prevent duplicate assessment. The PDQ-39 was only administered to the PD patients. Only one investigator administered the questionnaires to all the patients to ensure uniformity of interpretation.

Statistical analysis

Data were inputted and analyzed using the Statistical Package for the Social Sciences version 23 (IBM SPSS Statistics for Windows, IBM Corp., Armonk, NY). Profile of participants in the study was represented by frequency tables and appropriate charts, with a central tendency based on the type of variable.

Variables in the study did not represent a normal distribution, and this was determined using the Shapiro–Wilk test. Therefore, nominal data were summarized using mode, ordinal, and continuous data using median and interquartile range (IQR).

The relationship between the categorical variables (including age groups, sex, the presence of comorbidities, smoking, alcohol consumption, and type of drug treatment) and the median NMS scores were tested using the Mann–Whitney U-test for two independent variables or Kruskal–Wallis test for more than two independent variables. The association between H and Y staging and NMSS scores was tested using the Kruskal–Wallis test. The relationship between duration of illness and NMS score as well as the relationship between NMS scores and PDQSI were assessed using the Spearman-rho correlation coefficient. $P < 0.05$ was considered as statistically significant.

Ethical considerations

This study was approved by the Health Research Ethics Committee of LASUTH. Informed consent was obtained from all the participants and data derived from the study was kept safe and confidential. All patient identifiers were removed from the questionnaires.

Results

Participants demographic and clinical characteristics

A total of 105 patients with PD completed the NMSS and the PDQ-39 questionnaires, while the 105 controls completed only the NMSS questionnaire. There were no invalid responses. The median age of the patients was 64 years (IQR

55–70), while that of controls was 64 years (IQR 54.5–70.5). Males accounted for 61.9% of participants compared with 62.9% of controls. Seventy-six (72.3%) of the participants had at least 6 years of education compared with 66 (62.9%) of the controls. There was no significant difference in the median age, sex, level of education, and marital status between the two groups.

Forty-seven (44.8%) of the PD patients also had hypertension compared to 50 (47.6%) of controls. There was no significant difference between the number of participants and controls with hypertension. There were significantly more smokers among the participants relative to controls (7 [6.7%] vs. 1 [1.0%] $P = 0.030$). There was no significant difference in the frequency of alcohol use between both groups. Levodopa was the most commonly used medication. A total of 23 (21.9%) participants were not on any medication at their enrolment in the study. There were 60 participants on more than one PD medication at the same time.

Among the PD patients, the NMS across the miscellaneous, mood/cognition, and sleep/fatigue domains were the most common, while perceptual problems were the least common [Figure 1]. The median total NMS score were significantly higher in patients with median (IQR) of 42 (13–72) as compared to controls with median (IQR) of 20 (14–29), $P < 0.001$).

Factors associated with nonmotor symptoms severity

About two-thirds of the participants were in H and Y Stage 2 and Stage 3, with the median NMS score progressively increasing from Stage 1 to 5 [Figure 2].

There were only two patients in Stage 5, and they were added to the patients in Stage 4 for the difference in NMS scores, as they did not meet the minimum number of five samples required for the appropriate statistical test. There were significant differences in median scores of each H and Y stage for all the domains and the overall total [Table 1].

The duration of PD had a positive correlation with the total NMS scores ($r_s = 0.063$; $P = 0.034$). There was no significant correlation between the age of patients and the total NMS scores ($r_s = 0.033$; $P = 0.590$). There was a significant difference in the median cardiovascular/falls and sexual function NMS score domains among male participants as compared to female participants [Table 2].

There was a significant difference in the median NMS score among participants who had a history of smoking (median (IQR) =115 (65–168)) as compared to nonsmokers (median [IQR] =38 [12-67.5]) ($P = 0.001$). There was no significant difference in the median NMS scores based on the type of PD drug used ($P = 0.531$). The median NMS scores in drug-naive patients (median (IQR) = 58 [14–89]) was not significantly different from those on drug treatment (median [IQR] =37 [13–69]) ($P = 0.362$).

The relationship between nonmotor symptoms score and Parkinson's disease questionnaire summary index score

There was a strong positive correlation between the total NMS score and the PDQSI. Analysis of the NMS score domains revealed a strong positive correlation between the domains of sleep/fatigue, mood/cognition, and the PDQSI. The other domains had a moderate-positive correlation [Table 3].

Discussion

The NMS in the domains of mood/cognition and sleep/fatigue were the most common in this study. This finding agreed with that of de Souza *et al*.[14] where anxiety and rapid eye movement (REM) sleep behavioral disorder were some of the identified most common symptoms. The PRIAMO study also found fatigue, anxiety, and insomnia to be the most prevalent symptoms.[15] Some other previous studies, however, found urinary symptoms to be most common.[16,17] These variabilities may be due to the difference in demographic characteristics of the study participants.

The difference in NMS scores between patients with PD and controls was consistent with previous studies.[16,18,19] However, we found no significant difference regarding the domains of

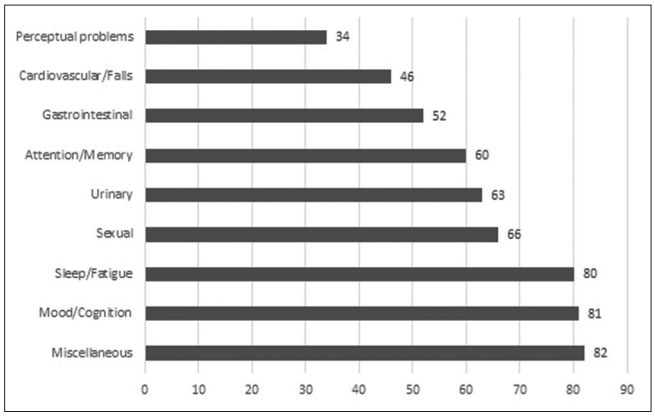

Figure 1: Frequency of nonmotor symptoms across different domains

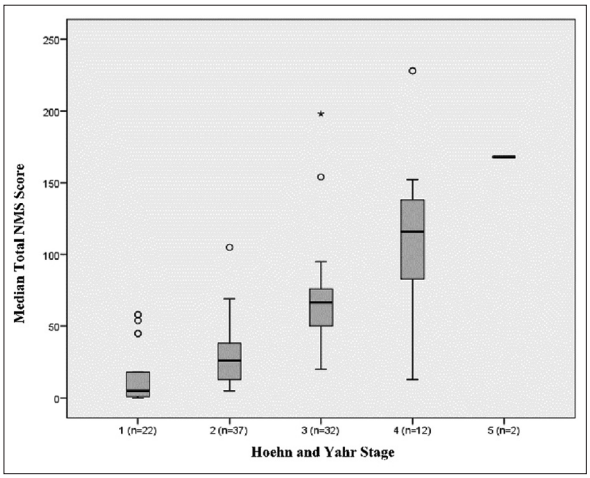

Figure 2: Median nonmotor symptoms score across Hoehn and Yahr stages

Table 1: Difference between median (interquartile range) nonmotor symptoms scores across Hoehn and Yahr stages

Domains	Stage 1 (*n*=22)	Stage 2 (*n*=37)	Stage 3 (*n*=32)	Stage 4/5 (*n*=14)	*P*
Cardiovascular	0 (0-0)	0 (0-1)	2 (0-6)	7.5 (2.25-15)	<0.001*
Sleep/fatigue	0 (0-1.75)	2 (1-4)	8 (4-12)	21.5 (8-24)	<0.001*
Mood/cognition	0.5 (0-2)	3 (0.5-8)	8.5 (4-19.5)	37.5 (13.5-42)	<0.001*
Perceptual problems/hallucinations	0 (0-0.25)	0 (0-0.5)	0 (0-4)	0 (0-11.25)	0.013*
Attention/memory	0 (0-1.25)	1 (0-4)	2.5 (0-8)	10 (0-22)	0.019*
Gastrointestinal	0 (0-0)	1 (0-4)	1.5 (0-9)	5 (2-24)	<0.001*
Urinary	0 (0-1)	0 (0-5)	6.5 (2-17.5)	10.5 (3-28)	<0.001*
Sexual function	0 (0-12)	2 (0-6)	10.5 (0-24)	12.5 (11.25-19.5)	<0.001*
Miscellaneous	1 (0-6)	5 (0.5-12.5)	11 (2.25-15)	12 (0-25)	0.006*
Total score	5 (1-24.75)	26 (11-41)	66.5 (50-76.5)	120.5 (98.5-168)	<0.001*

*P<0.05

Table 2: Difference in total and domain nonmotor symptoms scores among male and female Parkinson's disease cases

Domains	Median (IQR) by sex		*P*
	Male (*n*=65)	Female (*n*=40)	
Cardiovascular/falls	1 (0-6)	0 (0-1)	0.004*
Sleep/fatigue	4 (0.5-11)	4 (1-9)	0.899
Mood/cognition	4 (0-14)	3 (1-10)	0.707
Perceptual problems/hallucinations	0 (0-4)	0 (0-1)	0.294
Attention/memory	1 (0-6)	1 (0-7)	0.981
Gastrointestinal	0 (0-6)	0 (0.5-3.75)	0.623
Urinary	4 (0-9.5)	0 (0-7)	0.069
Sexual function	8 (1-12)	0 (0-18.75)	0.030*
Miscellaneous	6 (1-12.5)	8.5 (1-15.75)	0.453
Total score	42 (18-73.5)	44 (8-69)	0.378

*P<0.05. IQR - Interquartile range

Table 3: Correlation between nonmotor symptoms scores (domains and total) and Parkinson's Disease Questionnaire Summary Index score

Domains	r_s	*P*
Cardiovascular	0.556	<0.001*
Sleep/fatigue	0.713	<0.001**
Mood/cognition	0.740	<0.001**
Perceptual problems/hallucinations	0.417	<0.001*
Attention/memory	0.353	<0.001*
Gastrointestinal	0.533	<0.001*
Urinary	0.621	<0.001*
Sexual function	0.494	<0.001*
Miscellaneous	0.539	<0.001*
Total	0.851	<0.001**

*Moderate correlation, **Strong correlation

perceptual problems/hallucinations and attention/memory which is in contrast with a previous study on cognitive dysfunction in PD patients that reported a higher rate of cognitive dysfunction in PD patients.[20] This discordance may be due to the participants in our study being mostly in the early stages of PD. This study, like Crosier *et al*. and Kadastik-Eerme *et al*.,[17,21] found that the NMS severity increases with increasing H and Y stages. An earlier study by Ray Chaudhuri *et al*.[18] found that participants with higher severity of motor symptoms based on grouping of the H and Y staging had significantly worse NMS count. This finding suggests that the NMS progress with advancing disease, like the motor symptoms on which the H and Y staging is based. The significant worsening of the NMS scores with progression of H and Y staging is similar to the findings in a later study by Ray Chaudhuri *et al*.[8] However, they found a weaker agreement between the staging and the NMS severity. Contrary to our study, Ray Chaudhuri *et al*. compared the staging to the NMSB rather than the raw scores, which may explain the difference seen in our study compared to theirs.

The age of the patients did not correlate the overall severity of NMS; however, the older age groups were found to have worse symptoms in the attention/memory, gastrointestinal, and urinary domains which could be due to additional confounders such as senile dementia, obstructive uropathy, and constipation which are more common with increasing age.[22-24] The findings in this study were contrary to the results of another study in Estonia, where age was found to be associated with worsening NMS. However, the tool for assessment of NMS in that study was different from the one used in this study; it was based on a count of NMS rather than severity and frequency.[21] Findings from previous studies support the correlation of disease duration with NMS severity.[14,15,17,20,25] This is not unexpected since PD is characterized by progressive neuronal death and Lewy body accumulation, hence the worsening of symptoms with time.[26] Males had significantly higher NMS scores in the domains of cardiovascular/falls and sexual function. Similar findings were seen in a study in Hungary and another in Spain, where males had worse sexual domain scores compared to females. However, the former study found worse scores in the cardiovascular/falls, mood/cognition, and miscellaneous domains among females.[27,28] Explanations for these observations are unclear from the present study. Smokers had strongly significantly higher NMS scores than nonsmokers comparable to the findings from a previous study.[29] The number of smokers in this study was few and could affect the reliability of this finding. Although previous studies found smoking to

confer a lower risk of PD, the rationale is not well understood, with suggestions of biological protection against nigral neuronal damage. The effect of smoking in a PD patient on the severity and progression of NMS are still being debated.[30,31] The lack of significant relationship between being on PD drug treatment or the type of treatment and the NMS severity was different from previous studies where drug-naive participants were found to have less severe NMS compared to those on long-term PD treatment.[32] The PD medications mainly focus on treatment of the motor symptoms and were associated with side effects that could contribute to the NMS. There were also NMS that are primarily due to the pathogenesis of PD itself such as fatigue, constipation, and sleep disturbance.[10]

The positive correlation of NMS severity with PD-related QoL in this study was comparable to findings from several previous studies.[5,11,21,33-36] The strongest correlation was seen in the domains of sleep/fatigue and mood/cognition which corroborates the report by Lawson *et al*. and Berganzo *et al*.,[37,38] who found cognitive decline to be strongly associated with reduced QoL in PD patients. Kadastik-Eerme *et al*.[36] also found depression, which is in the domain of mood/cognition, to be the strongest determinant of poor QoL. Many of the nonmotor functions affected by PD are required for normal day-to-day physical, mental, emotional, psychological, and social functioning and therefore consistent with the impact of these dysfunctions on QoL.

This study is not without limitations; it may be limited by relatively small sample size. In addition, since this study was hospital based, it was difficult to generalize the findings to the rest of the population of Nigerians with PD. The NMS scale are a broad overview of the NMS seen in PD which does not give a detailed analysis of each domain. There is a need for further studies in specific domains, using standardized assessment tools. The potential for recall bias was also present, especially in patients with advanced PD who had problems with communication and required an informant for response to some of the questions.

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Conflicts of interest

There are no conflicts of interest.

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