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Parkinson's disease in University Hospital, Kuala Lumpur

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Abstract

Objectives: A clinical descriptive study of the Parkinson's disease (PD) patients seen in University Hospital, Kuala Lumpur (UHKL). *Methods:* The study population was the PD patients seeking treatment in the University Hospital. Interviews were done using a standard questionnaire. *Results:* 153 patients were studied. The mean age of onset was low at 56.8 years. The mean age at the time of study was 64.2 years. 20.9% were younger-onset PD (<45 years). The male-female ratio was 1:1.04. There was disproportionate number of Chinese patients with the racial composition of: Chinese (70.6%), Indians (18.3%) and Malays (9.9%). Family history in the first degree relatives was present in only 2% of cases despite a large mean number of siblings at 5.5. Slowness (82.4%) and tremor (82.0%) were the most common presenting symptoms. Motor complications was seen in 49.7% of patients with mean treatment duration of 5.9 years. The mental complications were: psychosis (8.5%), depression (8.5%) and anxiety (1.4%). There was more mental side effects among the females. The prevalence of dementia was low at 3.3 %. There was apparently a faster progression of disease among the older-onset PD as compared to the younger-onset group with shorter disease duration at similar Hoehn & Yahr stage. *Conclusion:* The PD seen in UHKL was characterised by lower age of onset with less dementia and mental side-effects. There was disproportionately high proportion of Chinese patients as compared with the Malays. Family history of PD was rare. The females were more likely to have mental-side effects. The older-onset PD has apparently a more aggressive disease.

Key words: Parkinson's disease, clinical features, Malaysia

INTRODUCTION

University Hospital is a teaching Hospital in Kuala Lumpur which serves as a community Hospital for the 3.5 million population in Kuala Lumpur and Selangor (mid-1998 population census). It is also a national tertiary medical referral centre. The racial composition of Kuala Lumpur and Selangor in 1990 consisted of Malays (43.5%), Chinese (40.1%) and Indian (15.6%). The different races in Malaysia has their own respective cultures and lifestyles. It is now held that the aetiology of PD is an interplay between genetic and environmental factors. There has been no previous published study on PD in Malaysia. This study aims to characterise PD in Malaysia, in particular to explore the role of ethnic factor in the disease.

MATERIALS AND METHODS

The study consisted of interviewing the patients currently in the PD register of the Hospital. All patients were seen by one of the study neurologists. A standard questionnaire was used to procure the information from the patients and the relatives. Questions asked included the age of onset, symptoms at onset, motor complications (motor fluctuations and dyskinesia) and mental side-effects (psychosis, depression, anxiety). The diagnosis of dementia was based on Diagnostic and Statistical Manual of Mental Disorders, DSM-III criteria. Hoehn & Yahr (HY) staging was used to grade the progress of the disease. The diagnosis of PD was based on the Ward and Gibb criteria.[1] Secondary parkinsonism and parkinsonism-plus syndromes were excluded from the study. The data were subsequently analysed statistically using Student's t test and Chi-square test.

RESULTS

Age at onset, gender and race

153 patients were included in the study. The mean age of patients was 64.2 years (SD:11.7). The mean age of onset was 56.8 years (SD 12.9). There was no difference between the sexes (males: 56.3 years, SD 12.5; females: 57.2

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years, SD 13.3, p=0.682) and ethnic groups in the mean age of onset (Chinese: 56.6 years, SD 13.0; Indians: 58.0 years, SD 14.2; Malays 55.7 years, SD 11.0, p=0.809). 20.9% of patients were younger-onset PD (age 20-45 years) and 28.8% were older-onset PD (65 years or older). The male-female sex ratio was 1:1.04 (75 males, 78 females). The racial composition was: Chinese (70.6%), Indians (18.3%), Malays (9.9%) and others 1.3%.

Family history

Family history of PD in first-degree relatives was present in 3 patients (1.96%). Two Indian patients had affected brothers while one Chinese patient had affected mother. Consanguineous marriage was seen in the parents of two Indians, one Chinese and one Malay patients (2.6%). The mean number of siblings (excluding patients) was 5.5 (SD 3.1). Only 0.2% of the siblings and 0.3% of parents had PD.

Symptoms at onset

The symptoms at onset is as shown in Table 1. The most common symptoms were slowness (82.4%) and tremor (82.0%). The mean duration of symptoms before presentation was 22.1 months (SD 21.6). There was no difference between the sexes (p=0.966) and the different ethnic groups (p=0.114) in the mean duration of symptoms before presentation.

Progress, treatment and complications

The mean HY stage for all patients was 2.4 (SD 1.1) with the mean duration of disease at 7.3 years (SD 6.2).There was no difference in HY stage and disease duration between the sexes (p=0.960, 0.563) and the ethnic groups (p=0.615, 0.134).

96% of the patients were on levodopa, half were on levodopa monotherapy while the other half also had adjuvant therapy. The mean dosage of levodopa was 472.8 mg/day (SD 270.8). There was no difference in the dosage of levodopa between the sexes (p=0.721) and ethnic groups (p=0.126). The mean duration of treatment was 5.9 years (SD 6.0). The duration of treatment was again similar between the sexes (p=0.849) and ethnic groups (p=0.186). The adjuvant drugs used were benzhexol, bromocriptine, amantadine and selegiline. The mean number of drugs given in combination was 1.7 (SD 0.7). 2% of the patients did not receive any prescribed known anti-Parkinsonism medication.

The complications is as shown in Table 2. As shown, motor complications were present in 49.7% of the patients. It consisted of motor fluctuation (49.7%) and dyskinesia (24.2%). Those with motor complications had significantly longer treatment duration (8.7 years, SD 6.5 versus 2.8 years, SD 3.3, p<0.001) and higher levodopa dose (570.7 mg/day, SD 298.4 vs 367.9 mg/day, SD 189.6, p<0.001). There was no difference in the frequency of motor fluctuation between the sexes (p=0.795) and the ethnic groups (p=0.200). Dyskinesia (37 patients, 24.2%) occurred as choreo-athetoid movement in 30 patients (19.6%) and dystonia in 7 patients (4.6%). The later occurred mainly as "off" period foot dystonia. The frequency of dyskinesia was also not different between the sexes (p=0.745) and the ethnic groups (p=0.715).

Mental side-effects occurred in 17.0% of patients consisting of psychosis (8.5%), depression (8.5%) and anxiety (1.4%). 2 of 13

TABLE 1: Symptoms at onset

Slowness	82.4%
Difficulty walking	77.1%
Difficulty writing	53.6%
Stiffness	50.0%
Tremor	82.0%
Tremor alone	12.0%
Speech difficulty	34.0%
Muscular symptoms	11.3%
Falls	11.3%
Depression	6.0%
Anosmia	5.3%
Sensory symptoms	4.7%
Weakness	4.7%

TABLE 2: Complications

Motor fluctuation	49.7%
a) end-of-dose	37.3%
b) on-and-off	8.5%
c) freezing	3.9%
Dyskinesia	24.2%
Dystonia	4.6%
Psychosis	8.5%
Depression	8.5%

TABLE 3: Comparison of mental side-effects between sexes

	Mental side-effects	Levodopa dose in mg, mean (SD)	Duration of treatment in years, mean (SD)	No. of drugs, measn (SD)	Age at time of study in years, mean (SD)
Male	8%	481 (293)	5.8 (5.4)	1.8 (0.8)	63.6 (11.3)
Female	25.6%	465 (250)	6 (6.5)	1.7 (0.7)	64.6 (12.1)
p value	<0.005	0.721	0.849	0.515	0.603

patients with depression were attributed to drugs, one each for benzhexol and selegiline. Among the 13 patients with psychosis, the cause was attributed to levodopa in 6 patients, benzhexol in 2 patients, bromocriptine and pergolide for one patient each. 10 out of 13 patients who developed psychosis were female, but the difference was not statistically significant (p=0.051). There were more mental side effects among the female as compared to male patients when all the mental side-effects (psychosis, depression, anxiety) were combined. This was true although there was no difference in the levodopa dose, duration of treatment, age at time of study and the mean number of drugs given between the two groups (Table 3). There was also no difference in the occurrence of mental side-effects among the different ethnic groups (p=0.759).

Only 5 patients (3.3%) had dementia based on DSM III diagnostic criteria. None had stroke nor other known causes of dementia.

Younger-onset vs older-onset PD

Table 4 is a comparison between 32 patients with younger-onset PD (age 20-45 years) and 44 patients with older-onset PD (age ≥65 years). As shown, although the HY stage was similar between the two patient groups, the duration of disease and the duration of levodopa treatment was much longer in the younger-onset group. The mean levodopa dose was slightly higher in the younger-onset group although it was not statistically significant. The younger-onset group was also given more drugs. Table 5 showed that there was higher proportion of younger-onset PD who developed dyskinesia. The duration of disease and duration of levodopa treatment prior to onset of dyskinesia was much longer among the younger-onset PD patients. Motor fluctuation (75% versus 20.5%, p<0.001) and mental side-effects (40.6% versus 11.4%, p< 0.005) were also more common in younger-onset PD. However, the duration of disease and duration

TABLE 4: Comparison between younger-onset and older-onset PD

	Onset 20-45 years (n = 32)	Onset ≥65 years (n = 44)	p value
M:F ratio	1:1.5	1:1.2	0.676
Presentation:			
Tremor alone	5 of 32 (15.6%)	4 of 44 (9.1%)	0.645
Bradykinesia/rigidity alone	4 of 32 (12.5%)	7 of 44 (15.9%)	
Mixed (tremor & bradykinesia/rigidity)	21 of 32 (70.0%)	31 of 44 (73.8%)	
Hoehn & Yahr stage (SD)	2.7 (1.1)	2.4 (0.8)	0.147
Duration of disease in years (SD)	11.1 (8.1)	3.9 (3.1)	<0.001
Duration of Ldopa therapy in years (SD)	8.6 (6.3)	2.8 (3.0)	<0.001
Mean Ldopa dose, mg/day (SD)	541.7 (266.6)	434.9 (220.8)	0.066
No. of drugs (SD)	2.3 (0.8)	1.4 (0.5)	<0.001

TABLE 5: Comparison of dyskinesia in younger-onset and older-onset PD

	Onset 20-45 years	Onset ≥65 years	p value
No. of patients with dyskinesia	19 of 32 (59%)	4 of 44 (9%)	<0.001
Duration of disease prior to dyskinesia, mean (SD)	7.8 years (5.2)	4 years (0.8)	<0.01
Duration of Ldopa therapy prior to dyskinesia, mean (SD)	6.2 years (4.1)	2.2 years (1.1)	<0.005

levodopa treatment prior to onset of the motor fluctuation and mental side-effects were not available.

DISCUSSION

The age of onset of PD in Western and Asian countries[2-7] published ranged from 53.5 years in Italy[2] to 70.4 years in Japan.[3] However, most studies gave the figure in the range of 61-65 years. The age of onset in our patients was 56.8 years (SD 12.91). The earlier onset of PD among our patients is likely to be due to the lower mean age of the general population in Malaysia. The mean age of Malaysian population in 1996 was 26 years. The age of onset was similar between the sexes and this was consistent with most studies.[3,6,8,9,10] There was also no difference in the age of onset between the ethnic groups. The male:female sex ratio in the published literature ranges from 1:0.5 to 1:2.4.[3-6,9,10] The male:female sex ratio in our study at 1:1.04 was within the published range.

The racial breakdown of the population in Kuala Lumpur and Selangor was: Chinese (40.1%), Malays (43.5%) and Indians (15.6%). The racial breakdown of the patients seeking treatment at the Emergency Unit of the University Hospital in 1998 was: Chinese (31%), Malays (37%) and Indians (24%). The racial breakdown of the PD patients in the University Hospital were: Chinese (70.6%), Malays (9.9%) and Indians (18.3%). Thus, there was an apparent higher prevalence of PD among the Chinese particularly when compared with the Malays. As the age of onset, duration of symptoms before presentation and disease duration were not different among the ethnic groups, the difference in racial composition could not be explained by the Chinese patients presenting themselves earlier to the Hospital and thus was over-represented in a Hospital based sample.

Familial PD has been said to occur in 6% to 24% of the PD patients.[11] Only 2% of our patients has a family history of PD with 0.2% of the siblings and 0.3% of the parents had PD. This suggests that genetic factor play a relatively minor role in the aetiology of PD among our patients. It could be argued that as our PD patients were younger than those reported in other series, some of their siblings may not be old enough to manifest the disease, thus under-estimating the number of PD cases among the siblings. Among our familial PD were two Indian patients with affected brothers and one Chinese patient with affected mother. Thus, genetic factor did not account for the higher occurrence of the disease among the Chinese.

As for the environmental toxins, none of our patients were exposed to known toxins that is known to cause Parkinson's disease. Epidemiological evidence suggests that rural living and exposure to agricultural chemicals are important etiologic factors for PD.[12] Vegetables in Malaysia have been shown to contain excessive amount of pesticides.[13] Chinese have a preference for half-cook leafy vegetables. This could have exposed them to higher quantity of pesticides than other races and may be a reason for the higher prevalence of PD among Chinese. Only 2 of our patients were farmers.

67.3% of the patients had both tremor and bradykinesia at the onset of illness. In the recent series by Hughes et al[8], 69% of the patient had tremor. In 42% of Hughes' series, tremor was the lone symptom. By comparison, 82% of our patients had tremor and in only 12% of patients, it was the lone symptom. The difference could be attributed to a high index of suspicion with early diagnosis in Hugh's series from UK, where a larger proportion of patients were diagnosed when only have bradykinesia or tremor as lone symptom.

The clinical progress based on HY staging showed that 36.8% of our patients were of stage

TABLE 6: Comparison of disease duration between UH and Hoehn.[14]

Hoehn & Yahr stage	Disease duration, years (mean)	
	UHKL	Hoehn
1	3.6	
2	6.6	9
3	8.4	12
4	9.4	13
5	15.8	18

3-5, indicating a significant health burden from the disease. Table 6 is a comparison of the mean disease duration to the various HY stage between our series and Hoehn's. As shown, the mean duration in reaching each HY stage was shorter in our patients when compared to Hoehn's series.[14] However, the mean dose of levodopa used in Hoehn's series was higher at 658mg/day (SD 352.5) as compared with 473mg/day (SD 270.8) among our patients. The shorter mean duration in reaching each HY stage among our patients could thus be due to less aggressive treatment although a more aggressive disease could not be excluded. It has been said that over 50% of patients developed motor problems after 2-5 years of treatment.[15] Half of our patients (49.7%) had motor complications with a mean duration of treatment of 5.9 years. The less aggressive treatment with lower dosage of levodopa used could again be the explanation for the lower frequency of motor complication among our patients. The similar dosage of levodopa and mean duration of treatment in both sexes and the different ethnic groups among our patients suggest that there is no difference in the progression of the disease between the sexes and the different ethnic groups.

Psychosis was said to occur in 10-50% of PD patients[16] and depression in 40-60%.[17] Dementia, advanced age , premorbid psychiatric illness and high levodopa dose was said to predispose to psychiatric adverse effects.[17] Psychosis (8.5%) and depression (8.5%) were less commonly seen among our patients. This could be due to younger age of PD population and lower dosage of levodopa used. Diamond[9] and Hughes[8] reported that age of onset, progression of disease and motor complications were not different between the sexes. Our results was consistent with this. However, we found mental side-effects occurred more frequently among the females. This may be related to a higher prevalence of neurosis and psychosis among females in rural Malaysia.[18]

The prevalence of dementia in PD varies depending on the diagnostic criteria used. Mayeux et al[19] estimated the prevalence of dementia to be 10.9% based on DSM III criteria. As the prevalence of dementia increases with advancing age, the low prevalence of dementia among our patients could also be due to the younger mean age of our PD population.

When the older-onset PD was compared to the younger-onset PD, the duration of disease was shorter for reaching a similar disease severity according to the HY staging (11.1 years versus 3.9 years). This suggested a more aggressive disease among our older-set PD patients. This was similar to findings by Pederzoli et al[2] who suggested that ageing aggravated the degenerative process in PD. However the difference could be distorted by the younger-onset patients being given more drugs (2.3 vs 1.4) and higher dosage of levodopa (541.7mg vs 434.9mg daily). This reflected the extra caution practised by neurologists when treating the older-onset PD in order to minimise side-effects.

Dyskinesia was reported by some authors to be more common in younger-onset PD[2,20,21] but not by others.[22] The occurrence of dyskinesia is said to be dependent on the dosage and duration of levodopa therapy.[14] Although there were more patients with dyskinesia among our younger-onset PD patients as compared to older-onset PD (59% vs 9%), the duration of disease and levodopa therapy prior to dyskinesia was significantly longer among our younger-onset PD patients. This was despite the larger number of drugs and higher dosage of levodopa given among the younger-onset patients. Thus our study did not support a more common occurrence of dyskinesia among the younger-onset PD patients. The higher frequency of mental side-effects among our younger-onset PD could also be due to the larger number of drugs and higher dosage of levodopa used.

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