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The Effect of Non-Motor Symptoms on Quality of Life of Idiopathic Parkinson's Disease Patient Attending in a Tertiary Level Hospital of Bangladesh.

Pulin Bihari Dhar[1*], Abul Kalam Mohammed Shoab[2], Mohammad Shah Jahirul Hoque Chowdhury[3], Nayeem Anwar[4], Rakib Hasan Mohammad[5], Niloy Ranjan Roy[1], Shubharthi Kar[6], Md. Ahasan Habib[7]

Abstract

Background: Non-motor symptoms (NMS) are common in Parkinson's disease (PD), affecting up to 90% of patients during their illness. They may appear at early pre-symptomatic stage of the disease as well as throughout the disease course of illness. Motor symptoms decrease the quality of life in patients of Parkinson's disease. At the same timeNon-motor symptoms (NMSs) are also a burden in Parkinson's disease (PD). Herein we reviewed the impact of common Non-motor symptoms (NMSs) on quality of life (QOL) for patients with Parkinson's disease (PD).

Aim of the study: The aim of this study was to see the effect of non-motor symptoms with Quality of life in Parkinson's disease.

Methods: This cross-sectional study was undertaken in Department of Neurology, BMU, patients were selected by non-randomized purposive sampling methodwere recruited. Study subjects were taken from movement Disorder Clinic, Inpatient and Outpatient Department of Neurology, BMU accordingto inclusion and exclusion criteria. Duration of study was October 2019 to September 2020. A total of 76 patients diagnosed as idiopathic Parkinson's disease with Non Motor symptoms was taken as study population. Detailed history, physical examination, previous medical were records. Quality of life was calculated by Validated Bengali version of WHOQOL-BREF and non-motor symptoms (NMSs) by the 30-item Parkinson's Disease Questionnaire (PDQ-30). Statistical analysis was done by SPSS method. The aims and objectives of the study along with its procedures, risks and benefits was explained to each respondent in easily understandable local language and informed written consent were taken.

Result: Among the study population (65%) above 50 years of age and below 50 years of age was (35%). Maximum patients were stage 2 to 3(57%) according to Hoehn and Yahr staging system. NMSs were found in almost 100% of the study population. The most common NMSs werefeeling of nervousness (78%), fatigue or lack of energy limit the patient day time (78%), difficulties in falling sleep (75%), dizziness (68%), mood/cognition (67%), forgetfulness (59%), pain perception (57%), alter sex interest (49%), constipation (38%), difficulty swallow (20%) and excessive sweating (18%). Positve significant correlation was found between Hoehn and Yahr stage (score) and Total Score Domain 1 to Domain 9. Positve significant correlation was found between diseases duration of the patients vs Domain 2: Sleep/ fatigues, Domain 5: Attention/memory and Domain 6 Gastrointestinal

Affiliation:

[1]Assistant Professor, Department of Neurology, Sylhet MAG Osmani Medical College, Sylhet, Bangladesh.

[2]Associate Professor, Department of Neurology, Sylhet MAG Osmani Medical College, Sylhet, Bangladesh.

[3]Professor of Clinical Neurology, National Institute of Neurosciences & Hospital, Dhaka, Bangladesh.

[4]Associate Professor, Department of Neurology, Bangladesh Medical University, Dhaka, Bangladesh.

[5]Assistant Professor, Clinical Neurology, Colonel Malek Medical College, Manikgonj, Bangladesh.

[6]Associate Professor, Department of Nephrology, Sheikh Hasina Medical College, Habiganj, Bangladesh.

[7]Professor, Department of Neurology, Bangladesh Medical University, Dhaka, Bangladesh.

***Corresponding author:**

Pulin Bihari Dhar, Assistant Professor, Department of Neurology, Sylhet MAG Osmani Medical College, Sylhet, Bangladesh.

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tract. Positve significant correlation was found between Domain 1: Cardiovascular including falls and Domain 2: Sleep/fatigues and Domain 3: Mood/cognition Positve significant correltion was found between Domain 4: Perceptual problem and Domain 5: Attention/memory. Positve significant correltion was found between Domain 5: Attention/memory and Domain 6: Gastrointestinal tract.

Conclusion: The present study was intended to see the impact of non-motor symptoms on quality of life of patients with Parkinson's disease. This study will help to manage Non-motor symptoms (NMSs) of Parkinson's disease and thereby improve Quality of life.

Keywords: Non-Motor Symptoms (NMSs); Quality of Life (QoL); Parkinson'sdisease (PD)

Introduction

Parkinson's Disease represents the second neurodegenerative disorder in the world after Alzheimer's disease with an estimated prevalence of 3% in the elderly and overal 0.3% of population is affected [1-3]. This condition, is caused by degeneration of the dopaminergic neurons of the substantia nigra in the midbrain, is associated with motor symptoms like bradykinesia, rest tremor, rigidity and postural instability and various non motor sympyoms [4]. The hallmark is bradykinesia, leading to slow gait, difficulty standing from sitting, small stride length, reduced arm swing, rigidity in trunk movements, propulsion and retropulsion [5]. Non-motor symptoms (NMSs) include neuropsychiatric features (anxiety, depression, apathy, hallucinosis/ psychosis) sleep disturbance and hypersomnolence, fatigue, pain, sphincter disturbance and constipation, sexual problems (erectile failure, loss of libido or hypersexality), drooling and weight loss [6-8]. Cognitive impairment, including dementia is the symptom most likely to impair quality of life for patients and their carers. These symptoms constitute a burden on the caregiver and the public health system. In the PRIAMO study, up to 98.6% of PD patients had NMS. Recently, the correlation between NMS and PD patients' health-related quality of life (HRQoL) has been emphasized [9]. Several studies indicate that NMS, rather than motor symptoms, are a major cause of poor health related quality of life (HRQoL) [10,11]. Recently, two complementary instruments to assess non-motor symptoms in PD have been developed: The Non Motor Symptoms Questionnaire (NMS Quest) and the Non motor Symptoms Scale (NMSS) [12,13]. The NMS screening questionnaire (NMS Quest), a self-completed questionnaire comprising 30 items, used as rapid screening tool, for the early detection of patient's non-motor symptoms (NMSs) [14,15]. Also NMSs is used for NMS burden assessment. Several studies have compared non-motor symptoms (NMS) in different countries and showed more prevalent gastrointestinal symptoms in Asian countries, probably due to ethnic and economic differences [16,17]. NMS have a deep impact on PD patients' quality of life [14]. The purpose of my study is to investigate NMS in PD patients attending in Neurology department BMU and the impact of NMS on HRQOL. This hospital-based cross-sectional study was conducted to examine the clinical factors, on the occurrence of non-motor symptoms (NMSs) and health related quality of life (HRQOL). 30-item Parkinson's Disease Questionnaire (PDQ-30) and Validated Bengali version of WHOQOL-BREF were usedto explore the correlation [17].

Methodology & Materials

This cross-sectional study was conducted in the movement disorder clinic, out patient and in patient department of Bangladesh Medical University (BMU), Dhaka over a period one year from October 2019 to September 2020. A total of 76 patients diagnosed as idiopathic Parkinson's disease with Non Motor symptoms was taken as study population. Patients with anti psychotic drug induced NMSs, secondary cause of parkinsonism, those who will not provide consent and atypical parkinson's disease were excluded from the study. Approval from the Institutional Review Board (IRB) of BMU was obtained prior to the commencement of this study. Idiopathic Parkinson's Disease patients was diagnosed on brain bank criteria. Parkinson's disease of patient was selected from movement disorder clinic, outpatient and inpatient Department of Neurology of BMU. After taking proper history, physical and neurological examination and relevant investigations were done. Informed written consent was taken from each patient. After diagnosis of idiopathic Parkinson's disease detected by non-motor symptoms assessment scale (developed by the international Parkinson's disease non-motor group) Quality of life in idiopathic Parkinson's disease detected by who quality of life scale. Proper diagnosis and treatment was ensured for each patient. Collected data were compiled and appropriate analyses were done by using computer based software, Statistical Package for Social Sciences (SPSS) version 23.0. Qualitative variables were expressed as percentage and quantitative variables as median or mean. Pearson's correlation coefficient was calculated between Hoehn and Yahr stage with total Score Domain and also Pearson's correlation coefficient was calculated between Diseases duration vs Nonmotor Symptom Domain 1 to Domain 6. A 'p' value of <0.05 was considered as significant.

Result

Out of 76 patients, among the patients highest (27.6%) were in the age group between 61 to 70 years of age and the lowest (2.6%) were in the age group of 81 to 90 years. The age mean and standard deviation (±SD) of the patients were 3.25 ±1.45 years. Among the patients most of them (72.4%) were male and the rest of (27.6%) were female. Among the 76

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Table 1: Distribution of the patients by baseline charactreristics.

Baseline charactreristics	Number	Percentage	Mean±SD
Age (years)			
31 to 40	7	9.2	3.25±1.45
41 to 50	20	26.3	
51 to 60	16	21.1	
61 to 70	21	27.6	
71 to 80	7	9.2	
81 to 90	2	2.6	
21 to 30	3	3.9	
Total	76	100	
Sex			
Male	55	72.4	
Female	21	27.6	
Total	76	100	
Treatment duration			
Bellow 1 Year	4	5.3	
(1 to 4) Years	49	64.5	
(5 to 14) Years	23	30.3	
Total	76	100	

Table 2: Domain 1: Cardiovascular including falls (score) and Domain 2: Sleep/fatigues

Variables	Range		Frequency	Percentage
Domain 1				
Dizziness Score	Valid	0	24	31.8
		≥1	52	68.4
		Total	76	100
Fall Score		0	71	93.4
		≥1	5	6.6
		Total	76	100
Domain 2				
Daytime sleep		0	56	73.7
		≥1	20	26.3
		Total	76	100
Difficulties fall and staying sleep		0	19	25
		≥1	57	75
		Total	76	100
Restless in legs		0	31	59.2
		≥1	45	40.8
		Total	76	100

patients most of them (64.5%) treatment duration was between 1 to 4 years and the lowest (5.3%) diseases duration were bellow one year (Table-1). Among the patients score highest (42.11%) Hoehn and Yahr stage (score) were 2 followed by (39.37%) were 1 and lowest (3.94%) were 0 (Figure-1). In domain 1 among the patients score highest (68.4%) dizziness score was >1 and highest (93.4%) fall score were zero (0). In domain 2 among the patients score highest (73.7%) daytime sleep score was zero (0) and highest (75%) Difficulties fall and staying sleep score were >1 and highest (59.2%) were restless in legs score were zero (0). The following table 11 shows in details (Table-2). In domain 3 among the patients score highest (59.2%) lots of interest in his/her surroundings score were zero (0) and highest (65.8%) Lost of interest in new activities score were >1 and highest (77.7%) feeling of nervous score were >1 and highest (62.4%) depressed mood score was >1 and highest (61.8%) flat mode score was >1 and highest (59.2%) lack of pleasure score were >1 (Table-3). In domain 4 among the patients score highest (90.8%) see the things are not there/hallucination score were zero (0) and highest (92.1%) belief that you are not real/delusions score were zero (0) and highest (88.2%) double vision score was zero (0). In domain 5 among the patients score highest (50%) Problem of concentration driving activities score were zero (0) and highest (59.2%) Short term memory lost score were >1 (Table-4). Positve significant correlation (r=0.409; p=0.001) was found between Hoehn and Yahr stage (score) and Total Score Domain 1 to Domain 9 (Table-5). Positve significant correlation was found between diseases duration of the patients and Domain 2: Sleep/fatigues (r=0.227; p=0.049). Positve significant correlation was found between Domain 1: Cardiovascular including falls and Domain 2: Sleep/fatigues (r=0.257; p=0.025) and Domain3: Mood/cognition (r=0.328; p=0.004) (Table-6). Positve significant correltion was found between diseases duration of the patients and Domain 5: Attention/memory (r=0.315; p=0.006) and Domain 6: Gastrointestinal tract (r=0.316; p=0.005). Positve significant correltion was found between Domain 4: Perceptual problem and Domain 5: Attention/memory (r=0.225; p=0.026). Positve significant correltion was found between Domain 5: Attention/memory and Domain 6: Gastrointestinal tract (r=0.352; p=0.002) (Table-7).

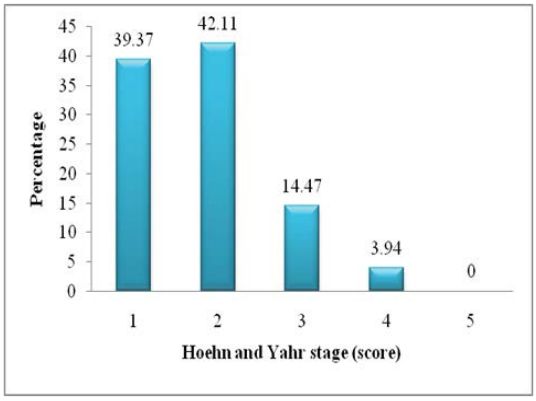

Figure 1: Hoehn and Yahr stage (score)

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Table 3: Domain 3: Mood/cognition.

Variables	Range		Frequency	Percentage
Lost of interest in his/her surroundings score	Valid	0	45	59.2
		≥1	31	40.8
		Total	76	100
Lost of interest in new activities		0	26	34.2
		≥1	50	65.8
		Total	76	100
Feeling of nervousness		0	17	22.3
		≥1	59	77.7
		Total	76	100
Depressed mood		0	21	27.6
		≥1	55	62.4
		Total	76	100
Flat mode		0	29	38.2
		≥1	47	61.8
		Total	76	100
Lack of pleasure		0	31	40.8
		≥1	45	59.2
		Total	76	100

Table 4: Domain 4: Perceptual problem & Domain 5: Attention/ memory.

Variables	Range		Frequency	Percentage
Domain 4				
See the thing are not there/ Hallucination	Valid	0	69	90.8
		≥1	7	9.2
		Total	76	100
Belief that you are not real/Delusions		0	70	92.1
		≥1	6	7.9
		Total	76	100
Double vision		0	67	88.2
		≥1	9	11.8
		Total	76	100
Domain 5				
Problem of concentration driving activities		0	38	50
		≥1	38	50
		Total	76	100
Short term memory lost		0	31	40.8
		≥1	55	59.2
		Total	76	100

Table 5: Hoehn and Yahr stage with total Score Domain.

Description		Hoehn and Yahr stage (score)	Total Score Domain 1 to Domain 9
Hoehn and Yahr stage (score)	**Pearson Correlation**	**1**	**.409****
	Sig. (2-tailed)		**0**
	N	**76**	**76**
Total Score Domain 1 to Domain 9	**Pearson Correlation**	**.409****	**1**
	Sig. (2-tailed)	**0**	
	N	**76**	**76**
****. Correlation is significant at the 0.01 level (2-tailed).**			

Table 6: Diseases duration vs Nonmotor Symptom Domain 1 to Domain 3 Correlations.

Description		Diseases duration of the patients	Domain 1: Cardiovascular including falls (score)	Domain 2: Sleep/ fatigues	Domain 3: Mood/ cognition
Diseases duration of the patients	Pearson Correlation	1	0.064	.227*	-0.077
	Sig. (2-tailed)		0.584	0.049	0.506
	N	76	76	76	76
Domain 1: Cardiovascular including falls (score)	Pearson Correlation	0.064	1	.257*	.328**
	Sig. (2-tailed)	0.584		0.025	0.004
	N	76	76	76	76
Domain 2: Sleep/ fatigues	Pearson Correlation	.227*	.257*	1	0.07
	Sig. (2-tailed)	0.049	0.025		0.55
	N	76	76	76	76
Domain3: Mood/ cognition	Pearson Correlation	-0.077	.328**	0.07	1
	Sig. (2-tailed)	0.506	0.004	0.55	
	N	76	76	76	76
*. Correlation is significant at the 0.05 level (2-tailed).					
**. Correlation is significant at the 0.01 level (2-tailed).					

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Table 7: Diseases duration vs Nonmotor Symptom Domain 4 to Domain 6 Correlations.

Description		Diseases duration of the patients	Domain 4: Perceptual problem	Domain 5: Attention/memory	Domain 6: Gastrointestinal tract
Diseases duration of the patients	Pearson Correlation	1	-0.034	.315**	.316**
	Sig. (2-tailed)		0.771	0.006	0.005
	N	76	76	76	76
Domain 4: Perceptual problem	Pearson Correlation	-0.034	1	.255*	0.116
	Sig. (2-tailed)	0.771		0.026	0.32
	N	76	76	76	76
Domain 5: Attention/memory	Pearson Correlation	.315**	.255*	1	.352**
	Sig. (2-tailed)	0.006	0.026		0.002
	N	76	76	76	76
Domain 6: Gastrointestinal tract	Pearson Correlation	.316**	0.116	.352**	1
	Sig. (2-tailed)	0.005	0.32	0.002	
	N	76	76	76	76
**. Correlation is significant at the 0.01 level (2-tailed).					
*. Correlation is significant at the 0.05 level (2-tailed).					

Discussion

Parkinsons Disease affect about 1-2% of the population over 65 years of age & upto 3-5% of people 85 years of age & older [18]. The results show a high prevalence of NMSs in our patients, in whom at least one NMS has been found. The results are NMSs prevalence rate of 100%. Other study NMSs of Parkinsons disease and impact on quality of life in Moroccanpeatients alsoprevalence rate of 100% [19,20]. The total patients of study were 76 whereas male were 55(72.4%) and female were 21 (27.6%). In another study conducted in Thailand, there was 76% respondent was male and rest of them are female. The age of the patients was above 50 years (>64.5%) and below 50 years (35.5%). This finding is similar to the study finding of Li et al. [19]. Among the 76 patients most of them (64.5%) treatment duration was between 1 to 4 years and the lowest (5.3%) disease duration below one year. Longer disease duration, advanced disease, longer levodopa use and higher daily dose are associated with the higher occurrence of non-motor symptoms of PD [9,21,22]. This study's Hoehn and Yahr stage 2 to 3 is 56.58% and stage 1 is 39.37%. Previous study showed the predominant population in stage 2 to 3 [23]. In this study the most frequent NMSs were dizziness, mood or cognition impairment, difficulties falling and staing sleep and feels of pain. The urinary disturbances were most frequent NMSs in previous studies [10]. But other study sleep and mood/cognition disorder were found in 88.3% and 80.6% of the patients, constituting the non-motor symptoms with the greatest impact on quality of life [24]. In domain 1 among the patients score highest (68.4%) dizziness score and lowest score 6.6% were fall. Almost similar symptoms of dizziness were present in more than half of patients [25]. In domain 2 were difficulties falling and staing sleep up to 75% and day time sleep up to 26.3% participant. Where sleep disorder more frequent NMSs upto 90% of people with PD [26,27]. This study was restless in legs upto 40.8%. Previous studies 8 to 20 % participants were RLS [28]. In domain 3 among the patients were cognition/mood more markly effect such as feeling of nervousness 77.7%, loss of interest in new activities 65.8%, depressed mood 62.4%, flat mode 61.8 % lack of pleasure 59.2% and lost of interest in his/her surroundings 40.8%. Cognitive dysfuntion affects 24% of patients with newly diagnosed PD [29]. Other previous studies 44.7-54% was cognitive impairment [9,22]. However, 63% of our patients admitted having cognitive problems only at slight or mild level. The correlation between cognitive impairment and QoL in patients with PD has been well-established [30,31]. In domain 4 among the patients' perceptual problem/ hallucination were upto 9%. But previous study was upto one third patients suffer from hallucination chronically treatment PD patients [32]. In domain 5 among the patients were forgetfulness upto 59.2% and loss of concentration 50%. Another study also found that participants with attentional/ memory deficits reported increased PD-39 scores [9]. In this study in domain 6 were constipation 38.2%, difficulty in shallow 19.7% and dribbling of saliva 11.8%. In a previous study constipation was most common symptom and swallowing difficulties were around 20% [9,14]. In domain 7 among the patients were urinary frequency 44.7%, urgency 43.4% and nocturia 34.2%. The most frequent NMSs were the urinary disturbances, which is in line with several previous studies [10]. In domain 8 among the patients were altered interest in sex 48.5% and problem having sex 27.6%. We trivialize the existing troubles and relate them to their advanced age. In a previous study

reported that the question relating to sex were frequently left unanswered [14]. In domain 9 among the patients were pain 56.6%, smell disturbance 45.7%, excessive sweating (not related to hoy weather)18.4% and change in weight (not related to dieting) 15.8%. Previous study was pain affects upto 74% of PD patients and due to its heterogenous aetiology, presents a complex diagnostic and management issue.33 Regarding olfactory disorders, they exist in a large majority of PD patients (up to 90%) and most often are present at the time of diagnosis. Overal the relative NMSs occurrence, as evaluated by NMS-30 is consistent dizziness (68.4%), mood/ cognition (67%), difficulties falling sleep (75%), restless in leg (40.8%) and urinary symptoms 40%. Though, in more than 70% of cases, patients are unware of their smell changes. Previous study there is a paucity of work examining the impact of sweating on QoL in PD despite studies showing that it affects almost half of the patients [34]. In this study there was pearson correlation between Hoehn and Yahr symptoms with non-motor symptoms domains 1 to 9. Most of the correlation were significant (<0.05). NMSs have considerable correlation with PDQ-39 scores with p value being significant like that observed in study with p value of (0.000) [10,35]. This study's disease duration vs non-motor symptom were pearson correlation and most of domain were significant (<0.05). Retrospective study with a long mean duration from PD diagnosis of 7.6±5.6 years, reported 98.9% of subjects experienced prodromal symptoms preceding a diagnosis of PD similar [36]. Hoehn and Yahr stage vs QoL were pearson correlation also significant (<0.05). The Hoehn and Yahr stage correlated more strongly with QoL scores than the motor part of the UPDRS [37]. Identifying the specific patterns of NMSs occurrence concerning time of symptoms has been pivotal in understanding the evoluation and its contribution to disease morbidity of PD individuals. Routine assessment of NMSs by using simple Questionnaires like NMSs quest and their impact on life by using PDQ-30, PDQ-39, PDQ-8 and Hoehn and Yahr scoring [23].

Limitations of the study: Several limitations exist to the present study, the sample size was small (worth to mention the COVID-19 situation which severely hampered sample collection), tt was single centered, study period was short, no further follow up was done, comorbid neurologic disorder were not assessed, motor symptoms also hamper the quality of life and control group was no concideration.

Conclusion

In this study we obseserved significant association of non–motor symptom with QoL NMSs are common in patients with PD, although they are often overlooked. NMSs result in a significant burden for people with PD and negatively affect QoL. Further studies are needed to assess the effect of treating NMSs on improving QoL.

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