Time interval to definite diagnosis of Parkinsonism

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Background
Parkinsonism is a clinical syndrome characterized by tremors rigidity, bradykinesia, and postural instability. Over the past decade there has been an increasing recognition of the broad clinical presentations of the neurodegenerative forms of Parkinsonism. Nonmotor symptoms in these diseases, including psychiatric, cognitive, autonomic, and gastrointestinal dysfunction, appear to have a major impact on quality of life and disability.

Aim of the study
The aim of this study is to detect the time lapse till definite diagnosis of Parkinsonism and possible etiologies and social factors that cause prolongation of that time in a hospital based study.

Patient and methods
We studied 80 patients with definite diagnosis of parkinsonism with specific questionnaire designed to detect the cause of delayed diagnosis applied for two weeks on a sample of patients in our department.

Results
Median time from the first symptom till the first medical contact was 4 months with range between 1 and 12 months. It was noticed that duration from the first medical contact till definite diagnosis was significantly shorter in those who had neurological consultation as the first contact.
Time interval till first contact and time interval till definite diagnosis were significantly lower in males than females [7 (1–29) vs. 12 (1–45) months].

Conclusion
Patient knowledge about Parkinsonism plays a major role in early diagnosis; most patients did not immediately recognize that their symptoms could be part of a disease.
Attending non-neurological doctors plays an important role in late diagnosis.

Keywords:
delayed diagnosis of Parkinsonism, Parkinsonism, Misdiagnosis of parkinsonism

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Introduction

Neurodegenerative diseases such as Parkinson's disease (PD) are incurable debilitating disorders that affect approximately 30 million people worldwide [1].

Parkinson's disease (PD) is now recognized as a multisystem disorder with motor and non-motor features [2]. Some motor and non-motor features are prodromal symptoms: symptoms that are already present before the onset of the typical motor signs of PD [3]. Patients seem to have prodromal symptoms years before they are diagnosed with PD [3-5].

Unfortunately, epidemiological studies have shown that between 12 and 78% of PD cases are undiagnosed which may occur if individuals under-report relevant symptoms [6, 7].

Patients and methods

This study is a cross-sectional hospital based study that was conducted at Neurology and Psychiatry Department, Assiut University Hospitals between 1 June 2016 and 31 May 2017 [8,9].

Eighty patients with definite diagnosis of Parkinsonism and presented at Inpatient Department and Out-Patient Neurology Clinic of Assiut University Hospitals were included in the study.

All patients received a description of the study and they were informed about the purpose, benefits, and risks.

Informed consent was obtained from each participating patient.

Inclusion criteria

(1) Patient with definite diagnosis of Parkinsonism relying on the presence of tremors, rigidity,

bradykinesia, and postural instability [10]
(2) Both male and female sex whether educated or noneducated, employed, or nonemployed were taken for this study.

Exclusion criteria

(1) Tremors rather than Parkinsonian tremors: orthostatic tremors, physiological tremors, and senile tremors [11]
(2) Severely demented patients
(3) Multiple etiologies
(4) Lack of caregiver regarding history.

Data collection

Systematic history

(1) Type and date of first motor symptom
(2) Date of first physician consultation about symptoms
(3) Time of definite diagnosis
(4) Date of first neurologist visit
(5) Family history of any relative diagnosed with Parkinsonism.

Dates were recorded to the month.

Scales

(1) Unified Parkinson's disease rating scale (UPDRS)
The UPDRS is a six part rating scale, which is frequently used to measure severity of Parkinsonism. It includes sections evaluating mentation, behavior, and mood (Section I: total four questions), subjective patient report of limitations on specified activities of daily living and Parkinsonian features (Section II: 13 questions), motor examination with clinician rated severity of motor features (Section III: 14 questions) [12]
(2) Modified Hoehn and Yahr scores:
The Hoehn and Yahr [13] stage is rated from 0 to V, based on distribution of Parkinsonism (unilateral, bilateral, and axial involvement), postural stability, and disability.

Specific questionnaire designed to detect the cause of delayed diagnosis applied for 2 weeks on a sample of patients in our department

(1) Type of first contact (neurologist, other specialty)
(2) Type of second contact (neurologist, other specialty)
(3) Type of first symptom
(4) First informed diagnosis
(5) Time of definite diagnosis
(6) Type of physician that reached the definite diagnosis
(7) Investigations done (cranial, extracranial)
(8) Type of treatment received (specific or not)
(9) Compliance on treatment
(10) Patient knowledge about his illness.

Statistical analysis

Data were collected and analyzed using Statistical Package for the Social Science (version 20; IBM, Armonk, New York, USA). Continuous data were expressed in form of mean ± SD or median (range) while nominal data was expressed in form of frequency (percentage).

χ^2 test was used to compare the nominal data of different groups in the study while Student's *t* test was used to compare mean of different two groups in case of normally distributed data. Correlation between duration till diagnosis and UPDRS score was done by Pearson's correlation. *P* value was significant if less than 0.05.

Table 1 Demographic data of the studied patients

Demographic variables	Frequency	Percentage
Age, range (years)	58.07±13.90 (31-82)	
Sex		
Male	49	61.3
Female	31	38.7
Level of education		
Illiterate	20	25
Primary school	16	20
Secondary school	19	23.8
University or above	25	31.3
Occupation		
Farmers	23	28.6
Employee	30	37.5
House wife	21	26.3
Retired	4	5
None	2	2.6
Residence		
Assiut	33	41.3
Sohag	29	36.3
Minia	9	11.3
Qena	4	5
New Valley	3	3.8
Aswan	2	2.6
Smoking		
Yes	17	21.3
No	63	78.8
Handedness		
Right	74	92.5
Left	6	7.5
Comorbidities		
Diabetes mellitus	4	5
Hypertension	4	5
Diabetes mellitus and hypertension	3	3.8
Chronic obstructive pulmonary disease	3	3.8
Osteoarthritis	2	2.5
Cervical disc	11	13.75

Data was expressed in form of frequency and percentage with exception of age in form of mean±SD.

Ethical consideration

(1) Review the proposal will be carried out before starting data collection via the Ethics Committee Faculty of Medicine
(2) Privacy and confidentiality of all the information will be assured
(3) The aim of the study will be explained to each participant before filling the questionnaires. Informed consent will be obtained from those who welcome to participate in the study.

Results

Patients' knowledge about his illness

Based on patients' knowledge, delayed medical consultation may be attributed to one or more of the following (Table 1):

(1) Patients did not immediately recognize that their symptoms could be part of a disease; presented in 25 (31.25%) patients in the current study
(2) Patients found an alternative explanation for their symptoms (aging, anxiety, general weakness, etc.); presented in 16 (20%) patients
(3) Patients adapted their lifestyle to relieve their symptoms; presented in 15 (18.5%) patients
(4) Previous negative experiences in the communication with health care providers and they tried with traditional medication; presented in 13 (16.25%) patients
(5) Patients feared of the diagnosis; presented in five (6.25%) patients
(6) Patients only knew what advanced Parkinsonism looked like, based on information from books or television and not taken early Parkinsonian features into consideration; presented in three (3.75%) patients
(7) Patients identified their symptoms as a disease or even as Parkinsonism; presented in three (3.75%) patients.

It was noticed that duration from the first medical contact till definite diagnosis was significantly shorter in those who had neurological consultation as the first medical contact ($P = 0.02$) (Tables 2-5).

Table 2 Frequency of medical visit and time interval till definite diagnosis (in months)

	Median (range)
Number of medical contact till definite diagnosis	2 (1-3)
Time interval from first symptom to first contact (months)	4 (1-12)
Time interval till definite diagnosis (months)	11 (1-45)

Table 3 Time interval till the first contact and the time interval till definite diagnosis from the first complaint in both sexes

	Males (*n*=49)	Females (*n*=31)	*P*
Age at first complaint (years)	50 (20-70)	50 (30-80)	0.26
Time interval till first contact (months)	3 (1-12)	6 (1-12)	0.02
Time interval till definite diagnosis (months)	7 (1-29)	12 (1-45)	0.03

Table 4 Time interval till definite diagnosis based on first symptom

First symptom	Median (range)
Tremors	8 (1-45)
Abnormal gait	9 (3-19)
Rigidity	8 (3-19)
Bradykinesia	8 (1-12)
Dysarthria	7 (1-24)
P	0.09

There was no significant difference regarding duration till definite diagnosis in different varieties of first symptom (*P*=0.09).

Table 5 Type of first contact and time interval till the definite diagnosis

	Neurological consultation (*n*=48)	Non-neurological consultation (*n*=32)	*P*
Duration till definite diagnosis from the first contact	4 (1-16)	8 (6-28)	0.02

Data was expressed in form of median (range). *P* value was significant if less than 0.05.

Discussion

The pathway to the diagnosis of Parkinsonism can be divided into three time intervals: recognition of the symptoms by the patient or his caregiver, the decision to seek help and the process of diagnosing Parkinsonism. Impeding and stimulating factors concerning the patient, the health care provider, and the disease itself can influence each of these time intervals.

According to the model of Walter *et al.* [14], the intervals of the pathway to diagnosis are influenced by patient, health care provider, and disease-related factors.

Patient-related factors

Many factors which are patient related are responsible for delayed medical consultation in the patients with Parkinsonism.

Patient knowledge about Parkinsonism plays a major role. Most patients did not immediately recognize that their symptoms could be part of a disease, and others had alternative explanations for the symptoms as a common illnesses (aging [15], inflammation of joints, general weakness). Although in considerable percentage of patients, they thought that symptoms were due to anxiety, depression [15], or dramatizing.

Our study showed that the patient's attitude toward health care providers, influenced by their previous experiences or even their family members or friends, can

also influence the decision to seek help. Some patients mention they are hesitant to present their nonspecific symptoms to their general practitioner, afraid they might be seen as somatizers. This is in line with earlier research that showed that patients carefully consider when to consult their general practitioner and are concerned about going with nonspecific symptoms [16–19].

With regarding sex differences, we observed a significant difference in the time to first medical consultation in men (3 months) compared with women (6 months) and so, the duration till definite diagnosis 7 (1–29) versus 12 (1–45) months in males and females, respectively [Table 3].

Saunders-Pullman *et al.* [20] found that the expected duration from onset of symptom to movement disorder specialist visit for women was 61% greater than for men ($P = 0.003$) in the unadjusted model.

It was proposed that women experience disease onset later because they have a slower preclinical course but do not differ significantly once Parkinson's disease is present [21].

It has been postulated that the milder early progression may be due to hormonal benefits that are most prominent early in a woman's life but decrease postmenopausal [22,23].

Moreover, nonspecific or nonmotor Parkinson's disease symptoms such as muscle pain or depression may be prominent, and hence misdiagnosed, for longer periods of time in women [24].

Health care provider-related factors

In our study, the median time from the first symptom onset (as recognized by the patient or his caregiver) till the first medical contact was 4 months with range between 1 and 12 months while median time for definite diagnosis of Parkinsonism from the first complaint was 11 month with range between 1 and 45 months. This could be explained by significant difference in duration till definite diagnosis based on the type of first medical contact where median duration was 4 (1–16) months in case neurological consultation and 8 (6–28) months in case of non-neurological consultation (40% of patients) (Table 5).

In our study, we found that most patients who were in contact with neurologist as the first medical consultation (48 patient), were diagnosed with Parkinsonism in the first visit (44 patients, 91.6%) and others had been diagnosed in the second or third neurological visit.

Although in case of non-neurological consultation as the first medical contact (32 patient) time wasted either in unneeded investigations [in 48 (60%) patients, physicians recommended extracranial investigations whereas in 10 (12.5%) patients cranial investigations were ordered] or the diagnosis could be missed without referral to neurologist [chronic fatigue was the diagnosis obtained in (12.5%) of patients, stroke (8.75%), cervical disc (13.75%), osteoarthritis (2.5%), and anxiety disorder (2.5%)].

In this group of patients, all of them sought another medical consultation with lack of response of the nonspecific medication and progression of symptoms, and definite diagnosis of Parkinsonism in the second or third visit with neurologist had been done.

Even in case of neurological consultation as the first medical contact, median duration for diagnosis was 4 (1–16) months (taking into consideration that varying duration till second or third neurological visit) and there was no significant difference regarding duration till definite diagnosis in different varieties of first symptom (that was mainly motor).

This can be explained by an absence of diagnostic test for Parkinsonism, and the therapeutic diagnostic test (Dopaminergic challenge test) is rare to be used in our locality.

Disease-related factor

Disease-related factors are of influence on the diagnostic pathway, in particular on the decision to seek help. Since most prodromal symptoms of Parkinsonism are not acute or life threatening, patients can decide to postpone seeking help and making adaptations in lifestyle to relieve the hinder and the restrictive influence on daily life. Early gait dysfunction, for example, can be subtle and nonspecific, often attributed to normal ageing or medical conditions such as osteoarthritis [25].

We found that patients are more inclined to seek help when their symptoms become worse or do not recover spontaneously. However, this requires patients who are aware of bodily changes and are capable to carefully monitor their symptoms [26].

On the other hand, nonmotor symptoms including constipation [27], sleep disturbances [28], and mood changes and anxiety [29] that may be the earliest harbingers of disease, an absence of diagnostic test for parkinsonism, and the therapeutic diagnostic test (Dopaminergic challenge test) is rare to be used in our locality, doctors even specialists may find difficulty in suspecting Parkinsonism.

Conclusion

(1) The pathway to the diagnosis of Parkinsonism can be divided into three time intervals: recognition of the symptoms, the decision to seek help and the process of diagnosis
(2) Patient knowledge about Parkinsonism plays a major role; most patients did not immediately recognize that their symptoms could be part of a disease
(3) It was noticed that duration from the first medical contact till definite diagnosis was significantly shorter in those who had neurological consultation as first contact than those who had non-neurological consultation
(4) Nonspecific symptoms of Parkinsonism, slow progression of the disease, symptoms are not acute or life threatening and absence of diagnostic test also attribute to delayed diagnosis of Parkinsonism
(5) With regarding sex differences, we observed that it took women longer duration from onset of symptoms to medical consultation compared with men and so, the duration till definite diagnosis with Parkinsonism.

Recommendations

In order to facilitate an earlier diagnosis of Parkinsonism which enables shared decision making between patients and health care providers, educating general population and even general practitioners on possible prodromal symptoms of Parkinsonism should be considered.

The image of Parkinsonism, as it is spread by the media, has to be modified from the classic image of the old man with advanced symptoms to a more complete representation of the disease.

Ideally, we need reliable biomarkers capable of diagnosing Parkinson's disease in the premotor phase, but until they exist we will continue to rely on the timely identification of motor symptoms in the community.

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Conflicts of interest

There are no conflicts of interest.

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