ORIGINAL ARTICLE

Evaluation of Sleep Disorders in Parkinson's Diseases and Correlation of the Risk Factors with Anxiety

Ayesha Aslam[1], Naeem Amjad[2], Meer Wasiq Buzdar[3*], Nauman Mazhar[4], Ikram-ul-Haq[5], Mubashir Ahmed[6]

ABSTRACT

Objective: To determine the prevalence of sleep disorders in a patient with Parkinson's disease (PD) and to identify the risk factors that might develop anxiety among the patients with Parkinson's disease.

Study Design: A cross sectional study.

Place and Duration of Study: The study was conducted from 16th June to 16th November 2020 at Cardiology Department of Ch.Pervaiz Elahi Institute of Cardiology, Multan.

Materials and Methods: A total of 200 participants were part of the study, out of which 100 were diagnosed with Parkinson's disease while the other half were healthy subjects. Prior diagnosis of Parkinson's disease was reconfirmed through standard criteria of movement disorders and disease staging was done through Hoehn Yahr staging. All the participants were inquired of understudy variables through one-to-one interviews and a structured questionnaire was administered. Hamilton Anxiety Rating Scale was utilized to evaluate the existence of anxious tendencies. SPSS 20.0 was used for statistical analyses. T-test was used for comparison of sleeping disorders between control subjects and patients. Risk factors for anxiety were measured as odd ratios. A *P*-value less than 0.05 was considered statistically significant.

Result: Among patients with PD sleep initiation problems (37%), nocturia (66%), and body movement problems (50%) were found to be significant. Moreover, a majority of patients, 75%, were on sleeping pills. The data was suggestive of significant occurrence of Obstructive Sleep Apnea Syndrome (OSAS), restless leg syndrome (RLS), and Rapid eye Movement (REM) REM Sleep Behaviour Disorder (RSBD). Further, anxiety was significantly correlated with disease duration, severity, and age of the patient.

Conclusion: Parkinson's disease not only presents with motor symptoms but has severe non-motor manifestations. Similar to the external world, sleeping disorders are also prevalent among PD patients of Pakistan. Moreover, several factors play role in the development of anxiety in these patients which require critical management.

Key Words: *Anxiety, Non-motor Symptoms, Parkinson's Disease, Prevalence, Sleeping Issues.*

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[1]*Department of Neurology, Mayo Hospital King Edward Medical University (KEMU), Lahore*
[2]*Department of Psychiatry/Medicine*[5] *Shahida Islam Medical College Lodhran*
[3]*Department of Neurology/Psychiatry*[6] *Ch. Pervaiz Elahi Institute of Cardiology, Multan*
[4]*Department of Psychiatry Institute of Medical Science Services Hospital, Lahore*

Correspondence:
Dr. Meer Wasiq Buzdar
Consultant, Neurology
Ch. Pervaiz Elahi Institute of Cardiology, Multan
E-mail: buzdar.meer@yahoo.com

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Introduction

Parkinson's disease (PD) is the second most prevalent disorder among neurodegenerative diseases which is described as the prominent loss of cells in substantia nigra and other parts of the brain.[1] PD is classified in two-four stages based on the distribution of α-synuclein-immunoreactive inclusions, termed as Lewy bodies, in the brain.[2] These Lewy bodies then cause damage to dopaminergic nigrostriatal neurons; thus accounting for motor impairment.[3] Studies state that every 2nd person out of 1000 is affected by the disease and risk is multiplied with aging, affecting 1% of the

population who cross 60 years.[4] The clinical manifestations of PD are classified as either motor symptoms[5] or non-motor symptoms.[6]

Among patients with PD, around 98% document a minimum of 1 non-motor symptom which becomes apparent in the prodromal, undiagnosed, stage of PD.[7] Among which sleep and anxiety disorders are prevalent. Since the diagnosis of PD in history, sleep disorders have been a critical feature of this disease. Even the First ever definition of PD given by James Parkinson also referred to sleeping disturbances in the course of disease.[8] The significance of the study of sleep disturbances can be validated from the fact that 60-70% of PD patients report them.[9] To date, literature seems to be unsure about the actual causes behind sleep disorders and contrasting views are presenting. Some believe they are the primary manifestation of pathological changes of PD while others View them as secondary symptom.[10] However, it is jointly accepted that they negatively impact the quality of life.[11] Clinical studies have documented multiple sleep disturbances, including witnessing violent dreams are known as REM sleep behavior, sleep apnea, restless leg syndrome, disturbed circadian rhythms among others, which gain severity with time.[12]

Similarly, mood disorders such as depression and anxiety are also prominent in PD. On average, 2.7-90% of patients with PD suffer from anxiety throughout their lives.[13] However, the causes of anxiety are still not well-established. Some studies suggest that severity of motor disturbances, depression, social conditions, age, and anti-parkinsonism medication act as a predisposing factor of anxiety.[14]

Although, several studies are documenting the general prevalence of sleeping disorders; yet to our knowledge Pakistan still lags in this research area. The rationale of this study is to ascertain the sleep disorder which might affect the quality of life of the patients. Additionally, the evaluation of anxiety-associated risk factors will further help in improving the quality of life of patients. The study was designed to determine the prevalence of sleep disorders in a patient with Parkinson's disease and to evaluate the risk factors that might develop anxiety among the patients with PD.

Materials and Methods

A cross sectional study was conducted for six months from 16th June 2020 to 16th November 2020 at Cardiology Department of Ch.Pervaiz Elahi Institute of Cardiology, Multan. Patients from any age group, and gender with Parkinson's disease and under treatment for the last four years were included in the study after seeking their informed consent. The data of the patients were collected from the hospital registry. Patients who were having a history of any other neurological disorder, comorbidities, or movement disorders were excluded from the study. Standard criteria of movement disorders were employed by movement disorder specialists to reconfirm idiopathic Parkinson's disease and staging of the disease was done through Hoehn Yahr staging (H-Y stage). All the information regarding sleeping disorders and anxiety were collected through face-to-face interviews. A simple questionnaire was addressed to the participants to evaluate sleeping disorders. Participants were supposed to answer yes or no to sleeping issues such as difficulty in sleep initiation, experience disturbed sleep and involuntary movement of the body, witness violent dreams, or had a frequent awakening. Participants were also inquired of the reasons for frequent awakening and if they were any sleeping pills or not. To access daytime sleep quality Epworth sleeping scale (ESS) was also included.[15] Similarly, patients were then administered another questionnaire to evaluate the prevalence of anxiety. Hamilton Anxiety Rating Scale was used for the interpretation of responses to determine anxiety level.[16] Moreover, to predict the risk factors of anxiety, PD-specific and non-specific question, including information about demographics, financial condition, marital status, family support, smoking habits, disease progress and duration, and medication therapy were asked. A similar size of healthy individuals was included in the study. Patients with others were excluded from the study.

Statistical Analysis

Computer software SPSS 20.0 was used for data entry and analyses. Percentages of prevalent sleep disturbances were produced. Control subjects and Parkinson's disease patients were compared for continuous variables using the student's t-test. Logistic regression analyses were used to identify

risk factors for anxiety. Risk factors were presented as odds ratio (OR) with a 95% confidence interval. A *P*-value less than 0.05 is considered significant.

Results

A total of 200 participants, 100 patients, and 100 control subjects, answered the questionnaire. Patients who were suffering from Parkinson's Disease had a mean age of 62±5 years and a median H& Y score of 2.7 (range 0-5) where 60% of patients were diagnosed with the disease 7 or more years ago. Evaluation of responses recorded various significant sleep disturbances in patients with PD which are summarized in Table 1. The interpretation of responses was found to be highly suggestive of Obstructive Sleep Apnea Syndrome (OSAS), Restless Leg Syndrome (RLS), and REM sleep behavior disorder (RSBD). The score referring to the severity of disturbances was higher in older patients than younger ones. ESS scale responses were used to calculate mean naps duration. Moreover, 28 (28%) patients were diagnosed with anxiety. Table 2 represent the correlation of risk factor of anxiety with disease among patients.

Table 1: Prevalence of Sleep Disorders in Patients with Parkinson Disease (n=100)

Sleep Disorders	Frequency (%)	*P*-value
Sleep initiation problem	37(37%)	0.03
Nocturia	66(66%)	0.003
Inability to turn in bed	50(50%)	0.05
Nightmares	75(75%)	0.001
Mean Duration of Nap	27	0.021
Intake of Sleeping pills	20(20%)	0.075
Suggestive of OSAS	15(15%)	0.091
Suggestive of RLS	53(53%)	0.043
Suggestive of RSBD	10(10%)	0.07

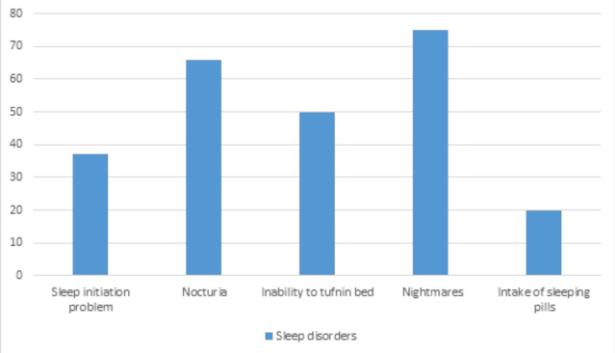

Fig 1: Graphical Representation of Sleep Prevalence among Patients with Parkinson Disease (n=100)

Table 2: Correlation of Risk Factors with Anxiety by Logistic Regression Analysis Adjusted for Age

Risk Factors	Adjusted OR (95% Confidence interval)	*p*-value
Age (years)	1.032 (1.015-1.053)	0.001
Income less than 25,000	0.92 (0.309-2.74)	0.883
Marital Status (broken or stressed relationship)	1.49 (0.678-3.59)	0.605
Smoking habits	1.45 (0.67-3.02)	0.56
H-Y Stage	3.32 (1.5-4.679)	<0.001
Disease Duration	3.38 (1.34-3.87)	<0.001
Medication	1.56 (1.003-2.45)	0.03

Discussion

Parkinson's disease is the second most prevalent neurodegenerative disorder which is significantly affecting a major segment of the world population. While the external world is rapidly making progress in grasping its pathology and symptomatic manifestations, Pakistan remains unsuccessful in making any significant change in this respect. In this study, we have tried to evaluate the prevalence of sleep disorders and anxiety among the population of Pakistan. Further, we tried to ascertain the predisposing risk factors that could contribute to the presentation of anxiety in patients with Parkinson's disease.

Evaluation of patients reflected that majority of the diseased population experience the issues of nocturia (66%) and nightmares (75%). These findings are consistent with already established literature.[17] Balta et al. reviewed that multiple causes of nocturia in these patients, including the reduced functional capacity of the bladder, nocturnal polyuria, and disturbances in circadian rhythms are to name a few.[18] A study documented incidences of isolated nightmare disorders in almost 40% of the general population; however, recurrence is majorly linked with psychiatric disorders.[19] The finding of anxiety in our study can be interpreted as that these patients suffer from psychiatric disorders which manifest as nightmares.

Further, 37% of patients reported difficulty in sleeping and complained of a mean of 4hrs to sleep after being in bed. In a study conducted by Tholfsen et AL., different insomnia types were reported during the early stages of PD however the problem began to reside after 5 years. The increase in sleep initiation problem is linked to consumption of dopamine antagonist and secondary to the onset of depression.[20]

The evaluation of responses also suggested the occurrence of RLS, OSAS, and RSBD among the population. Previous studies suggest that restless leg syndrome is positively correlated with Parkinson's disease, thus validating our results. It is claimed that defect in dopaminergic pathways in PD results in the development of RLS; however, changes in iron metabolism is also reported.[21] The actual cause of the coexistence of two disorders is still a mystery for researchers.

Similarly, REM behavior disorder (RBD) is previously being reported among such patients. It is reported that the emergence of RBD is associated with further worsening of motor symptoms and a decline in cognitive presentations. This association is stronger in patients with greater synuclein, amyloid, and dopaminergic pathology.[22] Besides, occurrences of sleep breathing disorders are a recent research area; therefore, literature is depleted with its mechanisms. However, upon comparing patients with Parkinson's disease with control subjects, 4% of patients suffered from OSAS than 2% of control subjects. Moreover, other sleep breathing disorders are also reported.[23]

The other important aspect of our study was the prevalence of anxiety in patients with sleep disorders and detecting the possible risk factors. It was found that around 28% of patients were anxious and the percentage was significantly high than healthy subjects. The study found that age, disease duration, disease severity, and medication are significant contributors to anxiety. Patients complained that with increasing age they found their disease getting more severe and slight improvement in symptoms since the start of symptoms is a disturbing agent for them. They also reported that medication seemed to aggravate their anxious tendencies. Similar results are found in previous studies where depression is also found to be coexistent with anxiety and a positive contributor of psychic symptoms.[13,24,25]

Conclusion

Parkinson's disease not only presents with motor symptoms but has severe non-motor manifestations. Similar to the external world, sleeping disorders are also prevalent among PD patients of Pakistan. Moreover, several factors play role in the development of anxiety in these patients which require critical management.

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