*Original Article*

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# A Comparative Study of Sleep Disorders between Familial and Sporadic Parkinson's Disease

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**Abstract**

*Background*: Parkinson's disease (PD) is associated with many non-motor features including various types of sleep dysfunction. So, the present study was conducted to compare pattern and prevalence of sleep disturbances in sporadic and familial PD. *Materials & Methods:* The patients in present study were recruited from movement disorders clinic of tertiary teaching hospital after approval from the institution ethics committee and written informed consent from all patients. Patients with comorbid illness likely to cause sleep dysfunction were excluded from the study. Familial and sporadic PD patients who participated in the study were interviewed using standardised questionnaires using Parkinson's Disease Sleep Scale (PDSS) and Epworth Sleepiness Scale (ESS). All patients underwent Polysomnography (PSG) using Biological Sleep Scan machine and results were evaluated with the help of a Qualified Sleep Specialist. *Results*: There was no significant difference with respect to PDSS total score and ESS total score between the two groups of PD. The overall prevalence of any sleep disturbance on PSG in Familial PD patients was 80% and it was 90% in Sporadic PD patients. There was no significant difference in the prevalence of Sleep disordered breathing, sleep fragmentation and periodic limb movements between the two groups. *Conclusion*: Sleep disturbances were common in both Familial and Sporadic PD patients in present study. No difference was found in overall nocturnal and daytime sleep symptomatology except less severe nocturnal akinesia and morning dystonia in Familial group.

**Keywords:** Familial; Sporadic; Parkinson's Disease; Sleep Disorders; Polysomnography.

## Introduction

A good night's rest/sleep is essential for a person to feel well. Disturbed and disrupted sleep can affect person health, mood and overall quality of life. Parkinson's disease (PD) is a disease which is characterized by degeneration of dopaminergic neurons in the substantia nigra pars compacta coupled with intracytoplasmic proteinaceous inclusions known as Lewy bodies [1]. The cardinal clinical features of PD include an asymmetric onset of bradykinesia, rigidity and resting tremor. Most idiopathic PD patients present with one or more of these motor features. It is well known that PD is also associated with many non-motor features including various types of sleep dysfunction. A community based study found that nearly two thirds (60-70%) of the patients with sporadic PD had sleep disorders, significantly more than among patients with diabetes (46%) and healthy control subjects (33%) [2].

Patients with PD can have excessive daytime somnolence (EDS) as well as nocturnal sleep problems [3]. The etiology of sleepiness in PD patients is multifactorial; dopaminergic medications as well as disease related factors like duration and severity are associated with EDS in PD [4-6].

Nocturnal sleep disturbances may be grouped into four broad categories; insomnia, secondary to motor dysfunction, urinary and neuropsychiatry problems [7]. Patients with PD have significantly less total sleep time and reduced sleep efficiency [8]. Sleep fragmentation and early awakening are seen more frequently than age matched controls [3]. The motor function related sleep disturbances include nocturnal akinesia, restless leg syndrome and periodic limb

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movements during sleep; the neuropsychiatry problems include rapid eye movement (REM) behavior disorder, hallucinations, nocturnal vocalizations and nightmares [9]. The sleep disturbance correlates with disease severity and duration, Schwab and England Score, Unified Parkinson Disease Rating Scale (UPDRS) motor score and levodopa dose [10].

Due to the presence of sleep centers in brainstem, sleep related problems often predate classic motor manifestations of PD. There have been various studies on sleep disorders in sporadic PD. However, sleep disorders have never been systematically evaluated in familial forms of PD. So the present study was conducted to compare pattern and prevalence of sleep disturbances in sporadic and familial PD.

## Material & Methods

The present comparative study was conducted in a teaching hospital after taking approval from the institution's Technical Advisory Committee and the Ethics Committee. The patients were recruited from Movement Disorders clinic of SCTIMST, Thiruvanan-thapuram, Kerala. Written informed consent was obtained from all patients prior to enrolment.

Parkinson's disease was diagnosed by UKPD Brain bank diagnostic criteria [11]. One or more of the family members with a documented diagnosis of were included in Familial PD group and no PD family member with a documented diagnosis of PD (other than proband) in preceeding three generations or any successive generation were included in sporadic PD group. Patients with comorbid illness/condition likely to cause sleep dysfunction (like substance abuse, obstructive airway disease, cardiac failure) were excluded from the study.

Familial and sporadic PD patients who participated in the study were interviewed using the structured proforma during their routine clinic visits. All patients underwent a detailed clinical examination and symptoms indicating sleep dysfunction were collected using standardised questionnaires using Parkinson's Disease Sleep Scale (PDSS) [12] and Epworth Sleepiness Scale (ESS) [13]. PDSS is a visual analogue scoring method, addressing 15 commonly reported symptoms associated with sleep disturbances in PD, with good test- retest reliability [12]. A higher PDSS score reflects better sleep quality. The patients completed the PDSS based on their experience in the past week. The severity of symptoms was reported by marking a cross along a 10 cm line (labelled from worst to best state). Thus scores for each item range from 0 (symptom severe and always experienced) to 10 (symptom-free). The maximum cumulative score for the PDSS is 150 (patient is free of all symptoms). The items of the PDSS address overall quality of night's sleep (item 1), sleep onset and maintenance insomnia (items 2 and 3), nocturnal restlessness (items 4 and 5), nocturnal psychosis (items 6 and 7), nocturia (items 8 and 9), nocturnal motor symptoms (items 10–13), sleep refreshment (item 14), daytime dozing (item 15). In addition to PDSS, ESS was filled by all patients. ESS consists of 8 items intended to measure daytime sleepiness [13]. The scoring varies from 0 (no daytime somnolence) to 24 (severe daytime somnolence).

All patients underwent an 8-hr standardized overnight Polysomnography (PSG) using Biological Sleep Scan machine in the Sleep Disorders Centre and results were evaluated with the help of a Qualified Sleep Specialist.

### PSG Technique

All patients were instructed to reach sleep lab at least 90-120 min before their usual sleep time in night. Before coming to the study the patients were advised to prepare a sleep diary of preceding 2 weeks. Patients were instructed to drink less water and not to take tea or coffee after 4' O clock on the

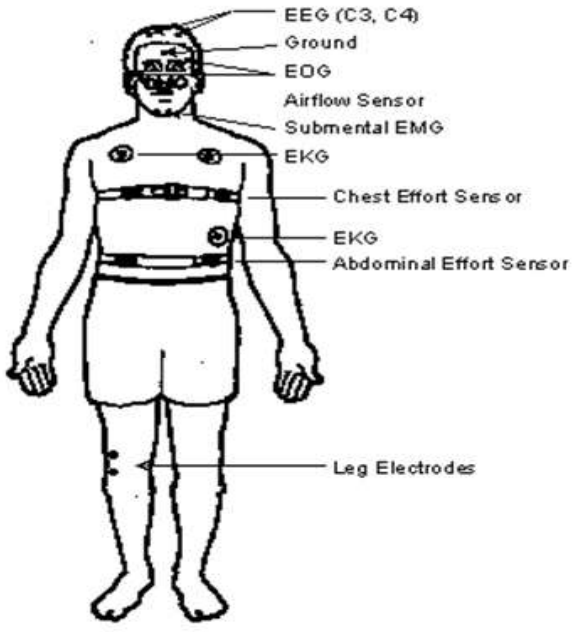


**Fig. 1:** Various places of sensor/electrodes in body for Polysomnography

day of scheduled PSG. Also they were told to keep their hair clean.

The study was started with biological calibration (like eyes open, eyes closed, blink 5 times, mimic snoring, hold breath for 10 seconds, move the right and left leg, grind teeth, etc.). Same was done at the study end. EEG recording, electrooculogram, chin EMG, tibialis anterior (TA), EMG, Nasal and oral airflow, oxygen saturation, electrocardiogram, snore electrode, the abdominal or thoracic belt sensor for thorax and abdominal movements were used to record total sleep time (TST), sleep latency (duration to sleep onset), sleep efficiency (percentage of total sleep duration over total time in bed), duration of Stage 1, 2, slow wave and REM sleep, apnea–hypopnea index (AHI), arousal index (AI), periodic limb movement index (PLMI) [14]. SPSS version 17 was used for data analysis. For categorical variables, percentages were compared by Fisher's exact test. For quantitative variables, Mann-Whitney test was used. p value ≤ 0.05 was considered significant.

## Results

A total of 20 cases of Familial and 20 cases of Sporadic PD were finally compared for sleep disorders. There was no significant difference with respect to PDSS total score and ESS total score between the two groups of PD.

However, individual PDSS item analysis showed higher mean scores of PDSS item 9 and 12 in Familial PD compared to Sporadic group suggesting lesser impairment in Familial PD patients as highlighted in Table 1.

The overall prevalence of any sleep disturbance on PSG in familial PD patients was 80% and it was 90% in sporadic PD patients.

There was no significant difference in the prevalence of SDB, sleep fragmentation and periodic limb movements between the two groups. Table 2 shows the prevalence of different PSG quantified sleep disturbances in familial and sporadic PD patients.

PSG quantified sleep parameters and indices showed lower mean AHI and mean nocturnal oxygen desaturation in Familial PD patients than Sporadic ones as shown in Table 3. No parasomnias including REM sleep behaviour disorder (RBD) were noted in any patient.

**Table 1:** Comparison of questionnaire items between familial and sporadic PD patients

| Questionnaire item | Familial PD Mean ± SD (N=20) | Sporadic PD Mean ± SD (N=20) | p value |
|---|---|---|---|
| PDSS 1 | 7 ± 2.3 | 6.2 ± 2.3 | 0.35 |
| PDSS 2 | 7.6 ± 3.6 | 7.8 ± 2.4 | 0.67 |
| PDSS 3 | 5.7 ± 4 | 5.5 ± 2.8 | 0.36 |
| PDSS 4 | 7.8 ± 3.7 | 7.2 ± 2.8 | 0.18 |
| PDSS 5 | 6.8 ± 4.1 | 8.1 ± 2.7 | 0.64 |
| PDSS 6 | 8 ± 2.7 | 7.3 ± 3.1 | 0.47 |
| PDSS 7 | 8.6 ± 2.8 | 9.1 ± 2.1 | 0.73 |
| PDSS 8 | 4 ± 4.4 | 6.2 ± 2.7 | 0.2 |
| PDSS 9 | 9.3 ± 1.4 | 6.7 ± 3.8 | **0.04** |
| PDSS 10 | 7.3 ± 4 | 7.3 ± 2.8 | 0.56 |
| PDSS 11 | 8.2 ± 2.6 | 6.3 ± 3.2 | 0.06 |
| PDSS 12 | 9.5 ± 1.7 | 7.3 ± 3 | **0.02** |
| PDSS 13 | 6.4 ± 4.4 | 7.7 ± 2.8 | 0.58 |
| PDSS 14 | 6.3 ± 4.1 | 7.5 ± 3 | 0.52 |
| PDSS 15 | 6.0 ± 4.3 | 8.1 ± 3.3 | 0.16 |
| PDSS (Parkinson's Disease Sleep Scale) total score | 108.9 ± 29.1 | 108.1± 21.8 | 0.71 |
| ESS (Epworth Sleepiness Scale ) total score | 6.6 ± 3.7 | 5.5 ± 5.4 | 0.18 |

**Table 2:** Prevalence of sleep disturbances in Familial and Sporadic PD patients

| Sleep Disturbances | Familial PD N (%) | Sporadic PD N (%) |
|---|---|---|
| Overall | 16 (80) | 18 (90) |
| Sleep disordered breathing | 6 (30) | 8 (40) |
| Sleep fragmentation | 14 (70) | 15 (75) |
| Periodic limb movement | 10 (50) | 9 (45) |

**Table 3:** Comparison of PSG parameters between Familial and Sporadic PD patients

| Parameter | Familial PD Mean ± SD (n=20) | Sporadic PD Mean ± SD(n=20) | p value |
|---|---|---|---|
| Sleep latency (min) | 10.3 ± 13.3 | 4.7 ± 3.8 | 0.1 |
| Total sleep time (min) | 348.9 ± 54.4 | 327.6 ± 66.3 | 0.36 |
| Duration Stage I sleep (min) | 59.8 ± 42 | 53 ± 34.9 | 0.65 |
| Duration Stage 2 sleep (min) | 194.6 ± 55.7 | 182.7 ± 53.8 | 0.49 |
| Duration Slow wave sleep (min) | 50.5 ± 38.4 | 46 ± 35.4 | 0.86 |
| Duration REM sleep | 43.9 ± 23.5 | 45.8 ± 38.7 | 0.67 |
| Sleep efficiency (%) | 81.1 ± 9.5 | 82.5 ± 8 | 0.69 |
| Apnea hypopnea index (AHI) | 3.8 ± 6.5 | 7.9 ± 8.5 | **0.02** |
| Snoring index | 3.2 ± 7.6 | 7.5 ± 9.6 | 0.22 |
| Max O2 desaturation (%) | 88.4 ± 8.4 | 84.8 ± 5.3 | **0.005** |
| Arousal index (AI) | 20.1 ± 13.9 | 25.4 ± 15.6 | 0.25 |
| Periodic limb movement index (PLMI) | 6.9 ± 9.7 | 12.4 ± 20.7 | 0.96 |

## Discussion

Nearly 98% of patients with Parkinson's disease (PD) may suffer at some time from nocturnal symptoms that can disturb their sleep [15]. A community-based study reported 60% of patients with PD with sleep problems, compared with 33% of healthy controls with the same age and sex distribution [16]. Oerlemans et al using a sleep questionnaire mailed to around 400 PD patients, found a high prevalence of abnormalities including restless leg syndrome (RLS) and REM sleep behavior disorder (RBD) [16]. In spite of this high prevalence neurologists fail to recognize the sleep disturbances in Parkinson's disease patients in nearly half of the routine office visits [17].

To our knowledge, this is the first study to compare the pattern of sleep dysfunction in two etiological subtypes of PD. The prevalence of PSG-quantified sleep disturbances in our patients with PD was 80-90%, which is comparable to previous studies in Sporadic PD in other population groups [2,16]. There are no studies of sleep disturbances in Familial PD. Our study compared nocturnal as well as daytime sleep dysfunction using sleep scales and PSG in Familial and Sporadic PD patients.

There was no significant difference in nocturnal sleep problems and daytime somnolence between the two groups as reflected in comparable total PDSS and ESS scores. However, in our study, PDSS item 9 and 12 scores were significantly higher in familial PD patients implying milder degree of symptoms attributable to nocturnal akinesia and early morning dystonia than sporadic group.

The overall prevalence of sleep disturbances on PSG was not different between the two groups. Also basic quantitative and qualitative sleep parameters like sleep latency, total sleep time, sleep efficiency and duration of individual sleep stages (NREM & REM) were comparable. Juan et al performed PSG studies in 4 of the 7 patients and in 2 asymptomatic carriers of a novel mutation in the α-synuclein gene (E46K) presenting with parkinsonism and dementia [18]. A severe loss of both REM and non-REM sleep was observed in 3 patients and mild sleep dysfunction in carriers. Though 2 patients complained of bizarre behavior at night, RBD could not be recorded in any case. They concluded that sleep disorders were common in synucleinopathies.

Previous studies showed high prevalence of SDB in Sporadic PD patients which was comparable to our prevalence in both Sporadic and Familial cases [19]. However, SDB severity (reflected in mean AHI and nocturnal O2 desaturation) was less in Familial PD patients compared to Sporadic cases. The pathogenesis of sleep apnea is complex but the central regulation from medullary centres is postulated. Whether the difference in severity of SDB could be due to difference in the pattern of involvement of brainstem centres in two subtypes of PD requires further studies.

The prevalence and severity of sleep fragmentation and PLM on PSG were not significantly different between the two groups, so also, the insomnia & nocturnal restlessness subitems on PDSS. However, the percentage of patients having sleep fragmentation & PLM were high in both the groups, as previously seen in many studies on Sporadic PD [8,20]. Tuin et al performed sleep interviews and PSG study in a Spanish family with PINK1 mutations (PARK6) [21]. They found that all siblings had good subjective and objective sleep quality. Restless legs syndrome and rapid eye movement (REM) sleep behaviour disorder (RBD) were not observed. They postulated that good sleep quality and the absence of RBD might be a useful diagnostic guide in the differential diagnosis of sporadic PD versus PARK6.

## Conclusion

Sleep disturbances were common in both Familial and Sporadic PD patients in present study. No difference was found in overall nocturnal and daytime sleep symptomatology except less severe nocturnal akinesia and morning dystonia in Familial group. PSG showed less severe sleep apnea in Familial PD patients. This may arise from differences in the pathophysiological processes affecting brainstem centres in the two forms of the disease. However larger studies are needed as sample size was small and many patients had PSG detected sleep disturbances without corresponding symptoms measured by PDSS & ESS which could be ascribed to the 1st night effect.

## References


1. Forno LS. Neuropathology of Parkinson's disease. J Neuropathol Exp Neurol 1996;55:259-72.
2. Tandberg E, Larsen JP, Karlsen K. Excessive daytime sleepiness and sleep benefit in Parkinson's disease: a community-based study. Mov Disord 1999;14:922–7.
3. Adler CH, Thorpy MJ. Sleep issues in Parkinson's disease. Neurology 2005;64(Suppl 3):S12–S20.
4. Ondo WG, Dat Vuong K, Khan H, Atassi F, Kwak C, Jankovic J. Daytime sleepiness and other sleep disorders in Parkinson's disease. Neurology 2001;57:1392–6.
5. Tan EK, Lum SY, Fook-Chong SMC, Teoh ML, Yih Y, Tan L, et al. Evaluation of somnolence in Parkinson's disease: comparison with age- and sex-matched controls. Neurology 2002;58:465–8.
6. Gjerstad MD, Alves G, Wentzel-Larsen T, Aarsland D, Larsen JP. Excessive daytime sleepiness in Parkinson's disease. Is it the drugs or the disease? Neurology 2006;67:853–8.
7. Chaudhuri KR. Nocturnal symptom complex in PD and its management. Neurology 2003;61(Suppl. 3): S17–S23.
8. Wetter TC, Collado-Seidel V, Pollmacher T, Yassouridis A, Trenkwalder C. Sleep and periodic leg movement patterns in drug-free patients with Parkinson's disease and multiple system atrophy. Sleep 2000;23:361-7.
9. Dhawan V, Healy DG, Pal S, Chaudhuri KR. Sleep related problems of Parkinson's disease. Age and Ageing 2006;35:220-8.
10. Kumar S, Bhatia M, Behari M. Sleep disorders in Parkinson's disease. Mov Disord 2002;17:775-81.
11. Hughes AJ, Daniel SE, Kilford L, Lees AJ. Accuracy of clinical diagnosis of idiopathic Parkinson's disease: a clinico-pathological study of 100 cases. J Neurol Neurosurg Psychiatry 1992;55:181-4.
12. Chaudhuri KR, Pal S, DiMarco A, Whately-Smith C, Bridgman K, Mathew R, et al. The Parkinson's disease sleep scale: a new instrument for assessing sleep and nocturnal disability in Parkinson's disease. J Neurol Neurosurg Psychiatry 2002;73:629-35.
13. Johns MW. A new method for measuring daytime sleepiness: the Epworth Sleepiness Scale. Sleep 1991; 14:540–5.
14. Noradina AT, Hamidon BB, Roslan H, Raymond AA. Risk factors for developing sleep-disordered breathing in patients with recent ischaemic stroke. Singapore Med J 2006;47:392–9.
15. Lees AJ, Blackburn NA, Campbell VL. The nighttime problems of Parkinson's disease. Clin Neuropharmacol 1988;11:512–9.
16. Oerlemans WG, de Weerd AW. The prevalence of sleep disorders in patients with Parkinson's disease: A self-reported, community-based survey. Sleep Med 2002;3:147-149.
17. Shulman LM, Taback RL, Rabinstein AA, Weiner WJ. Non-recognition of depression and other non-motor symptoms in Parkinson's disease. Parkinsonism Relat Disord 2002;8(3):193-7.
18. Zarranz JJ, Bedoya AF, Lambarri I, Esteban JCG, Lezcano E, Zamacona J, et al. Abnormal Sleep Architecture Is an Early Feature in the E46K Familial Synucleinopathy. Mov disord 2005;20:1310-5.
19. Norlinah MI, Afidah KN, Noradina AT, Shamsul AS, Hamidon BB, Sahathevan R, et al. Raymond. Sleep disturbances in Malaysian patients with Parkinson's disease using polysomnography and PDSS. Parkinsonism Relat Disord 2009;15(9):670-4.
20. Gjerstad MD, Wentzel-Larsen T, Aarsland D, Larsen JP. Insomnia in Parkinson's disease: frequency and progression over time. J Neurol Neurosurg Psychiatry 2007;78:476–9.
21. Tuin I, Voss U, Kessler K, Krakow K, Hilker R, Morales B, et al. Sleep quality in a family with hereditary parkinsonism (PARK6). Sleep Med 2008;9:684-8.