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Clinical and neuropsychological profile in idiopathic parkinson's disease: About an Algerian hospital series

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Abstract:
Background:
Parkinson's disease (PD) is a common neurodegenerative disorder. It has not been well studied in Algeria.
Objectives: *To identify the clinical, neuropsychological and neuropsychiatric profile of Algerian patients with PD.*
Materials and Methods: *Retrospective study in the neurology department of the specialized hospital establishment (EHS) of ALI AIT Idir, between January 2015 and March 2022.The diagnosis of idiopathic PD was made according to the Brain Bank criteria of the UK-PD Society . The clinical characteristics of 80 patients with PD were obtained from their medical records. These records were carefully reviewed with the following data: age, sex, history, education level, age of onset of symptoms and age of diagnosis, signs of onset, associated motor and non-motor signs, cognitive and psychiatric assessment, stage of the disease as well as therapeutic data with their complications.*
Results:
In this cohort, 34 (42.5%) were men and 46 (57.5%) were women. The mean age of onset of the disease was 56.61 ± 12.76 years. Family history of PD was present in 8 patients (10%). The mean score of the UPDRS (motor section) in off was 19 .5 ± 9.08 and the mean score of the modified Hoehn and Yahr scale was 2.36 ± 0.89. The most frequent non motor manifestations were bowel and sleep disturbances. Cognitively, 55 patients (68.75%) had mild cognitive impairment and psychiatrically, 66.18% had depression and 69.70% had anxiety. Therapeutically, 71 patients (88.75%) were on L-dopa (mean dose 420 ± 208,27). The complications of the treatment were dominated by akinesia at the end of the dose (45.07%) and dyskinesias at the beginning and end of the dose (28.17%).
Conclusion:
The profile of our patients was similar to that of other populations. Non-motor signs such as sleep disorders, intestinal disorders as well as depression, anxiety and cognitive deficit are common.
Key words: *Parkinson's disease, Mild cognitive impairment, Depression, Anxiety*

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I. Introduction

Parkinson's disease is the second most common degenerative disease after Alzheimer's disease. Its increasing prevalence gives it a growing socio-economic weight. Worldwide, the number of cases of PD has been estimated to be nearly 9.4 million in 2020, a figure significantly higher than the 6.1 million cases previously reported in 2016. [1].

The incidence of Parkinson disease has been estimated to be 4.5-21 cases per 100,000 population per year, and estimates of prevalence range from 18 to 328 cases per 100,000 population, with most studies yielding a prevalence of approximately 120 cases per 100,000 population. [2.] The frequency of PD is 2 to 5 times higher in industrialized countries than in developing countries.[3]. Generally, the lowest prevalences are observed in Eastern and African countries, while the highest prevalences are in Western countries and Caucasian subjects. Exceptions are Denmark and Sweden, which have low prevalences .[3].

In Africa, it seems that the disease is more frequent in North Africa than in sub-Saharan Africa [4]. In Algeria, PD is becoming increasingly prevalent [5], with nearly 24,250 patients estimated in 2016[4]. Yet, very little work has been done on the disease [5].

This study was designed to provide the demographic and clinical profile of PD in the patients of the EHS of ALI AIT IDIR in Algiers.

II. Material And Methods

We present a retrospective and descriptive study, carried out in the neurology department of the EHS of Ali Ait Idir in the Casbah of Algiers. The study focused on 80 medical records of patients with PD, who were hospitalized during the period from January 2015 to March 2022 at the EHS of Neurosurgery Ali Ait Idir (Algiers).

We included in our study all patients, regardless of age, with diagnosed PD with a fairly complete record archived at the institution. However, patients with Parkinson's syndrome or other neurodegenerative pathologies than PD were excluded from the study.

In these patients the diagnosis of PD was based on the United Kingdom Parkinson's disease Society Brain Bank diagnostic criteria [6].Our exploitation of the different parameters from the patient's medical records allowed us to collect sociodemographic, clinical, paraclinical, neuropsychological, evolutionary and therapeutic data.

1-Sociodemographic data:

For each patient, we collected the following information: Age at onset of symptoms, Age of diagnosis, Sex, Personal medical history, Similar cases in the family, Consanguinity, Profession, Educational level of the patients and Time interval between the onset of symptoms and the diagnosis of PD.

2- Clinical data:

In addition to the different forms of the disease which are: The mixed form (akineto-rigid and tremor), the akineto-rigid form and the tremor form, we have collected all the motor and non-motor signs observed in the patients including the inaugural signs of the disease without forgetting the complications of the disease.

Motor signs: including the three major signs: tremors, akinesia and rigidity, as well as other signs such as: swallowing disorders (hypersalivation), walking disorder (walking with small steps), the notion of falling, postural instability, frezzing, speech disorders and micrography.

Non-motor signs: For each patient, non motor symptoms of PD were systematically sought, including: Sleep disorders (insomnia, early or nocturnal awakenings, sleepwalking, acted dreams and nightmares, inversion of the nycthemeral rhythm.), digestive disorders (mainly nausea and constipation), olfactory disorders (such as hyposmia), sexual disorders (loss of libido and impotence), urinary disorders (incontinence, urinary urgency), pain, fatigue, weight loss and hypersudation.

Complications of the disease: Represented mainly by visual and auditory hallucinations and dyskinesias, the most common forms of which are choreic, dystonic and ballic movements.

The stage of the disease was determined by the by the Hoehn and Yahr scale **and the severity and progression of PD** was measured by the Movement Disorders Society- Unified Parkinson's Disease Rating Scale Section III (MDS-UPDRS).

3-Neuropsychological data: Patients were evaluated neuropsychologically during the medication phase (ON) according to their level of education in order to look for the presence of a dysexecutive syndrome with disorders of planning, mental flexibility, programming, susceptibility to interference and loss of inhibitory control, as well as other cognitive impairment such as disorders of short-term and long-term memory, attention and visuospatial functions.

The level of education was determined according to the Barbizet scale which distinguishes between subjects with a low level of education (EL<3) "illiterate and self-taught" and subjects with a medium or high level of education having at least the primary school certificate (EL ≥).

Cognitive impairment were investigated by a battery of neuropsychological tests including:

-For a Global Cognitive Assessment, the MMSE "Mini Mental State Exam", the MMP "Mini Mental Parkinson" and the MOCA "Montreal Cognitive Assessment**"**.

-For the Assessment of Executive Functions, the Frontal Assessment Battery (FAB). It is a tool for assessing frontal executive functions (executive and motor components) in a single instrument, namely Conceptual Elaboration, Mental Flexibility, Environmental Autonomy, Programming, Interference Sensitivity and Inhibitory Control.

-**For attention and visuo-spatial selective attention**, the Barrier Test. Divided attention was assessed by the Trail Making Test (TMT) A and B.

-**For the evaluation of verbal episodic memory**, the nine image test (TNI-93).

-**For the evaluation of categorical verbal fluency**, the ISAACS Set Test.

-**For the impact of cognitive impairment on activities of daily living,** the instrumental activities of daily living (IADL).

4-Neuropsychiatric data: Assessment of affective and emotional disorders was done by Hamilton - Depression and Hamilton - Anxiety.

5- Statistical analysis:

All statistical analyses were conducted with the Graph Pad 9.0.0 software (Graph Pad Inc).

Categorical variables were compared using the chi-square statistical test. The threshold for a difference was set at $p<0.05$.

III. Results

1- Demographic data:

During the study period, 80 patients admitted to the neurology department of the EHS Ali Ait Idir, presented characteristics compatible with PD: 34 men (42.5%) and 46 women (57.5%) aged 35 to 85 years. However, this difference was not statistically significant (ns, p=0.2185, khi deux test) (Cf.Table1).

The mean age of onset of the disease in our cohort was 56.61 ± 12.76 years. These patients were divided into 3 categories according to the age of disease onset:

The early form with an age of onset between 20 and 40 years. This group includes 10 patients (12.5%). The common form, the most common with an age of onset between 40 and 60 years includes 41 patients(51.25%) and the late form with an age of onset greater than 60 years includes 29 patients (36.25%). We did not find any juvenile form with an age of onset less than 20 years. 8 patients (10%) had a family history of PD.

Mean interval between symptoms and diagnosis of PD: 1.46 ± 1.35 years. 24 patients (30%) had consulted 2 years or more after the onset of symptoms.

The distribution of PD patients according to cultural level and in particular the number of years of education, revealed that 60 patients namely 75 % have a low cultural level, in contrast to 20 patients (25%) who have a medium or high level of education. The average number of years of education of the patients was 4.22 ± 5.78 years (0-17).

66 patients (82.50%) had associated pathologies, a fairly high percentage compared to patients with no concomitant pathologies (17.50%) (n=14). They were mainly represented by hypertension found in 31 patients (38.75%) and diabetes in 15 patients (18.75%).

Table n° 1: Demographic data

Demographic characteristics of the sample		N=80
Age (Years) Mean		62,25 ± 12,03
Sex- n(%)	**Men**	34 (42.5 %)
	Women	46 (57.5 %)
Sex ratio women men		1,35
Age of onset (years) - mean ±SD		56.61± 12.76
Age of onset ≥ 60 years		29 (36,25 %)
Age of onset between 20 and 40 years		10 (12.5 %)
PD duration (years) - mean ±SD		5.68±5.25
Years of education - average		4,22 ± 5,78 (0-17)
Educational Level (EL) < 3		60 (75%)
Educational Level (EL) ≥3		20 (25%)

2-Clinical Data:

Main symptoms of disease onset were represented by Rigidity or bradykinesia (46 cases: 57.5% of cases) . Tremor as a sign of onset found in 34 cases (42.5 % of cases).

The clinical picture in the state phase was dominated by mixed forms (Trembling with rigidity and bradykinesia): 43 cases (53.75 %), followed by akineto-rigid forms: 23 cases (28.75 % of patients) and trembling forms: 14 cases (17.5% of patients).This predominance is statistically significant, ****, p=0.0001, Chi-square test.

As for the non-motor signs, we notice within our cohort, the predominance of sleep disorders and digestive disorders, found in more than 50% of the patients (63.75% and 51.25% respectively), followed by urinary disorders from which 37.5% of the patients suffer (Cf.Table 2).

Table n° 2: Non-motor signs of PD

Non -motor signs	**N=80**	**%**
Hyposmia	18	22.5
Sleep disturbances	51	63.75
Digestive disorders	41	51.25
Vesicosphincterian disorders	30	37.5
Hypersudation	18	22.5
Sexual disorders	8	10
Pseudo-rheumatic pain	23	28.75
Visual hallucinations	8	11.27

The classification of the patients according to the Hoen and Yarh scale made it possible to distinguish a predominance of stage 2 (n=28) with a percentage of 35%, compared to the other stages of the disease: stage 1 (n=11) 13.75%; stage 1.5 (n=2) 2.5%; stage 2.5 (n=16) 20%; stage 3 (n=16) 20%; stage 4 (n=4) 5% and stage 5

(n=3) 3.75% (Cf. Table3).Statistical analysis showed that this predominance of stage 2 over the other stages was highly significant, ****, p <0.0001, chi-square test.

Table n° 3: Stage of Hoen and Yarh of Parkinson's disease

Parkinson's disease stage	**N=80**	
Hoehn & Yahr - n(%) **(Scores 1-5)** **(Slight- Grabber)**	1	11 (13.75 %)
	1.5	2 (2.5 %)
	2	28 (35 %)
	2.5	16 (20 %)
	3	16 (20 %)
	4	4 (5 %)
	5	3 (3.75%)
Average stage of the disease according to the H&Y scale	2,36 ± (0,89)	
Section III of the MDS-UPDRS scale **Motor UPDRS - average (OFF)**	19 .5 ± 9.08 (4 - 40)	

Drug therapy was initiated in 88 , 75% of patients with a mean dose of 420 mg ± 208, 27 and a mean duration of 4.61 years ± 4.52. The main complications were fluctuations in efficacy in the form of end-of-dose akinesias in 45.07% of cases and dyskinesias (33.80%), in particular dyskinesias at the beginning and end of doses (28.17%). Mid-dose dyskinesias were observed in 5.63% of cases (see Table 4). The number of patients with complications was significantly higher in those with >10 years of disease progression compared to those without, *, p= 0.0391, chi-square test.

Table n°4: Dopa therapy and complications

Features	**N =80**	
Dopa therapy	71	88 , 75%
Average dose Dopa therapy (mg)	420 ± 208, 27	
Average duration of Dopa therapy (Years)	4,61 ± 4,52	
Dyskinesias	24	33,80 %
Early - Late Dose Dyskinesias	20	28,17 %
Mid-dose dyskinesias	4	5,63 %
Fluctuations in efficacy End-of-dose akinesia	32	45,07 %

3- Neuropsychological evaluation:

The neuropsychological evaluation revealed that 55 patients (68.75%) had mild cognitive impairment (PD-MCI) and 25 patients (31.25%) did not. This difference is statistically highly significant, ****, p<0.0001, chi-square test. The cognitive deficit involved one cognitive domain in 12.5% of cases and multiple cognitive domains in 56.25% of cases. The cognitive deficit involved one cognitive domain in 12.5% of cases and multiple cognitive domains in 56.25% of cases.

The global cognitive evaluation showed a cognitive deficit on the MMSE, the MMP and the MOCA.

The MMSE evaluation according to the level of education showed a more frequent deficit in subjects with a low cultural level (66.67%) than in those with an average or low cultural level (10%) (see Table 5). This difference is statistically significant, *, p=0.0215.

Cognitive deficits were dominated by attention disorders found in 56.06% of cases (n=37/66), followed by executive function disorders in 45.76% of cases (n=27/59). Memory evocation disorders were found in 39.39% of cases (n=26/66) and a decrease in verbal fluency in 18.18% of cases (12/66).

Table n° 5: Neuropsychological evaluation

Cognitive Scales	**N=80**	**Score**
MMSE -mean ±S D	19 (23,75 %)	24,10 ± 4,84
MMSE pathological	7 (36, 84 %)	18,5 ± 3,3
MMSE Normal	12 (63,16 %)	27, 33 ± 1,84
MMSE (<CL 3)	9 (47,37 %)	22 ± 4,57
	6 (66,67 %)	
MMSE < 22	3 (22,23%)	
MMSE ≥ 22		
MMSE (≥ CL3)	10 (52,63 %)	26 ± 4,27

MMSE < 26 **MMSE ≥ 26**	1 (10%) 9 (90%)	
MMP -moyenne ±S D	36 (45%)	26,47 ± 5,13
MMP <29 pathological **MMP ≥ 29 Normal**	19 (52,78%) 17 (47,22 %)	22,79 ± 4,47 30, 5 ± 1,84
MOCA - mean ±SD **MOCA Classification - n(%)** **< 26 (With cognitive impairment)** **≥ 26 (Without cognitive impairment)**	7 (8,75%) 2 (28.57%) 5 (71,43%)	23,14 ± 8,11 20,8 ± 8,5 28,86 ± 2,88
FAB - mean ±SD **FAB Classification - n(%)** **≥ 15 (Without cognitive impairment)** **< 15 (With cognitive impairment)** **Conceptualization disorder** **Mental flexibility disorder** **Environmental Autonomy Disorder** **Programming disorder** **Loss of inhibitory control**	59 (73,75 %) 32 (54,24%) 27 (45.76%) 11 (40,74%) 16 (59,26%) 9 (33,33%) 26 (96,30%) 21 (77,77%)	Total 14 ± 3,69 16,78 ± 1,17 10,57 ± 2,88

No significant correlation was found between the age of onset of the disease and cognitive deficits on the MMSE and/or FAB (p= 0.248). On the other hand, a close and significant correlation was observed between the duration of the disease and the global cognitive deficit observed on the MMSE (P-Value < 0.00001) (Cf.Figure1). The highest MMSE scores were observed at the beginning of the disease. As the disease progressed, the MMSE score was lower.

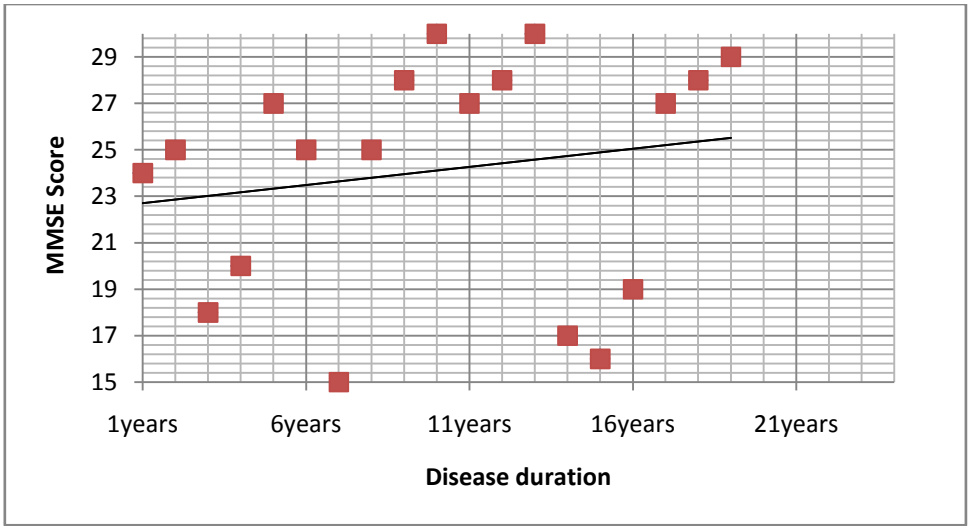

Figure n° 1: Correlation between MMSE total score and disease duration (years).

This significant correlation was also observed between the duration of the disease and the FAB score (P-Value <0.00001 , which were higher at the beginning of the disease (Cf. Figure 2).

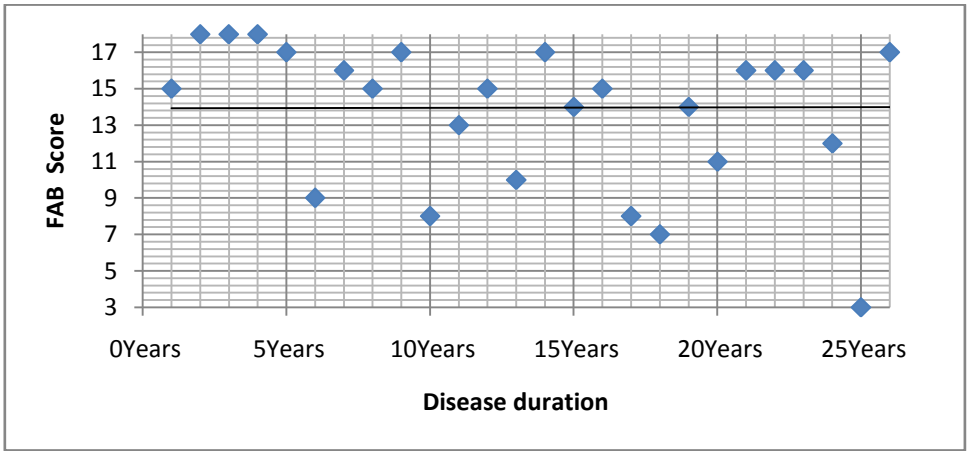

Figure n°2: Correlation between MMSE total score and disease duration (years).

4-Neuropsychiatric evaluation:

66.18% (n=45/68) of the PD patients had depression, whereas the 43.75% (n=35/68) were free of depression. Statistical analysis revealed no significant difference between the two groups, p=0.3143, chi-square test (see Table 5).

Among the 45 patients with depression, 51.11% (n=23) had mild depression, 40% (n=18) had mild to moderate depression and 8.89% (n=4) had a very significant difference between the different groups, ***, p=0.0004, chi-square test (Cf. Table 5).

Regarding the anxiety factor in the PD patients in our cohort, the rates were almost similar to those of depression with 69.70% (n=46/66) of patients with anxiety and 30.30% (n=20/66) without with no significant difference between the two groups, ns, p=0.2185, Chi-square test (Cf.Table 5).

Among the 46 patients with anxiety, 41.30% (n=19) had mild anxiety, 43.48% (n=20) had mild to moderate anxiety and 15.22% (n=7) had moderate to severe anxiety and 23.91% (n=11) . Statistical analysis revealed no significant difference between the different groups, ns, p=0.4060, chi-square test (Cf.Table 5).

Table n° 5: Neuropsychiatric evaluation

Neuropsychiatric Scales	**N=80**
Hamilton Depression Scale	**68 (85%)**
Normal	**23 (33,82%)**
Present depression	**45 (66,18%)**
Mild depression	**23 (51,11%)**
Mild to moderate depression	**18 (40%)**
Moderate to severe depression	**4 (8,89 %)**
Hamilton Anxiety Scale	**66 (82,5%)**
Normal	**20 (30,30%)**
Present Anxiety	**46 (69,70%)**
Mild Anxiety	**19 (41,30%)**
Mild to moderate anxiety	**20 (43,48%)**
Moderate to severe anxiety	**7 (15,22%)**

IV. Discussion

In our cohort, we observed no statistically significant difference in the frequency of occurrence of PD between men and women. Our results agree with those of de Rijk and al [7]. PD appears to be slightly more common in men than in women in most studies, usually ranging from a 1.2:1 ratio up to a 1.5:1 ratio.

The mean age of onset of PD in our cohort was 56.61 ± 12.76 years, a smaller mean age of onset than that reported in the literature, which is approximately 60 years [8].The age range of]40-60] years, representing the common form of the disease, includes the largest number of patients. Our results are thus comparable to those of Defebvre and colleagues [9], reporting that the disease is rare before 40 years of age and more rarely starts after 80 years of age.

Clinically, a predominance of the mixed form (53.75%) was observed in our results. This is in line with what was reported in a Russian study in 2004 [10], which found a marked predominance of the mixed and akineto-rigid forms. Note that several studies report instead the marked predominance of the akinetic-rigid form [11], or even the tremor form [12].

Sleep disorders are the most frequent non-motor signs found in our study (63.75% of patients suffer from them). This is in line with what has been reported in the literature. These disorders have a negative impact on the daily life of patients. They are expressed by insomnia, nightmares, early awakenings, delays in falling asleep or even by the inversion of the nycthemeral rhythm. Several factors are responsible for disturbed sleep in PD, including: PD-related symptoms including nocturnal akinesia, early morning dystonia, painful cramps, tremor and difficulty turning over in bed. However, these disorders may also be associated with PD drug treatments [13].

Digestive disorders (such as constipation or nausea) were the second most frequently found non-motor signs in our cohort (51.25%). This result is perfectly consistent with other studies [14]. These disorders can be explained by autonomic nervous system damage. Indeed, neuronal degenerations occur in the myenteric plexus and the central nervous system, causing many digestive disorders [15]. These degenerations are likely to develop even before the degeneration of dopaminergic neurons in the SN [16].

Our results showed a significant predominance of stage 2 (n=28) with a percentage of 35%, compared to the other stages of the disease, similar result to the study of Kang and colleagues in 2005 (34.6%) (n=53) [17].

Our results report a homogeneous distribution of most non-motor signs according to the clinical form of PD, including hyposmia or anosmia. However, Japanese research states that this symptom more frequently affects patients with the akineto-rigid form, suggesting that olfactory dysfunction depends on the clinical form of PD [18].

Neuropsychologically, 56.25% of the patients in our cohort had mild cognitive impairment (PD-MCI) in several cognitive domains. This is consistent with the results of a recent meta-analysis where the prevalence of PD-MCI was estimated to be 40% in a total sample of 7053 PD patients. The prevalence of multiple domain PD-MCI was estimated to be 31% and that of single domain PD-MCI was 9% [19]. Cognitive disorders in PD are common, and can appear in the early stages of the disease. They become more and more prominent as the disease progresses [20].In early PD, the Cognitive Profile is predominantly a non-amnestic cognitive decline in a single domain, affecting visuospatial, attentional or executive functioning [21].

Nearly half of the patients assessed had cognitive symptoms on both the FAB and MMP. Cognitive impairment was found on the MMP in 52.78% of the subjects. It was also found on the FAB in 45.76% of cases. On the MMP, the most affected items were related to executive functions. People with PD suffer from impaired executive functions, even in the initial stage of the disease [22].

The prevalence of MCI in PD patients is in the range of 20-50%. PD-MCI patients have a high risk of developing long-term dementia, which is found in more than 75% of patients, which is closely related to the duration of the disease of 10 years or more [23]. Impairments in tests assessing language and visuospatial functioning are highly sensitive in predicting conversion to dementia.

In our cohort, cognitive impairment is more frequent in subjects with low educational level. The MMSE is < 22 in 66, 67% of subjects with an education level < NC3. This is consistent with most of the literature which reports that patients with MCI-PD are less educated than patients without MCI-PD. A high level of education, considered as one of the indicators of cognitive reserve, could protect against cognitive decline in PD and is strongly associated with cognitive efficiency in advanced stages [24].

66.18% of the patients in our cohort suffer from depression, and 69.70% of them suffer from anxiety. These percentages are close to those reported in the study by Seritan and colleagues in 2019 [25] with (55.5% anxiety and 52.1% depression) . However, they are higher than those reported in an Egyptian study (31.25% for depression and 40.6% for anxiety) [26]. This could be explained by the short duration of the disease in our cohort, which averaged 5.68±5.25 years, knowing that these two non-motor signs may accompany or even precede the motor symptoms.

V. Conclusion

Our study provides data on the clinical, neuropsychological and neuropsychiatric profile of Algerian patients with Parkinson's disease and shows that it is similar to that of other populations, but was characterized by a high frequence of mood/cognition dysfunction and gastrointestinal / sleep disorders. The characteristics of cognitive impairment in our cohort are variable in terms of impaired cognitive domains.

It is important to understand the clinical and especially the cognitive profile in PD in order to determine prognosis and better manage patients.

Disclaimer Statements Contributors

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Conflicts of interest
The authors report no conflicts of interest in this work.

Ethics approval
Ethical approval was obtained.

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