



Frequency of Non-Motor Clinical Features of Parkinson Disease and the Associated Factors in Pakistan

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ABSTRACT

Parkinson's disease is an idiopathic disorder of the extrapyramidal system, resulting in impairment of movement with tremor, bradykinesia, rigidity, depression, shuffling gait and stooped posture. Among non-motor clinical symptoms, depression, anxiety, and apathy are the most prevalent symptoms. Although these are treatable but usually are not recognized at early stage in Parkinson's disease, so the current study aimed to find out the prevalence of non-motor clinical symptoms and the associated factors. A descriptive cross-sectional study was conducted at the Neuro-medicine Ward, (28), Jinnah Postgraduate Medical Center, Karachi during August 2019 to February 2020. Demographic information including; age, gender, residence, and duration of symptoms were collected by the investigator on prescribed proforma. ICD-10 was used to diagnose the presence of depression; BAI was used to detect anxiety while DSM-IV was used to diagnose the presence of insomnia. Data was entered and analyzed through Statistical Package for the Social Sciences (SPSS) version 20. The mean \pm SD of age, duration of symptoms and MMSE (mini mental status examination) score was 59.26 ± 5.95 years, 2.67 ± 2.04 months and 24.29 ± 1.59 respectively. About two thirds of patients were of age 50-60 years with male predominance. It was noted that depression was more prevalent with frequency of 54.3%, anxiety was 41.4% and insomnia was present in 32.9% patients of Parkinsonism. The non-motor symptoms were common among patients who were in their 6th decade of life. Likewise, male patients were much more affected with non-motor symptoms than females- but non-significantly. No any major difference was noted in frequency of non-motor symptoms of Parkinsonism between the rural and urban area patients. It was noted that anxiety decreased, insomnia increased while depression remained same with the decreasing duration of the disease but the results were non-significant. Lesser the mini mental status examination (MMSE) score, higher the frequency of depression, anxiety and insomnia. It is concluded that the non-motor symptoms are quite common among PD patients and out of all, the most common one is depression. Frequency of non-motor symptoms varies within different age groups as well as the gender and duration of disease.

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Authors' Contribution

This work was carried out in collaboration among all authors. JM designed the study. NI and AR performed the statistical analysis, wrote the protocol and wrote the first draft of the manuscript. GM and SMT managed the analyses of the study. SSM managed the literature searches. All authors read and approved the final manuscript.

Key words

Parkinson's disease, Non-motor clinical symptoms, Depression, Anxiety, Insomnia

INTRODUCTION

Parkinson's disease (PD) or Parkinsonism is one of the most common neurological disorder and second most

prevalent movement disorder in elderly people. Prevalence rate of Parkinson's disease in the United States is 187/100,000 and an annual incidence of 20 per 100,000. Worldwide, studies indicate a wide range of occurrence of PD, with prevalence rates ranging from 31 to 347 per 100,000 (Slaughter *et al.*, 2001). The prevalence of Parkinson's disease is not low in south Asian countries including Pakistan. Indian has prevalence of 70/100,000 population while as far as Pakistan is concerned there is no exact published data on statistics of this disease in Pakistan (Khealani and Baig, 2006). The average age at which the symptoms of Parkinson's disease begin (onset age) is about 60, but about five percent of those with Parkinson's disease experience the first symptoms before age 40,

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defined as young-onset Parkinson's disease (Jankovic, 2005; Khealani and Baig, 2006).

Parkinson's disease is an idiopathic disorder of the extrapyramidal system, involving primarily the degeneration of nerve cells in the basal ganglia, and in particular loss of neurons in the substantia nigra (A'campo *et al.*, 2010). The primary deficiency or with significant reduction of dopamine, the dopamine receptors in the striatum are not adequately stimulated, and the result is impairment of movement with tremor, bradykinesia, rigidity, depression, shuffling gait and stooped posture (Diederich *et al.*, 2003). Other clinical manifestations, usually less focused are also seen at the time of diagnosis including sensory symptoms like pain and tingling, hyposmia, sleep alterations, depression, anxiety, and abnormal executive, working memory-related functions (Pedersen *et al.*, 2009). Regarding non-motor clinical features of Parkinson's disease, it is estimated that cognitive deficits are present in early stage of disease in 20–40% of patients but are often overshadowed by motor features (Kulisevsky *et al.*, 2008).

Neuro-psychiatric symptoms which appear at any time, usually worsen as the disease progresses. Depression, anxiety, and apathy are the most prevalent symptoms (Aarsland *et al.*, 2009; Ilahi *et al.*, 2013). In day to day neurologic practice, many patients of Parkinson's disease are attended who have typical personality of emotional and attitudinal inflexibility, introversion. These patients are prone to develop non-motor symptoms like anxiety and also have a depressive tendency. Although these are treatable but usually are not recognized at early stage in Parkinson's disease therefore; these increases the suffering of these patients. So the current study aimed to find out the prevalence of non-motor clinical symptoms and the associated factors.

MATERIALS AND METHODS

A descriptive cross-sectional study was conducted at the Neuro-medicine Ward number 28, Jinnah Postgraduate Medical Center, Karachi during August 2019 to February 2020. Permission for the study was requested from Research evaluation unit, College of Physicians and Surgeons (CPSP) Pakistan. Permission for data collection was taken from the ethical review committee of the concerned institute. Estimated prevalence of anxiety taken at rate of 17% (Ilahi *et al.*, 2013), bound of error 9%, and level of significance 95%. Using least proportion formula, the calculated sample was 67–70. Non probability consecutive sampling technique was used.

Those patients were included who were having (1) Age >50 years and <70 years (2) diagnosed case of

Parkinson's disease since one month at least (3) Mini mental status examination score ≥ 22 while those were excluded who were already diagnosed case of (1) depression (2) hyperthyroidism (3) meningitis (bacterial, tuberculous, viral, TB) (4) brain abscess (5) uncontrolled diabetes mellitus (6) intracranial masses (e.g., tumor, abscess [often differentiated by CT]) (7) amyotrophic lateral sclerosis, Alzheimer's disease (8) subarachnoid hemorrhage and venous sinus thrombosis (9) epileptic seizures and normal pressure hydrocephalus (10) psychogenic disorders like panic disorder, or conversion reactions (11) or having previous history of accident with spine involvement and back pain (12) or the Mini mental status examination score <22. Informed and written consent was sought from all participating patients. The respondents were assured of the confidentiality of the information that they provided.

The patients presenting to out-patient department of Neuro-medicine ward were included in the study. Demographic information including; age, gender, residence, and duration of symptoms were collected by the investigator on prescribed proforma. International classification of disease (ICD-10) was used to diagnose the presence of depression. Back, anxiety inventory (BAI) questions was used to detect anxiety while Diagnostic and Statistical Manual of Mental Disorders (DSM-IV) was used to diagnose the presence of insomnia.

Data was entered and analyzed through Statistical Package for the Social Sciences (SPSS) version 20. Continuous variables like age, mini mental status examination score, duration of symptoms was analyzed as mean (+ SD) while frequencies and percentages were expressed for gender, non-motor clinical features (depression, anxiety and insomnia). Age, gender, residence, duration of symptoms, mini mental status examination score, were stratified to analyze the effect modification. Chi-square was applied to find out the association with a P value ≤ 0.05 taken as significant.

RESULTS

The mean \pm SD of age of patients was 59.26 ± 5.95 years. The mean \pm SD duration of symptoms among these patients was 2.67 ± 2.04 months while mean \pm SD of MMSE (mini mental status examination) score was 24.29 ± 1.59 . About two thirds (62.86%) of patients were of age 50-60 years while rest of patients (37.14%) were of age 61-70 years. Male to female ratio was 1.69: 1 as the males were predominant over females. It was also noted that 65.7% patients belong to urban areas while 34.3% were from rural areas. The main outcome variable of this study was frequency of non-motor clinical features of Parkinsonism, it was noted that depression was more prevalent with

frequency of 54.3%, anxiety was 41.4% and insomnia was present in 32.9% patients of Parkinsonism (Table I).

Table I. Characteristics of study participants (n=70).

Variables	Frequency	Percent
Age (years)		
50-60	44	62.8
61-70	26	37.1
Gender		
Male	44	62.8
Female	26	37.1
Residence		
Urban	46	65.7
Rural	24	34.3
Non-motor clinical symptoms		
Depression	38	54.3
Anxiety	29	41.4
Insomnia	23	32.9

Regarding the effect modification of results, age, gender, residence and duration of symptoms, the results showed that age of patient was an effect modifier such that non-motor symptoms (depression, anxiety and insomnia) were common among patients who were in their 6th decade of life (50-60 years) as compared to those who were elder (61-70 years) but these results were statistically non-significant (P values = 0.380, 0.447 and 0.053, respectively) as presented in Table II. Likewise, it was found that male patients of Parkinsonism were much more affected with non-motor symptoms than females- but non-significantly. (P values = 0.211, 0.263 and 0.062, respectively) as shown in Table II. No any major difference was noted in frequency of non-motor symptoms of Parkinsonism between the rural and urban area patients (P values = 0.593, 0.412 and 0.578, respectively) as reported in Table II. Evaluating the effect of duration of symptoms over frequency of non-motor symptoms including Depression, anxiety and insomnia, it was noted that anxiety decreased, insomnia increased while depression remained same with the decreasing duration of the disease but the results were non-significant (P values = 0.858, 0.889 and 0.949, respectively) as reported in Table II. The study also assessed the effect of mini mental status examination (MMSE) score on frequency of non-motor symptoms. Lesser the score, higher the frequency of depression, anxiety and insomnia (P values = 0.400, 0.184 and 0.879, respectively) shown in Table II.

DISCUSSION

Parkinson's disease (PD) is a chronic progressive disease of the nervous system characterized by tremors,

rigidity, akinesia, hypokinesia, bradykinesia, cranial nerve dysfunctions, autonomic nervous dysfunctions, sensory impairment, adhesive capsulitis of shoulder, perceptual motor and visuospatial defects (Jankovic and Kapadia, 2001; Khealani and Baig, 2006). Apart from these, the Parkinson's disease causes neuropsychiatric disturbances, which include mainly cognition, mood and behavior problems and can be as disabling as motor symptoms. Among these depression, anxiety and insomnia are the most common non-motor symptoms of PD. Because of lack of awareness many times these patients are very lately diagnosed (Aarsland *et al.*, 2009; Diederich *et al.*, 2003; Ilahi *et al.*, 2013).

Table II. Effect of age, gender, residence, frequency, disease duration and MMSE score on frequency of non-motor clinical features in Parkinsonism patients.

	Frequency of non-motor clinical features			
	n	Depression yes (%)	Anxiety yes (%)	Insomnia yes (%)
Age categories (Years)				
50-60	44	25(56.8%)	19(43.2%)	18(40.9%)
61-70	26	13(50.0%)	10(38.5%)	5(19.2%)
Total	70	38(54.3%)	29(41.4%)	23(32.9%)
P value		0.38	0.447	0.053
Gender				
Male	44	26(59.1%)	20(45.5%)	18(40.9%)
Female	26	12(46.2%)	9(34.6%)	5(19.2%)
Total	70	38(54.3%)	29(41.4%)	23(32.9%)
P value		0.211	0.263	0.062
Residence				
Urban	46	25(54.3%)	20(43.5%)	15(32.6%)
Rural	24	13(54.2%)	9(37.5%)	8(33.3%)
Total	70	38(54.3%)	29(41.4%)	23(32.9%)
P value		0.593	0.412	0.578
Disease duration				
Up to 1 month	20	10(50.0%)	8(40.0%)	6(30.0%)
>1 to 6 months	44	25(56.8%)	19(43.2%)	15(34.1%)
> 6 months	06	3(50.0%)	2(33.3%)	2(33.3%)
Total	70	38(54.3%)	29(41.4%)	23(32.9%)
P value		0.858	0.889	0.949
MMSE score				
22-24	50	29(58.0%)	24(48.0%)	17(34.0%)
25-27	19	9(47.4%)	5(26.3%)	6(31.6%)
28-30	1	0(0.0%)	0(0.0%)	0(0.0%)
Total	70	38(54.3%)	29(41.4%)	23(32.9%)
P value		0.400	0.184	0.879

The current study also found that non-motor symptoms are quite common in our patients who present with Parkinsonism. More than half (54.3% patients) had depression, anxiety was detected among 41.4% and insomnia was present in 32.9% patients. This shows that from one to one half of PD patients have non-motor symptoms. This arose the need of mandatory screening and treatment of such patients for these symptoms along with the primary pathology.

These findings are in concordance with other studies as well (Reijnders *et al.*, 2008). One such study documented that depression was present among more than one third (37%) PD patients while other 18% had insomnia, and anxiety was detected among 17% of Parkinsonism patients (Aarsland *et al.*, 2009). Another study has found much higher than current results. Accordingly; two thirds (63%) of Parkinsonism patients were depressed, about 27% had sleep disturbances and more than one third (37%) had anxiety (Behari *et al.*, 2002; Ilahi *et al.*, 2013).

Age distribution of patients of current study was more or less of those documented in other studies on PD patients (Diederich *et al.*, 2003; Lang, 2007; Reijnders *et al.*, 2008). Current study reported, the mean \pm SD age of patients was 59.26 ± 5.95 years. All our patients were in range of 50-70 years; among which two thirds (62.86%) of patients were of age 50-60 years while rest of patients (37.14%) were of age 61-70 years. This finding is as of contemporary studies on the subject because the parkinsonism rarely appears in younger age group (Behari *et al.*, 2002; Diederich *et al.*, 2003; Lang, 2007; Reijnders *et al.*, 2008). Further taking gender relation it was noted that majority (62.85%) of patients were males.

Current study also evaluated the relationship of age, gender, duration of Parkinsonism disease, and residence with frequency of non-motor symptoms among these patients. All the results were although non-significant but proportionally showed that some relationship existed between these variables. Male patients were more prone to non-motor symptoms of PD as compared to female patients. Frequency of depression, anxiety and insomnia slightly decreased with increasing age of Parkinsonism patients. The reason to this mechanism cannot be understood (Aarsland *et al.*, 2009; Khealani and Baig, 2006; Villarejo *et al.*, 2003).

Duration of PD itself also lead to an altered rate of non-motor symptoms. Non-significant results found that anxiety decreased, insomnia increased while depression remained same with the decreasing duration of the disease. Other studies do not rectify these findings. But findings of having no any major difference of living area/ setting on frequency of non-motor symptoms among out Parkinsonism patients is mimicking with international

literature that living vicinity do not have any effect over the disease progression, symptom or prognosis of PD (Shahed and Jankovic, 2007; Stefani *et al.*, 2007).

Mini mental status examination (MMSE) score was also found to have some relationship with the frequency of non-motor symptoms and higher score was associated with lower frequency of depression, anxiety and insomnia among PD patients. These findings have not been evaluated by other studies yet.

Although the current study was smaller study with limited time and short sample; yet it has focused and highlighted very crucial issue of PD patients. Worsening of quality of life occurs when the conditions is superimposed by psychiatric problems.

CONCLUSION

The current study noted that non-motor symptoms are quite common among PD patients and out of all, the most common one is depression. Frequency of non-motor symptoms varies within different age groups as well as the gender and duration of disease. The current study comes up with an important recommendation that all PD patients must be and thoroughly screened for presence of any non-motor symptom and should be treated simultaneously.

Statement of conflict of interest

The authors have declared no conflict of interest.

REFERENCES

- A'campo, L., Wekking, E., Spliethoff-Kamminga, N., Le Cessie, S., and Roos, R., 2010. The benefits of a standardized patient education program for patients with Parkinson's disease and their caregivers. *Parkinson. Relat. Disord.*, **16**: 89-95. <https://doi.org/10.1016/j.parkreldis.2009.07.009>
- Aarsland, D., Brønnick, K., Alves, G., Tysnes, O.B., Pedersen, K.F., Ehrh, U., and Larsen, J.P., 2009. The spectrum of neuropsychiatric symptoms in patients with early untreated Parkinson's disease. *J. Neurol. Neurosurg. Psychiatr.*, **80**: 928-930. <https://doi.org/10.1136/jnnp.2008.166959>
- Behari, M., Bhatnagar, S., Muthane, U., and Deo, D., 2002. Experiences of Parkinson's disease in India. *Lancet Neurol.*, **1**: 258-262. [https://doi.org/10.1016/S1474-4422\(02\)00105-9](https://doi.org/10.1016/S1474-4422(02)00105-9)
- Diederich, N.J., Moore, C.G., Leurgans, S.E., Chmura, T.A., and Goetz, C.G., 2003. Parkinson disease with old-age onset: a comparative study with subjects with middle-age onset. *Arch. Neurol.*, **60**: 529-533. <https://doi.org/10.1001/archneur.60.4.529>

- Ilahi, I., Khan, S., Khan, A.A., and Khan, M.Z., 2013. Parkinson's disease; Its occurrence and identification of risk factors in Khyber Pakhtunkhwa, Pakistan. *J. Biol. Life Sci.*, **4**: 172-180. <https://doi.org/10.5296/jbls.v4i1.2625>
- Jankovic, J., 2005. Motor fluctuations and dyskinesias in Parkinson's disease clinical manifestations. *Mov. Disord. Off. J. Mov. Disord. Soc.*, **20**(S11): S11-S16. <https://doi.org/10.1002/mds.20458>
- Jankovic, J., and Kapadia, A.S., 2001. Functional decline in Parkinson disease. *Arch. Neurol.*, **58**: 1611-1615. <https://doi.org/10.1001/archneur.58.10.1611>
- Khealani, B., and Baig, S., 2006. Clinical spectrum of Parkinson's disease from Pakistan. *Singapore med. J.*, **47**: 1075-1079.
- Kulisevsky, J., Pagonabarraga, J., Pascual-Sedano, B., García-Sánchez, C., Gironell, A., and Study, T.G., 2008. Prevalence and correlates of neuropsychiatric symptoms in Parkinson's disease without dementia. *Mov. Dis.*, **23**: 1889-1896. <https://doi.org/10.1002/mds.22246>
- Lang, A.E., 2007. The progression of Parkinson disease: A hypothesis. *Neurology*, **68**: 948-952. <https://doi.org/10.1212/01.wnl.0000257110.91041.5d>
- Pedersen, K.F., Larsen, J.P., Alves, G., and Aarsland, D., 2009. Prevalence and clinical correlates of apathy in Parkinson's disease: A community-based study. *Parkinson. Relat. Disord.*, **15**: 295-299. <https://doi.org/10.1016/j.parkreldis.2008.07.006>
- Reijnders, J.S., Ehrst, U., Weber, W.E., Aarsland, D., and Leentjens, A.F., 2008. A systematic review of prevalence studies of depression in Parkinson's disease. *Mov. Disord.*, **23**: 183-189. <https://doi.org/10.1002/mds.21803>
- Shahed, J., and Jankovic, J., 2007. Exploring the relationship between essential tremor and Parkinson's disease. *Parkinson. Relat. Disord.*, **13**: 67-76. <https://doi.org/10.1016/j.parkreldis.2006.05.033>
- Slaughter, J.R., Slaughter, K.A., Nichols, D., Holmes, S.E., and Martens, M.P., 2001. Prevalence, clinical manifestations, etiology, and treatment of depression in Parkinson's disease. *J. Neuropsychiat. clin. Neurosci.*, **13**: 187-196. <https://doi.org/10.1176/jnp.13.2.187>
- Stefani, A., Lozano, A.M., Peppe, A., Stanzione, P., Galati, S., Tropepi, D., Pierantozzi, M., Brusa, L., Scarnati, E., and Mazzone, P., 2007. Bilateral deep brain stimulation of the pedunculopontine and subthalamic nuclei in severe Parkinson's disease. *Brain*, **130**: 1596-1607. <https://doi.org/10.1093/brain/awl346>
- Villarejo, A., Camacho, A., García-Ramos, R., Moreno, T., Penas, M., Juntas, R., and Ruiz, J., 2003. Cholinergic dopaminergic imbalance in Pisa syndrome. *Clin. Neuropharmacol.*, **26**: 119-121. <https://doi.org/10.1097/00002826-200305000-00004>