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CLINICAL PROFILE OF PATIENTS WITH PARKINSON'S DISEASE IN HYDERABAD REGION

Neurology

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ABSTRACT

INTRODUCTION: Parkinson disease (PD) is the second most common neurodegenerative disorder that causes progressive motor and non-motor disability. This condition is diagnosed clinically and is characterized by the presence of bradykinesia, accompanied either by rest tremor or rigidity. The present study aimed to provide the demographic and clinical profile of PD in patients from Hyderabad and also to create a database on PD in this region.

METHODS: A prospective cross-sectional hospital based study was conducted over a period of 3 years commencing in December 2014. The study included cases of PD diagnosed in accordance with the United Kingdom PD Society Brain Bank criteria and analyzed its demographic and clinical features.

RESULTS: 40 patients (26 males, 14 females) were found to have features compatible with PD. The average age at onset was 51.55± 10.18 years. Majority of patients had onset of PD at an older age (≥50 years; 24 patients, 60%) when compared to the rest who were younger (age<50 years, 16 patients, 40%).The most common initial symptom was tremor (36 patients, 90 %). Postural instability was observed in 22% patients. The average progression from mild to moderate/severe PD (stage3) was seen to be 3.8±5 years among the young and 3.7±3.2 years among the older patients. Non motor feature of PD was observed in 25% patients and the most common non motor feature was found to be disturbance in sleep (15%)

CONCLUSION: Unilateral limb tremor was seen to be the most common initial symptom and disturbance in sleep was the most common non motor symptom. Male predominance and older onset of PD was observed in this region.

KEYWORDS

INTRODUCTION

Although Parkinson's disease (PD) was first described by James Parkinson in the early 19th century, [1] knowledge about PD had been present in India since ancient times. PD is the second most common neurodegenerative disorder seen in clinical practice. It is a chronic and progressive neurodegenerative disorder characterized by death of dopaminergic neurons in the substantia nigra pars compacta and widespread presence of an intracellular protein namely alpha synuclein. Classical PD motor symptoms include bradykinesia, tremor and rigidity. Postural instability occurs during later stages of the disease. Non-motor symptoms may precede motor symptoms by more than a decade. Non motor symptoms include autonomic dysfunction, behavior abnormalities, cognitive decline, sleep disturbances, and sensory abnormalities such as anosmia. During the later stage of PD, these non-motor symptoms turn out to be extremely burdensome for the patients.

The average prevalence of PD in India is 19 per 100,000 which is considerably low, except in the small Parsi community where a high prevalence of 328.3 per 100,000 has been reported from Western India. [2] .Moreover there have been very limited studies so far, on the clinical profile of PD, especially from India. [3, 4, 5] In this study, we aspired to present the demographic and clinical profile of PD in patients from Hyderabad and also to create a database on PD in this region.

METHODS

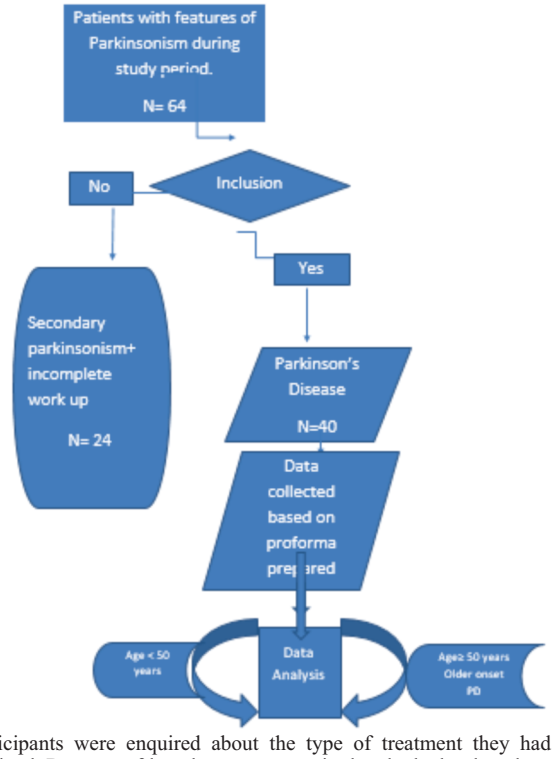
Study Design

This was a prospective cross sectional, hospital based study conducted at the Department of Neurology, at ESIC Superspeciality hospital, Hyderabad for a period of 3 years from December 2014 to December 2017 and patients diagnosed with PD based on United Kingdom Parkinson disease Brain bank criteria were enrolled. Clinical assessment of patients was done by a qualified neurologist. Computed tomography or magnetic resonance imaging (MRI) of the brain was done to exclude secondary Parkinsonism.

Participants

A total of 40 patients comprising inpatients as well as outpatients who visited the hospital and diagnosed with PD, were enrolled for the study. Patients with secondary Parkinsonism and prior stroke history were excluded. Those patients/relatives who were unwilling or reluctant to enroll for the study and those whose work up was incomplete were excluded from the study [flow chart]. Information regarding reliable variables in the study, comprising demographic details, age at onset of first symptom, duration of illness, family history of PD, risk factors, motor symptoms of PD (TRAP-tremor, rigidity akathisia, postural instability), asymmetry or symmetry at onset, first motor symptom, non-motor symptoms such as autonomic dysfunction, behavior abnormalities, cognitive impairment, sleep disturbances and sensory abnormalities, especially anosmia, were obtained from the patients. Hoehn and Yahr scale was used to make gross assessment of the progression of the disease. Cognitive impairment was confirmed/measured using Montreal Cognitive Assessment Test. The unified Parkinson's disease rating scale (UPDRS) was used for assessing disability and impairment, especially in those patients selected for Deep Brain Stimulations (DBS).

Flow chart



Participants were enquired about the type of treatment they had received .Dosages of levodopa were enquired and whether levodopa was prescribed alone or in combination with other dopamine agonist

such as pramipexole, ropinrole etc. And also whether these participants have underwent DBS were enquired. Information was also sought regarding the presence of phenomena such as morning dystonia and dyskinesia. In the event of the patient being unable to cooperate with the study procedure, all necessary information was obtained from his /her close relative.

Definition of study variables

Diagnosis of PD:

Based on United Kingdom Parkinson's Disease Society Brain Bank Diagnostic Criteria. [6]

STEP 1. Diagnosis of Parkinsonian syndrome

Bradykinesia (slowness of initiation of voluntary movement with progressive reduction in speed and amplitude of repetitive actions). And diagnosis was based on the presence of at least one of the symptoms, varying from muscular rigidity, 4–6Hz rest tremor to postural instability not caused by primary visual and vestibular, cerebellar or proprioceptive dysfunction.

STEP 2. Exclusion criteria for Parkinson's disease

History of repeated strokes with stepwise progression of Parkinsonian features, history of repeated head injury, history of definite encephalitis, oculogyric crises, neuroleptic treatment at onset of symptoms, more than one affected relative, sustained remission, strictly unilateral features after three years, supranuclear gaze palsy, cerebellar signs, early severe autonomic involvement ,early severe dementia with disturbances of memory, language and praxis, Babinski sign, presence of a cerebral tumor or communicating hydrocephalus on CT scan, negative response to large doses of levodopa (malabsorption excluded) and MPTP (1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine) exposure were exclusion criteria for PD.

STEP 3. Supportive prospective positive criteria for Parkinson's disease.

Apart from bradykinesia, three or more symptoms are considered essential for diagnosis of definite Parkinson's disease. These include unilateral onset, rest tremor at present, progressive disorder, persistent asymmetry mostly affecting the side of onset, excellent response (70–100%) to levodopa, severe levodopa-induced chorea, levodopa response for 5 years or more and clinical course of 10 years or more.

Disease Progression

Modified Hoehn and Yahr scale [7] was used to provide gross assessment of disease progression ranging from stage 0 (no signs of disease) to stage 5 (wheelchair bound or bedridden unless assisted).

0– no signs of disease,
1– unilateral disease (on one side)
1.5–unilateral disease plus axial involvement
2– bilateral disease, without impairment of balance
2.5–bilateral disease, with recovery on the pull test
3– mild to moderate bilateral disease; needs assistance to prevent falling on pull test; Physically independent
4– severe disability, but still able to walk or stand unassisted
5– wheelchair-bound or bedridden unless aided.

Older onset PD

Those with onset of PD at 50 years and above were considered as older onset PD patients. [8]

Young onset PD

Patients with onset of PD before attaining 50 years of age were considered as young onset PD. [8]

Statistical analysis

Data obtained in the study were subjected to statistical analysis with SPSS (version 18.0).Bivariate analysis was done using 2x2 Fisher's exact test for significance. A two tailed probability value less than 0.05 was considered significant.

Ethics Statement

The information obtained in this study was collected prospectively with the approval of the local ethics committee.

RESULTS

40 patients diagnosed to have PD were enrolled for the study.

Baseline characteristics

Mean age at onset of PD was 51.5±10.2 years (range 34-69); 26 (65 %) patients were male. Male to female ratio was 1.8:1. Majority of patients had older onset PD [Table 1].

Table 1: Baseline characteristics of study group

Study variable	Number n (%)
Total cases diagnosed to have PD	40
Male	26 (65%)
Female	14 (35%)
Average age at onset (in years)(Mean ± SD)	51.5± 10.2
Older onset (≥50 years)	24 (60%)
Young onset (<50 years)	16 (40%)
Age range in years	34-69

SD - Standard deviation

Clinical Characteristics

Tremor was the initial symptom noted in 36 (90%) patients. Asymmetry was observed in 28 (70%) patients.50% patients belonged to stage 1.5 and 2.5 as per Hoehn and Yahr scale of disease progression. Sleep disturbance was the major non motor symptom observed in 6 (15%) patients. Most of them had insomnia. Only 4 (10%) patients underwent DBS [Table 2].

Table 2: Clinical Characteristics of patients with Parkinson's disease.

Study variable	Number n (%)
Tremor as initial symptom.	36(90%)
Rigidity	40 (100%)
Bradykinesia	40 (100%)
Postural Instability (positive pull test)	8 (20%)
Stooped posture	22 (55%)
Asymmetry	28 (70%)
Mean duration of illness (Mean ± SD) in years	3.8±3.6 years
Stage 1*	6 (15%)
Stage 1.5*	10 (25%)
Stage 2*	4 (10%)
Stage 2.5*	10 (25%)
Stage 3*	6 (15%)
Stage 4*	4 (10%)
Sleep disturbances	6 (15%)
Psychosis	4(10%)
Morning dystonia	2(5%)
Treatment with levodopa with or without other drugs.	38 (95%)
Underwent DBS**	4 (10%)
Average age duration in years for DBS	11.6

*Hoehn and Yahr stages ** Deep Brain Stimulation

Those who had undergone DBS had sub thalamic DBS. Only 1 patient who underwent DBS belonged to young onset PD. Further subgroup analysis of patients based on young onset and older onset PD showed male predominance, especially in older onset PD, while both men and women were equally affected in young onset PD. The older onset PD presented the later stages of Hoehn and Yahr scale when compared to young onset PD [Table 3].

Table 3: Showing comparison between young and older onset Parkinson's disease

Variables	Young onset (<50 Years) Number n (%)	Older onset(≥50 years) Number n (%)	P value
Number of patients	16 (40%)	24(60%)	0.11
males	8 (50%)	18(75%)	0.17
females	8 (50%)	6(25%)	0.17
Postural instability	12(75%)	18 (75%)	1
*Average progression of disease in years. (mean ±SD)	3.8±5.0	3.7±3.2	0.93
tremor	16 (100%)	24(100%)	1
rigidity	16(100%)	24(100%)	1
Hoehn& Yahr stage	Stage 1,1.5,2 (early)	Stage 2,2.5,3,4 (advanced)	

*Average progression of disease from mild to moderate/severe disease

Risk factors

None of the patients with PD had any family history of PD. Only 4 patients had been diabetic, 2 patients had history of hypertension and 2 patients had history of smoking. None of the PD patients reported regular alcohol consumption or exposure to insecticides.

Disease progression

Among the 40 patients enrolled for the study, we observed mild PD (Hoehn & Yahr stage 1-2.5) in 30 (75 %) while moderate to severe PD (stage 3 to 5) was observed in 10 (25 %) cases. Progression from mild to moderate/severe PD required 3.8± 5 in young onset PD, while 3.7±3.2 years in older onset PD. The duration from initial symptom to mild PD was 4 years.

DISCUSSION

The available data on clinical profile of Parkinson's disease in Hyderabad region is negligible. We examined the demographic and clinical profiles of Parkinson's disease to create a database on PD in this region and to provide comparative data on Parkinson's disease phenotype, and progression in this region. We found a lower mean age of onset of PD [51.5 years] at presentation, when compared to studies reported from other parts [54-58 years] of India.[3,4,5] Further, mean age was lower in our study, even when compared to reports from Europe [61 years] [9] and Asia [66 years]. [10] The present study also revealed that a majority of patients had older onset PD which is similar to the result of previous studies. [3,4,5,9,10] Considerable risk factors described in the development of PD involved males with family history of PD, prior history of depression, well water drinking, farming and pesticide exposure. [11,12] 65% patients with PD in our study were men, thus male gender emerging as the major, non-modifiable risk factor for patients afflicted with PD. Demographic and clinical profile study of 557 PD patients in northern Karnataka district by Kadakola et al, [4] showed that males (64.8%) were the more affected in Northern Karnataka which may partly be attributed to the fact that women, when compared to men are less likely to seek medical attention.

The most common initial symptom in our study was tremor (90 %), which was higher than the range of 55%−74% reported in previous studies. [13] This higher incidence of tremor as the first symptom might have been an overestimation, as tremor is more perceptible than mild rigidity and bradykinesia. Clinical variants of PD described in related literature are tremor dominant PD (relative absence of other motor symptoms) and non-tremor dominant PD (includes akinetic rigid syndrome, postural instability and gait disorder).Tremor dominant PD was noted in a majority of our patients (90%).Tremor-dominant PD is often associated with a slower rate of progression and less functional disability than the non-tremor-dominant Parkinson's disease. [14] We found slower progression of disease in majority of our patients and none of them was in stage 5 of Hoehn and Yahr scale. We could not find any significant differences in onset of symptoms and disease progression, as the majority of patients had tremor (90%), rigidity (100%) and bradykinesia (100%). However, a greater sample sizes is recommended to determine whether tremor-first PD and non-tremor PD follow distinct progression.

Motor symptoms in PD are usually asymmetric at onset. The research on change in asymmetry over time has mixed results, with some studies suggesting a retained asymmetry and others suggesting a progression towards symmetry. Asymmetry in motor symptoms was noted in 70 % of our patients. This included either asymmetry in tremor, rigidity, bradykinesia, gait disturbance or postural instability. Our findings are in concordance with results of previous study, wherein TA Boonstra et al. reported balance asymmetry in 75% of patients. [15] However, the mechanism of such dissymmetry of symptom appearance is not properly understood. There is only scanty information about whether side predominance in PD is genetically coded and also about the determined years before symptom onset, or whether it is related to side differences in vulnerability of the degenerating neurons. [16]

Postural instability/gait disturbance occurs in the later stages of the disease and has been associated with rapid progression of the disease and cognitive dysfunction.[17,18] Postural instability comprising either abnormal pull test, gait disturbance or stooped posture and freezing of gait was noted in around 75% of the study group. These symptoms indicate a predisposition to recurrent falls and a higher degree of morbidity in this vulnerable group. Early identification and rehabilitation measures are needed to prevent further damage as they have only limited response to dopaminergic drugs, and falls are episodic and unpredictable.

There were several limitations in our study as it is cross-sectional, with a small sample size. The follow-up data and an unbiased assessment of the degree of response to levodopa therapy and mortality data may be lacking in our PD cohort. The study did not evaluate the predisposing factors, especially environmental factors, in the occurrence of PD in this region. Lastly, we could not perform a genetic study due to scarcity of laboratory facilities.

Our study of 40 PD patients in the Hyderabad region identified tremor as the most common initial symptom. Male gender was the major non-modifiable risk factor for PD. Most PD patients had late onset PD with average age being lower than that reported from other regions of India and worldwide. To the best of our knowledge, the present study is the first of its kind presenting the clinical profile of PD in Hyderabad's Telangana region.

CONCLUSION

Our study has successfully created a data base on the demographic and clinical profile of PD in the Telangana region, Hyderabad. A higher frequency of older age onset PD and male predominance were observed. And the average age of onset of PD was found to be lower than that reported from other parts of India and the rest of the world.

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