

## ORIGINAL ARTICLE

## PREVALENCE AND DETERMINANTS OF FATIGUE AMONG PARKINSON'S DISEASE PATIENTS IN ETHIOPIA

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## ABSTRACT

**Introduction:** Fatigue is a severe problem for many people living with Parkinson's disease. Best estimates suggest that more than 50% of patients with Parkinson's disease experience this debilitating symptom. Fatigue is related to excessive daytime sleepiness and in certain studies with disease progression. There has been no prior report on Fatigue among patients with Parkinson's disease living in Ethiopia.

**Objective:** The present study is aimed at assessing the prevalence and determinant of fatigue among patients with Parkinson's disease in Ethiopia.

**Methods:** A cross-sectional study of all Parkinson's disease patients attending the follow-up clinics of the Departments of Neurology at Tikur Anbessa and Zewditu Memorial Hospital in Addis Ababa, Ethiopia, from July 1 to October 30, 2015 was conducted. We collected information using a structured questionnaire which assessed demographic information, clinical history, the Parkinson's fatigue scale item sixteen (distressing fatigue defined as mean score  $\geq 3.3$ ) and the Epworth Sleepiness Scale.

**Results:** Of the 155 patients surveyed, 155 patients responded for PFS-16 items with mean ( $\pm$ SD) score of 3.88 ( $\pm 0.79$ ). Distressing fatigue was noted on 120 (79.5%) of the respondents. Excessive day time sleepiness according to the Epworth Sleep Scale  $\geq 10$  (OR 3.39; 95% CI 1.41 - 8.20,  $P=0.004$ ) and unemployment (OR 2.71; 95% CI 1.19 - 6.17,  $P=0.016$ ) associated with distressing fatigue. There was no statistical association with age, gender, Parkinson's disease stage, duration of Parkinson's disease symptoms, previous history of sleep disturbance, Levodopa or Trihexyphenidyl use and higher Parkinson's disease Sleep Scale version two score.

**Conclusions:** The prevalence of distressing fatigue in Ethiopian patients with Parkinson's disease is substantially high. Further investigations into contributors in our patients with Parkinson's disease are needed.

**Keywords:** Parkinson's disease, Fatigue, Ethiopia

## BACKGROUND

Parkinson's disease (PD) is a neurodegenerative disorder associated with a loss of dopamine-producing neurons in the substantia nigra pars compacta. The disease was described by James Parkinson in 1817, and his description remains remarkably accurate (1). It is characterized by abnormal motor symptoms such as bradykinesia, tremor, rigidity, and postural instability (2). However, the non-motor symptoms (NMS) of PD, including fatigue, cognitive impairment, depression, sleep disorders, and autonomic dysfunction are also equally important (3).

Since Fatigue is a subjective feeling, with no biological markers, it is difficult to describe and its definition is influenced by the background and culture of the patient (4). Subtypes of fatigues are peripheral fatigue and mental fatigue. Fatigue is a common problem for the general population and is particularly challenging for people with Parkinson's disease (PD) (5).

Available estimates suggest that more than 50% of patients' experience this debilitating symptom. Fatigue has been described to be the most troublesome aspect of PD in about one-third of patients, yet it is poorly understood. Fatigue could be present before, at the time of diagnosis of PD in untreated patients or during the course of the disease (4).

A cross-sectional study conducted in Italian patients revealed 33.8% reported Distressing fatigue (PFS-16 mean score  $\geq 3.3$ ) [6]. Patients with distressing fatigue were older ( $P=0.044$ ) and had a longer duration of PD ( $P<0.0001$ ) than those without distressing fatigue (6).

The presence of distressing fatigue was associated with higher total Unified Parkinson's Disease Rating Scale (UPDRS) scores, poorer quality of life, worse social and psychological behaviors.

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There have been limited recent studies published on PD in sub Saharan Africa (7-14) and far fewer from Ethiopia (15-21) and no published data on fatigue in people with PD living in Ethiopia. This study is aimed at filling this knowledge gap by assessing the prevalence of fatigue and their determinant factors in people living with PD in Ethiopia.

## METHODS

Addis Ababa University is the only training center for neurologists in Ethiopia. Its main hospitals include the Tikur Anbessa and Zewditu Memorial hospitals. A cross-sectional survey was conducted from July 1, 2015 to October 30, 2015 in the two referral hospitals. All patients diagnosed with PD attending the neurology clinics in these hospitals during the study period were the source population. Patients were included if they were  $\geq 18$  years old, fulfilled the UK Parkinson's Disease Society Brain Bank Clinical Diagnostic Criteria for the diagnosis of PD, and gave informed verbal consent for study participation.

The diagnostic criteria consisted of three major entirely clinical components: Diagnosis of Parkinsonian Syndrome, exclusion criteria for Parkinson's disease and supportive prospective positive criteria for Parkinson's disease (22). Patients were excluded if they had Parkinsonism due to other causes (like drug induced Parkinsonism, vascular Parkinsonism, Parkinson plus syndrome which were based on UK Parkinson's Disease Society Brain Bank Clinical Diagnostic Criteria for the diagnosis) or if they refused consent. Clinical data was collected using a structured questionnaire in English and Amharic which assessed demographic data, a detailed clinical history including symptoms and duration of PD, medication history and neurologic examination. We used two data collection instruments: the Parkinson Fatigue Scale 16 item (PFS-16), (23)] and the Epworth Sleepiness Scale (ESS) questionnaires (24, 25).

The PFS-16 is a scale addressing 16 commonly reported symptoms associated with Fatigue. The presence of Fatigue was evaluated using PFS-16 which consists of 16 items. Each item was rated on a scale from 1-5 one is for strongly disagree and 5 being strongly agree. The PFS-16 scale was designed to tap a single construct encompassing the physical aspects fatigue and their impact on the patient's daily function (26). The scale deliberately excludes emotional and cognitive features that may occur as part of the fatigue experience, but which may also occur independently in Parkinsonism. The scale has good intrinsic properties and satisfactory test-retest reliability.

It shows reasonable associations with other measures of fatigue and can identify patients who self-report the presence of fatigue, and particularly those in whom fatigue is a problem. Cut-off scores are provided in both cases with good specificity and sensitivity (26). The scale was also validated in different country (27, 28).

The ESS is used as a subjective measure of a patient's daytime sleepiness. This scale has a list of eight situations in which patients rate their likelihood of becoming sleepy on a scale of 0-3. Total score ranges from 0 to 24. A score of 10-15 suggests possible excessive daytime somnolence, and a score of 16-24 suggests definite excessive daytime somnolence (24, 25). Unfortunately, we didn't perform formal reliability/validity study considering the setup we are in, but the PFS-16 and ESS were translated from English into Amharic and pilot-tested on 10 subjects. These subjects were not included in the study results.

Findings from the pre-test were used to modify questions on the standard questionnaire. The slight amendments were done on ESS up on translation to Amharic version by using similar scenarios considering that some of our patients were not having television and car.

Analysis was performed using SPSS/PC version 20.0 software packages for statistical analysis (SPSS). Descriptive summaries were employed to describe socio-demographic and clinical characteristics. Appropriate measures of central tendency, frequency distribution, cross tabulation, Fisher's Exact test and binary logistic regression analysis were used in the analysis. Odds ratios with 95% confidence intervals were calculated to describe the strength of the association between the outcome and key determinant factors. A P-value  $\leq 0.05$  was considered a statistically significant association.

Protocol approvals were obtained from the ethical review Committee of the Department of Neurology and the Institutional Review Board and Research and Publication Committee of the College of Health Sciences of Addis Ababa University. Verbal informed patient consent was obtained before study enrollment. Patients were informed participation was on voluntary basis, and they had the right to withdraw from the study at any point without any consequences. Patient data was de-identified during subsequent analysis and dissemination.

## RESULTS

A total of 151 study participants were recruited in this study: 124 (82.1%) male and 27 (17.9%) female. Table 1 shows the demographics of our participants. The mean duration of symptoms, duration since PD diagnosis and duration of PD treatment were 6.37, 4.90, and 4.68 years, respectively. All patients were taking levodopa while 24.5% were taking trihexyphenidyl in addition to levodopa and 7.3% patients were taking medications for hypertension and diabetes mellitus.

No patient was taking other anti-parkinsonian agents (e.g. dopamine agonist, amantadine) or was on any other medications other than mentioned.

Presences of comorbidities were also assessed. Of the study participants only 11 patients were having medical comorbidities; five patients had diabetes mellitus and six had hypertension.

**Table 1:** Socio-demographic characteristics of patients with Parkinson's disease, Tikur Anbessa and Zewditu Memorial hospitals, Addis Ababa. July 1, 2015 to October 30, 2015.

Variables	Number (%)
Gender	
Female	27 (17.9)
Male	124 (82.1)
Age	
<60 years	70 (46.4)
≥60 years	81 (53.6)
Marital status	
Never married	6 (3.9)
Married	117 (77.6)
Widowed	19 (12.6)
Separated/divorced	9 (5.9)
Duration of PD symptom in years	
<5 years	63 (41.7)
≥5 years	88 (58.3)
Employment status	
Employed	42 (27.8)
Unemployed	109 (72.2)
Educational status	
No formal education	48 (31.8)
Primary education	44 (29.2)
Secondary education	35 (23.2)
More than secondary education	24 (15.8)
Hoehn and Yahr Stage	
Stage 1	36 (23.8)
Stage 2	46 (30.5)
Stage 3	41 (27.2)
Stage 4	23 (15.2)
Stage 5	5 (3.3)
Previous history of sleep disorder	
Yes	37 (23.9)
No	118 (76.1)
Trihexyphenidyl use	
Yes	37 (24.5)
No	114 (75.5)
Levodopa use	151 (100)

Table 2 shows the results of the PFS-16 scores with independent variables. Over a three fourth 120 (79.5%) of patients were having distressing Fatigue (Defined as PFS-16 Mean score  $\geq 3.3$ ) mean score ( $\pm$ SD) being 3.88 ( $\pm 0.79$ ). On univariate analysis, there was a statistically significant association between distressing fatigue and excessive day time sleepiness, ESS  $\geq 10$

(OR 3.39; 95% CI 1.41 - 8.20,  $P=0.004$ ) and unemployment (OR 2.71; 95% CI 1.19 – 6.17  $P=0.016$ ). On univariate analysis there was no statistical association with age, gender, Hoehn & Yahr stage, duration of PD symptoms, and presence of hypertension or diabetes mellitus, previous history of sleep disturbance, levodopa or trihexyphenidyl use, marital and educational status.

**Table 2:** Results of Parkinson Disease Fatigue scale item 16 with independent variables of the study participants, Tikur Anbessa and Zewditu Memorial hospitals, Addis Ababa. July 1, 2015 to October 30, 2015.

	PFS-16 mean score		OR (95% CI)	P-value
	<3.3	$\geq 3.3$		
ESS total score				
<10	23	55	3.39 (1.41 - 8.20)	0.004
$\geq 10$	8	65		
Employment status				
Employed	14	28	2.70 (1.19 – 6.17)	0.016
Unemployed	17	92		
Age				
<60yrs	17	53	1.54 (0.69 – 3.39)	0.195
$\geq 60$ yrs	14	67		
Sex				
Male	29	95	0.26 (0.06 - 1.17)	0.047
Female	2	25		
PD stage				
Hoehn & Yahr stage <3	19	63	1.43 (0.64 – 3.21)	0.251
Hoehn & Yahr stage $\geq 3$	12	57		
Previous history of sleep disorder				
Yes	9	27	1.39 (0.58 – 3.38)	0.302
No	12	92		
Trihexyphenidyl use				
Yes	11	26	0.50 (0.21 – 1.18)	0.080
No	20	94		
Duration of PD symptom				
<5Years	17	46	1.95 (0.88 – 4.34)	0.073
$\geq 5$ Years	14	74		
Marital Status				
Have partner living with	27	90	2.25 (0.73 – 6.95)	0.113
No partner	4	30		

A logistic regression analysis was performed to determine factors associated with a fatigue. On logistic regression there was no statistical association with age, gender, Hoehn & Yahr stage, excessive day time sleepiness, unemployment, duration of PD symptoms, and previous history of sleep disturbance, levodopa or trihexyphenidyl use, marital and educational status.

## DISCUSSION

The present study revealed that Ethiopian PD patients exhibit one of the highest prevalence of distressing Fatigue with more than three out of four patients reporting the problem (79.5%). This is substantially higher compared to estimates from countries such as Fatigue reported in 42.4% of Chinese (29), 57.9% of Polish (30) and 34% of Norwegian PD patients (31).

A study done on Italian PD patients using PFS-16 reported 33.80% of patients were having distressing fatigue (PFS-16 mean score  $\geq 3.3$ ) (6) which was much lower than our finding. This could be due to disparity in cultural and economic status of the population (4). In PD patients, the wide range of prevalence of fatigue (37–56%) is largely because of varying definitions of fatigue and populations tested (32). This difference could be due to the presence of diverse tools to assess fatigue in PD patients and its definition.

A study done on Slovakian PD patients using multi-dimensional fatigue inventory (MFI) showed that out of 119 PD patients (78.8% of the sample) were fatigued in at least one of MFI domain (33). This is nearly comparable with our finding. Our study revealed that distressing fatigue was associated with Excessive day time sleepiness ( $P=0.004$ ), which was also shown on other study that the severity of fatigue was positively associated with excessive daytime sleepiness ( $p = 0.009$ ) (29).

On our study 7.3% of the patients were having Hypertension and Diabetes Mellitus. However, the presence of these disease entities didn't show statistically significant association with the presence of distressing fatigue; this finding was also reported on Italian PD patients (6).

In contrary to our study finding, a cross-sectional study conducted on Italian PD patients revealed that patients with distressing fatigue were older ( $p = 0.044$ ) and had a longer duration of PD ( $P < 0.0001$ ) than those without distressing fatigue (6). This could be due to longer mean duration of PD symptom and higher mean age of the study participants of the Italian PD patients. Our study also discovered that unemployment is associated with distressing fatigue ( $P=0.016$ ) which was not revealed in other studies.

Our study had several limitations. One significant limitation of our study was the data were obtained from only two teaching hospitals in Ethiopia which may not fully representative of the overall PD patients in the country and the sample consisted predominantly of male patients.

The other significant limitation of our study was our inability to assess psycho-behavioral factors that contribute for fatigue like depression and anxiety. One study revealed that the presence of distressing fatigue was associated with worse psychological behaviors and a higher severity of depressive symptoms ( $p < 0.001$ ) (6).

**Conclusions:** The prevalence of distressing fatigue in Ethiopian PD patient is among the highest compared to earlier reports from several countries. Further studies need to focus on substantiating the current high prevalence and investigate contributing factors to better understand the extent and distribution of distressing fatigue in low income setting.

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### *Competing interest:*

The authors declare that this manuscript was approved by all authors in its current form and that no competing interest exists.

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