Clinical spectrum of Parkinson's disease from Pakistan

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ABSTRACT

Introduction: Parkinson's disease is an idiopathic disorder of the extrapyramidal system. It has a worldwide prevalence but data from developing countries is scanty. We describe the clinical spectrum of the disease from Pakistan, a developing country.

Methods: Patients with Parkinson's disease, over a period of 11 years, were identified by ICD-9 coding system of the hospital medical records. Demographical characteristics, clinical features, laboratory investigations and radiological investigations were recorded and analysed.

Results: A total of 80 patients were identified. 50 (63 percent) were males and 30 (37 percent) were females. Mean age of onset of the disease was 54 years. 47 (59 percent) patients had onset of illness during the sixth or seventh decade of life. Mean duration of illness at the time of presentation was five years. Rigidity, bradykinesia, tremors, hypomimia, primitive reflexes, difficulty in performing fine work and walking difficulty were the most common clinical features. 52 (65 percent) patients had stage I or II (Hoehn-Yahr staging) disease at the time of presentation. 56 (70 percent) patients had predominantly unilateral symptoms. 15 (19 percent) patients had cognitive impairment. Cognitive decline was more common in the elderly and in patients with disease duration of longer than ten years.

Conclusion: Parkinson's disease is more common in males. Tremor, rigidity, walking difficulty, bradykinesia and difficulty in performing fine work are the commonest clinical features. Disease severity increases with duration of the disease. Cognitive impairment is not uncommon in these patients and is associated with disease duration and age of onset of the illness.

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INTRODUCTION

Parkinson's disease is an idiopathic disorder of the extrapyramidal system characterised by tremors, rigidity and bradykinesia. Though James Parkinson is credited for his very clear description of Parkinson's disease, evidence exists that the disease has affected mankind since 2500 BC[1,2]. Little has been added to the clinical description since its first crisp description in the monograph "An essay on shaking palsy" by James Parkinson in 1817[3]. However, the management strategies have been revolutionised over time and much is now known about the pathogenesis. The most common clinical features of the disease are tremor, rigidity and bradykinesia. As the disease progresses, postural instability becomes a common disabling symptom. Although cognitive impairment is not a primary feature of this disease, it is not uncommon in advanced cases[4].

The disease has worldwide prevalence, with our part of world (South Asia), including Pakistan, not being excluded. The prevalence is however extremely variable, ranging from as low as 31/100,000 population in Libya to 300/100,000 and 328/100,000 population from Canada and India (Parsi community), respectively[5-7]. Except for the Parsi community, which has the highest prevalence of the disease in the world, the overall prevalence in India is about 70/100,000 population and this is lower than that reported in the West[8]. Despite the relatively low prevalence, the burden of disease in South Asia is enormous, as the population is huge. Little work has been done on this relatively common disorder in Pakistan and there is no published data on epidemiology and clinical presentation from our country. We describe the clinical spectrum of the disease from Pakistan a developing country.

METHODS

At the Aga Khan University Hospital, Karachi, Pakistan, patients with diagnosis of Parkinson's disease were identified by the ICD-9 coding system of the hospital medical records. The hospital is one of a few major tertiary care facilities, situated in Karachi, a provincial capital and the most populous city of Pakistan. The city has a population of about ten million and also attracts people from across the country to seek medical advice, in addition to employment and business. In the province of Sindh, almost all of the trained neurologists are practising in Karachi, the catchment area for neurological disorders in the whole province.

The charts were reviewed and the demographical, clinical, laboratory and radiological data were recorded. Cases with inadequate clinical data were excluded. Patients with a history of stroke(s) before the diagnosis of Parkinson's disease and patients whose clinical course and/or neuroimaging were suggestive of an alternative diagnosis (multisystem atrophy, progressive supranuclear palsy and normal pressure hydrocephalus) were also excluded. Only patients whose the diagnosis was based on presence of at least two cardinal clinical features (tremor, rigidity and bradykinesia) and response to levodopa therapy, were included.

101 patients were identified over a period of 11 years (January 1, 1988 to December 31, 1998) and 21 were excluded (data was inadequate in 12 patients, five patients had history of stroke before the diagnosis, two had hydrocephalus, one had progressive supranuclear palsy and one had multisystem atrophy). All of these patients were admitted for management of Parkinson's disease related problems. All the patients were evaluated by one or more qualified neurologists during their course of illness. The data was presented in mean ± standard deviation and percentages. Chi square and Fisher's exact tests were used to assess association between discrete variables.

RESULTS

101 patient charts were reviewed. 21 were excluded based on the criteria described in the Methods section. 30 (37%) were women and 50 (63%) were men. Their age at time of onset of the symptoms ranged from 27 to 87 (mean 56 ± 12, median 54) years. 47 (59%) patients had disease onset during the sixth or seventh decade of life, while ten (13%) of the patients started to have the symptoms before 40 years of age. Duration of symptoms prior to presentation was quite variable, ranging from <1 year to 30 years. 57 (71%) patients presented within five years of onset of symptoms of the illness.

Rigidity was recorded in 75 (94%), bradykinesia in 67 (87%), tremors in 66 (82%), difficulty in doing fine work in 58 (72%) and walking difficulty in 57 (71%) patients. In 11 (14%) patients, there was neither history of tremors nor was it noticed on examination. In three patients, data regarding tremor was lacking. Primitive reflexes and hypomimia were seen in 59 (74%) and 63 (79%) patients, respectively. About half of the patients had history of non-specific symptoms and hypophonic (monotonous) speech (Table I). Dysphagia, falls, depression and cognitive impairment were reported in less than 35% of the patients. Cognitive impairment was more common in the elderly, and in patients with a longer duration of illness. All patients with cognitive impairment had onset of illness after the age of 50 years ($p<0.004$) and their duration of illness was also comparatively longer than those who did not have the symptom. Three of eight (35%) patients with disease duration longer than ten years and 12/72 (17%) patients with duration less than ten years had cognitive impairment ($p=0.006$) (Table II).

Table I. Clinical features of patients with Parkinson's disease during the course of disease.

Symptoms	Number
1. Rigidity	75 (94)
2. Bradykinesia	67 (87)
3. Tremors	66 (82)
4. Hypomimia (Masked facies)	63 (79)
5. Primitive reflexes	59 (74)
6. Difficulty in doing fine work	58 (72)
7. Walking difficulty	57 (71)
8. Monotonous speech	48 (60)
9. Constipation	42 (52)
10. Non-specific symptoms*	41 (51)
11. Stiffness	29 (36)
12. Bladder symptoms	16 (20)
13. Cognitive impairment/decline	15 (19)
14. Falls	13 (16)
15. Dysphagia	11 (14)
16. Stooped posture†	16 (76)
17. Shuffling gait¶	24 (73)
18. Micrographia‡	11 (65)

Percentages in parenthesis.

* Bodyaches, generalised weakness, fatigue or dizziness.

† Data was available for only 21 patients.

¶ Data was available for only 33 patients.

‡ Data was available for only 17 patients.

Table II. Effects of disease duration and age of onset on cognitive decline.

Variables	Total no. of patients	No. of patients with cognitive decline	p-value
Disease duration at presentation			
≤10 years	72	12 (17)	<0.006
>10 years	8	3 (35)	
Age of onset			
≤50 years	24	0 (0)	<0.004
>50 years	56	15 (27)	

Percentages in parentheses.

56 (70%) patients had either predominantly unilateral symptoms or unilateral onset. Five (6%) patients had bilateral symptoms at onset. At the first visit, the majority of patients had either Stage (Hoehn-Yahr) I or II disease and after a mean follow-up of 3.5 years, the majority of the patients had Stage III or severe disease (Table III). Among 24 patients who had disease onset before age of 50 years, 21 (88%) presented with either Stage I or II disease as compared to 41/56 (73%) patients with disease onset beyond age of 50 ($p<0.001$). Patients, who had illness of longer duration at presentation, also had more severe disease (Table IV). There was no gender difference in disease severity at presentation. In both groups, two-thirds of patients presented with either Stage I or II disease.

Table III. Number of patients with Parkinson's disease in different stages of the disease.

Hoehn-Yahr Stage	No. of patients at presentation	No. of patients at last follow-up
I	15 (19)	8 (10)
II	37 (46)	25 (31)
III	8 (10)	24 (30)
IV	17 (21)	8 (10)
V	3 (4)	15 (19)

Percentages in parentheses.

Table IV. Relationship between disease duration and severity.

Disease duration	Total no. of patients	Stages I & II	Stages III & above	p-value
≤5 years	57 (71)	43 (75)	14 (25)	0.05
6-10 years	14 (19)	8 (50)	7 (50)	
>10 years	8 (10)	3 (38)	5 (62)	
Total	80	54 (67)	26 (33)	

Percentages in parentheses.

Thyroid function tests were done in 32 patients and were normal in 30 patients. In 32 patients, neuroimaging (computed tomography and magnetic resonance imaging) of the brain was done during the follow-up period after the clinical diagnosis of Parkinson's disease was made, mainly due to development of focal deficits and was found to be abnormal in 19 patients. Nine patients had infarctions, five had cerebral atrophy and five had both infarctions and atrophy. All patients received pharmacological therapy. The pharmacological agents used were levodopa and carbidopa, or levodopa and benserzide (94%), anticholinergics (72%), dopamine agonists (42%), selegeline (38%) and amantadine (33%). All the patients responded symptomatically to the therapy, at least early in the course.

During a mean follow-up period of 3.5 years, all the patients developed several complications in various combinations, such as on-off phenomenon, peak dyskinesias, wearing-off dyskinesias, freezing spells, dystonias, oro-facial dyskinesias, choreoathetosis, confusion, hallucinations and postural hypotension. In addition to these complications, which were the result of long-standing disease or the drugs or both, five (6%) patients developed bedsores and nine (11%) patients sustained fractures. All the patients with bedsores had Stage IV or V disease.

DISCUSSION

Parkinson's disease has a worldwide prevalence and is the second most prevalent movement disorder in elderly people[9]. However, it probably is an under-diagnosed disease in this part of the world (South Asia) because all of the major clinical features of the disease such as tremors, slowing of movements and gait as well as posture abnormalities, are considered as features of normal ageing by the general population. As they may never seek medical advice, the diagnosis may not be made. No epidemiological study has previously been published from Pakistan to report incidence and prevalence of the disease in this country. We identified 80 patients over a period of 11 years at a tertiary care centre but the actual number would be high as most of the patients with Parkinson's disease are managed in outpatient clinics and we were only able to retrieve records of inpatients.

Contrary to Western literature, where disease affects males and females almost equally, significant male preponderance (male:female = 1.7:1) was found in this study. This gender difference was also observed by other researchers in this country and has been attributed to the cultural rituals. This could also be a result of case ascertainment bias, however, we

believe that the difference is real. Our inference is based on results from the neighbourhing countries and overall male to female ratio of patients admitted to this institution. In China, Parkinson's disease was found to be three times more common in men[10]. An epidemiological study from India revealed that men were at increased risk of developing Parkinson's disease (odds ratio 1.98; 95% confidence interval 1.34-2.92)[11]. Over the study period (1988-1998) male to female ratio of all adult patients admitted to all medical subspecialties was 1.2:1. The reasons for the difference are not clear.

Dietary factors may be important, as dietary habits are different between genders in this part of the world, especially in the middle and lower socioeconomic groups. In these socioeconomic groups, especially in the rural areas, men would be provided with the best available diet while women would contend with whatever is available after the men and children have eaten. This discrepancy leads to provision of a relatively high protein diet to men. Only epidemiological studies can answer whether this observation is relevant to the development of Parkinson's disease or is just a coincidence. However, it has been shown that a number of heat-prepared meat and fish dishes contain variable levels of β-aromatic carbolines i.e. non-harmalins and harmalines, which are structurally similar to 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP)[12] and can potentially lead to Parkinson's disease. Age of disease onset, proportion of early onset disease and clinical features (Table II) were similar to those reported from the West[13-17].

11 (14%) patients in this series did not have tremors. Tremor-deficient disease has been reported variably from 10% to 30% of clinically-diagnosed patients in the Western literature[13] but interestingly, an autopsy series argues against it. In the series, Rajput et al found that none of the pathologically-proven patients had tremor-deficient disease[18].

Only 29% (23/80) of the patients presented within the first year of disease onset, but about three-quarters of the total study population presented within five years. The reasons for delay in medical consult are probably an insidious onset and slow progression of the disease, presumption by patients and family that the clinical features are age-related findings, and prominently non-specific symptoms early in the course.

Postural instability is the most disabling feature of the disease, which was found in 37% of patients of Hoehn-Yahr series, where the disease duration was more than five years[16]. In this series, the average duration at presentation was approximately five years and 35% of patients in this series had Stage III or more severe disease at initial visit. The severity of the disease was directly related to the duration of illness, a fact which has been observed throughout history since its first clear description by James Parkinson. We found that late onset of the disease also has a negative impact on the severity of the disease (Table IV). 13 (16%) patients had history of frequent falls and ten (77%) of them had Stage III disease. The results are compatible with the fact that this is the stage when patients are still mobile and begin to have postural instability.

Parkinson's disease is typically unilateral at onset. About 70% of patients had either predominantly unilateral disease at presentation or unilateral onset, 6% of patients had clearly bilateral onset and in 24%, a clear history regarding onset of the side of the symptoms could not be established. Dementia is not a feature of early Parkinson's disease; however, it has been found to be more common in patients with Parkinson's disease than in the general population. In a case control study, Rajput et al found that after five years of index date, a new diagnosis of dementia was made three times more commonly in patients with Parkinson's disease than in controls[19]. Similarly, other investigators also noted that dementia occurs in 20-30% of patients with the disease[20]. Because of the retrospective nature of this study, it was not possible to follow stringent criteria for dementia, but 15 (19%) of our patients were recorded to have cognitive impairment. Onset of illness in all these patients was beyond 50 years. Cognitive impairment was also more common in the patients with disease of longer duration (Table II). A similar relationship of dementia with the age of onset and disease duration was found by Aarsland et al[4].

Despite dramatic symptomatic response, the disease progressed relentlessly and the course was complicated by several complications in various combinations. These complications included various kinds of dyskinesias, unpredictable response to therapy, hallucinations, confusion, postural hypotension, aspiration pneumonias, fractures and bedsores. All the patients who developed bedsores were in Stage IV-V of the disease. Only three patients died, two from aspiration pneumonia. Since this study is limited by its retrospective nature, further details of the drug-related side effects and mortality could not be assessed. Detection of prevalence and incidence was not the objective of this study; therefore, a large-scale systematic study is required to detect prevalence and incidence of the disease in this country. We conclude that the disease exists in Pakistan and has a similar clinical profile to that reported in the West. Gender distribution is probably different from the West but is compatible with prior Asian literature. Cognitive impairment is not uncommon in patients

with Parkinson's disease and its frequency increases with disease duration and age of patient.

REFERENCES

1. Stern G. Did Parkinsonism occur before 1817? J Neurol Neurosurg Psychiatry. 1989; Suppl:11-2.
2. Lawrence IG, Jacob IS. Medical treatment of Parkinson's disease. In: Kurlan R, ed. Treatment of Movement disorders. Philadelphia: JB Lippincott, 1995: 1-57.
3. Parkinson J. An essay on shaking palsy. In: Wilkins RH, Brody IA, eds. Neurological Classics. Illinois: American Association of Neurological Surgeons, 1997: 87-92.
4. Aarsland D, Tandberg E, Larsen JP, Cummings JL. Frequency of dementia in Parkinson disease. Arch Neurol 1996; 53:538-42.
5. Ashok PP, Radhakrishnan K, Sridharan R, Mousa ME. Epidemiology of Parkinson's disease in Benghazi North-East Libya. Clin Neurol Neurosurg 1986; 88:109-13.
6. Rajput AH. Frequency and cause of Parkinson's disease. Can J Neurol Sci 1992; 19 (1 suppl):103-7
7. Bharucha NE, Bharucha EP, Bharucha AE, Bhise AV, Schoenberg BS. Prevalence of Parkinson's disease in Parsi community in Bombay, India. Arch Neurol 1988; 45:1321-3.
8. Behari M, Bhatnagar SP, Muthane U, Deo D. Experiences of Parkinson's disease in India. Lancet Neurol 2002; 1:258-62
9. Moghal S, Rajput AH, D'Arcy C, Rajput R. Prevalence of movement disorders in elderly community residents. Neuroepidemiology 1994; 13:175-8.
10. Tanner CM, Goldman SM. Epidemiology of Parkinson's disease. Neurol Clin 1996; 14:317-25.
11. Behari M, Srivastava AK, Das RR, Pandey RM. Risk factors of Parkinson's disease in Indian patients. J Neurol Sci 2001; 190: 49-55.
12. Pfau W, Skog K. Exposure to beta-carbolines norharman and harman. J Chromatogr B Analyt Technol Biomed Life Sci 2004; 802:115-26.
13. Rajput AH. Parkinsonism, aging and gait apraxia. In: Matthew BS, Kollar WC, eds. Parkinsonian Syndromes. New York: Marcel Dekker, 1993: 511-34.
14. Hoehn MM. The natural history of Parkinson's disease in the pre-levodopa and post-levodopa eras. Neurol Clin 1992; 10:331-9.
15. Gelb DJ, Oliver E, Gilman S. Diagnostic criteria for Parkinson's disease. Arch Neurol 1999; 56:33-9.
16. Henry LP, Matthew BS. Clinical manifestations of Parkinson's disease. In: Ray LW, Kollar WC, eds. Movement Disorders: Neurological Principles and Practice. New York: McGraw Hill, 1997: 183-300.
17. Parkinson Study Group. Mortality in DATATOP: a multicenter trial in early Parkinson's disease. Ann Neurol 1998; 43:318-25. Comment in: Ann Neurol 1999; 45:138-9.
18. Rajput AH, Rolzdilsky B, Arg L. Occurrence of resting tremor in Parkinson's disease. Neurology 1991; 41:1298-9.
19. Rajput AH, Offord K, Beard CM, Kurland LT. A case-control study of smoking habits, dementia, and other illnesses in idiopathic Parkinson's disease. Neurology 1987; 37:226-32.
20. Olanow CW, Koller WC. An algorithm (decision tree) for the management of Parkinson's disease: treatment guidelines. Neurology 1998; 50 (3 suppl 3): S1-S57.