Prevalence of Depression, Anxiety, Dementia and other Non Motor Features of a large Cohort of Egyptian Parkinson's Disease Patients

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Abstract: Background: There is a lack of awareness of the considerable disability associated with non motor symptoms (NMS) in PD among physician. The aim of the work is to estimate the prevalence of depression, anxiety, dementia and other NMS of Parkinson's disease (PD) Egyptian patients. **Material and Methods**: The study included, 112 patients with Parkinson's disease. Each individual was scored on the Unified Parkinson's Disease Rating Scale part III (UPDRS) and the the Hoehn and Yahr Scale (HY) to evaluate motor symptoms. Other symptoms were quantified with the Mini Mental State Examination (MMSE), Hamilton Depression and Anxiety Scales (HAM-D, HAM-A) and the Non-Motor Symptom Questionnaire and Scale (NMSQuest and NMSS). **Results**: According to HAM-A and HAM-D scales; anxiety and depression were noted in 78% and 54% of patients whilst dementia was recorded in 22%. According to NMSS, mood/cognition was the commonest domain (87.5%), and sleep disturbance/fatigue was the second frequent domain with a prevalence rate 78.6%, but all other non-motor symptoms also scored highly: gastrointestinal and urinary domains (76.8% for both), Sexual dysfunction (73%), cardiovascular (70.5%). Perceptual problems /hallucinations were the least frequently recorded domain (9.9 %%). There were significant correlations between UPDRS and HAM-D, HAM-A scores as well as with MMSE. UPDRS were also correlated with total NMSQuest and NMSS and each domain separately except cardiovascular and perceptual problems. Duration of illness was significantly correlated with UPDRS, depression, and dementia but not with other NMS. **Conclusions**: mood/cognition, sleep disorders, GIT, and sexual disorders were common non motor manifestations in PD patients. Patients with a longer duration of PK had higher scores on the UPDRS part 3 and were more likely to have depression, anxiety and dementia.

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1. Introduction

Parkinson's disease (PD) is a progressive neurological condition which is characterized and diagnosed by the presence of classical motor symptoms, such as tremor, rigidity, bradykinesia and gait disturbance. Although PD is primarily a movement disorder, it is accompanied by various non motor symptoms. The NMS of PD is very diverse. It includes psychiatric and behavioral problems, cognitive dysfunction, sleep disturbance, gastrointestinal, sexual dysfunction and cardiovascular symptoms. These symptoms are challenging in advanced stages of the disease, and they frequently limit the effective treatment of motor signs, leading to increased disability and poor quality of life [1,2,3]. Neuropsychiatric disorders are common in PD, but not frequently recognized by clinicians. The assessment of these conditions must be routinely conducted due to their impact on the motor signs and on the quality of life of patients and caregivers. Depression is considered the most common neuropsychiatric disorder associated with PD. The actual rate of depression in persons with PD is unknown but reported rates vary from 7 to 76%. Difficulty in diagnosing depression in PD is quite complex due, in part, to the overlap of symptoms of PD with those of depressive syndromes [4]. Up to forty percent of PD patients were clinically diagnosed with significant anxiety [5]. Nearly 80 to 90% of PD patients have some type of sleep difficulty [6], and virtually all patients with PD will experience a sleep disorder during the course of the disease [7]. Cognitive impairment is common in PD, and approximately 30 to 40% of patients with PD meet criteria for dementia. [8]. These symptoms may be also related to the effect pharmacological and non-pharmacological treatment. Early and accurate identification and appropriate management of the nature and severity of non-motor symptoms in PD will aid the holistic care of this progressive neurodegenerative illness, improve the quality of life of patient and career, and contribute to limiting the financial impact of PD. Because few studies have provided an integrated scale for the assessment of NMS in PD, NMS have not been regularly used to assess PD, especially in Egypt. Recently, the Non-motor Symptoms Scale (NMSS) for PD was developed to quantify the overall prevalence of NMS [9,10].

The primary purpose of this cross-sectional study was to estimate the frequency of depression, anxiety, dementia and other non motor manifestations among a

large cohort group of PD patients and to evaluate the influence of disease duration, severity and Motor scale on NMS.

2. Material and Methods

One hundred and twelve PD patients participated in the study. They were selected consecutively from those who attended the Department of Neurology, Assiut University Hospital, Assiut, Egypt, from December 2009 to December 2010. All patients fulfilled the UK Parkinson's Disease Brain Bank Criteria for idiopathic PD [11]. The mean age of the patients was 60.96 ± 12.7 ranging from 28- 88 years, 77 males and 35 were females, the mean duration of illness was 6.17 ± 5.9 with a ranging from 6 months to 25 years.

We rated motor and functional performance on PD patients using Unified Parkinson's Disease Rating Scale (UPDRS) part 3 [12] and the Hoehn and Yahr Scale [13].

Minimental State Examination (MMSE) [14], Hamilton Depression Scale (HAM-D) [15] and Hamilton anxiety scale [16] were applied for each patient. Patients underwent also clinical examination, including tests investigating for possible other NMS using a self reported questionnaire for non-motor symptoms (NMSQuest) [17]. NMSQuest comparises 30 common symptoms scored yes or no, and is designed to provide a rapid screen for problematic NMS as an aid for clinical management. Then Non-Motor Symptoms Scale for Parkinson's disease (NMSS) that contains nine dimensions were applied [9]. The nine relevant domains included: cardiovascular (2 items); sleep/fatigue (4 items); mood/cognition (6 items); perceptual problems/hallucinations (3 items); attention/memory (3 items); gastrointestinal tract (3 items); urinary (3 items); sexual function (2 items); and miscellaneous (4 items). Score for each item is based on a multiple of severity (from 0 to 3) and frequency scores (from 1 to 4).

During their interview, patients were usually assisted by a caregiver, in order to maximize data collection in case of cognitive impairment. All patients provided fully informed written consent. The local ethics committee of Assiut University Hospital had approved the experimental protocol.

Statistical analysis

Questionnaires and different scales were reviewed, and open-ended questions were coded and entered using a simple spread sheet. Analysis followed after data verification and correction. All data were analyzed with the aid of the SPSS ver. 16 (www.spss.com). The results were expressed as mean ± SD. Degree of dementia was classified mild (21-19), moderate (14-18) and severe dementia less than 14 for illiterate patients and 2 point above for educated patients [18].

Degree of anxiety was classified as mild (≤17), moderate (18–24) or severe (≥ 25) [16] and depression was also classified into; mild symptoms equated to a score of 7–17, moderate to 18–24 and severe to 25 or more[15]. Spearman's correlation coefficient was done between duration of illness, total UPDRS, self assessment scale, NMSS, NMSQ, HDS, HAS, and subscales.

3. Results

Of 112 PD patients, clinical and demographic data are illustrated in table 1. Seventy patients (62.5%) were illiterate and 42 patients (37.5%) were literate. The mean duration of illness was 6.17 ± 5.9 years ranging from 6 months to 25 years. Fifteen patients had an early age of onset (younger than 40 years), twenty patients (17.85%) had positive family history.

Most of the patients (107/112 or 95.5% of patients) had resting tremor, while bradykinesia and rigidity were recorded in 82.1% and 85.7% respectively. Using the Hoehn and Yahr rating, Most of the patients were presented in stage 1 to 2 (80.3%) while stage 5 was least frequent (3.6%) see table 2.

Table 3 shows the mean values of each scale and domain using in this study.

A mild degree of anxiety was commonest (52.7%), while only 17 patients (15.2%) had severe anxiety. Depression (HAM-D) was recorded in 53.6%, anxiety (HAS) in 77.7%. Comorbid depression with anxiety was observed in 60 patients (53.6%).

Dementia was recorded in 22.3% of patients, most of them having a mild degree of dementia according to MMSE (Table 4). Significant correlation between dementia and depression and anxiety (MMSE versus HAM_D r= -0.30 p = 0.001, HAM-A versus HAM-D r= 0.75 , P= 0.0001; MMSE versus HAM-A- versus r= -0.29 p = 0.001)

Table 5 illustrate the frequency and percent of each domain: Sleep disturbance/fatigue was the second commonest domain after mood/cognition domain (87.5%), with a prevalence rate of 78.6%, but all other non-motor symptoms also scored highly: gastrointestinal and urinary domains (76.8% for both), Sexual dysfunction (73.2%), cardiovascular (70.5%), Perceptual problems /hallucinations were the least frequently recorded symptoms (9.9%%). NMS were present in 108 (96.25%) patients and occurred during both on and off periods. Only 4 patients (3.75%) had no NMS. The average total frequency of symptoms noted in the NMSQuest as well as the total NMSS scores in each domain are shown in table 5.

As regards to the frequency of each symptom of NMSQuest: feeling anxious, fightened or panicky, (60.7%), getting up regularly at night to pass urine (59.8%), a sense of urgency to pass urine that makes rush to the toilet (54.5%), feeling lightheaded, dizzy or weak when standing from sitting or lying (53.6%) and

constipation (51.8%) were the most common symptoms among studied patients

Followed by unexplained pains (not due to known conditions such as arthritis (47.1%), feeling less interested in sex or more interested in sex (46.4%), and difficulty getting to sleep at night or staying asleep at night (46.4%). The least symptoms were the double vision (7.1%) and believing things and visual hallucination (9.8%) (Table 6).

There were no significant differences between males and females in scores on the different rating scales and no significant differences between scores from patients with early or late age of onset also in different rating scales. There was no significant difference between patients who had positive family history of cases versus sporadic cases.

Table 7 illustrated the correlation between age, duration of illness, and UPDRS on one hand and the different rating scales on the other hand. It was shown that: age was significantly correlated with MMSE only (P= - 0.009).

Duration of illness was significantly correlated with UPDRS, HAM-D, HAM-A, MMSE, NMSS, and NMSQuest, while only sleep/fatigue, Perceptual problems/hallucination and attention/memory domains were correlated with the duration of illness.

There was a significant positive correlation between UPDRS score and Hoehn and Yahr staging on one hand and HAM-D, HAM-A, and NMSQuest score, on the other hand, and significant negative correlation between UPDRS and MMSE) were shown in (Figure 1A, 1B, 2 and 1C) respectively.

Significant positive correlation between the UPDRS with sleep/fatigue, mood/cognition and attention/memory domain, details illustrated in Table 7.

Table 1: Demographic and clinical data of Parkinson's Disease patients

	Mean ± SD
Age (Years) Range Age of onset (≤ 40years/ < 40 years)	60.96± 12.1 28- 88 15/97
M/F	77/35
Positive family history/negative family history	20/92
Duration (years) Range	6.17 ± 5.9 0.5-25
Illiterate number (%) Literate <6 years >6years	70 (62.5%) 42 (37.5%) 13(11.6%) 29 (25.9%)
Symptoms of PK number (%) Bradykinesia Resting tremors Rigidity Postural instability	 92 (82.1%) 107 (95.5%) 96 (85.7%) 70(62.5%)

Table 2: Hoehn and Yahr Stages of Parkinson's Disease patients

Severity of Parkinson's disease	Frequency	Percent
Stage 1: Unilateral disease.	42	37.5
Stage 1.5: Unilateral plus axial involvement.	24	21.4
Stage 2: bilateral disease, without impairment of balance	24	21.4
Stage 3: Mild to moderate bilateral disease; some postural instability; physically independent.	9	8.0
Stage 4: severe disability; still able to walk or stand unassisted	9	8.0
Stage 5: Wheelchair bound or bedridden unless aided	4	3.6
Total	112	100%

TABLE 3. Score distribution of the applied measures and non-motor symptoms scale

Scales	Scores (mean ± SD)	Range
Total UPDRS part 3	18.5 ± 11.4	3 - 50
Hamilton Anxiety Score	13.9± 8.9	0 - 40
Hamilton Depression Score	11.17 ± 7.2	0 – 33
MMSE score	25.0 ± 4.5	7 – 30
NMS Scale Cardiovascular domain Sleep/fatigue domain Mood/cognition domain Perceptual problems/hallucination domain Attention/memory domain Gastrointestinal domain Urinary domain Sexual function domain Miscellaneous domain Total NMSS	 2.07 ± 1.9 3.04 ± 2.6 4.1 ± 3.3 0.18 ± 0.13 1.76 ± 2.2 3.2 ± 2.7 3.0 ± 2.5 2.3 ± 2.3 1.6 ± 1.8 20.88 ± 12.8	 0-6 0-15 0-16 0-1 0-6 0-12 0-10 0-8 0-9 0-58
NMS Questionnaire	9.9 ± 5.9	0-21

Table (4):Frequency of depression, anxiety, dementia among PD using Hamilton depression and anxiety and MMSE.

Manifestation	No manifestations	Positive manifestation	Mild degree	Moderate degree	Severe degree
Anxiety	25(22.3%)	87 (77.7%)	59(52.7%)	11(9.8%)	17(15.2%)
Depression	52(46.4%)	60 (53.6%)	21(18.8%)	22(19.6%)	17(15.2%)
Dementia	87(77.7%)	25 (22.3%)	18(16.1%)	6(5.3%)	1(0.9%)

Table 5: Frequency and percent of occurrence of each domain of NMSS

NMS Scale	Yes/No (number of cases) for each domain	Percent of each domain Yes/No Percent
Domain		
Cardiovascular	79/33	70.5/29.5
Sleep/fatigue	88/24	78.6/21.4
Mood/cognition	98/14	87.5/12.5
Perceptual problems	11/101	9.9/90.1
Attention/memory	81/31	72.3/72.7
Gastrointestinal	86/26	76.8/23.2
Urinary	86/26	76.8/23.2
Sexual function	82/30	73.2/26.8
Miscellaneous	72/40	64.3/35.7
Total NMSS	108/4	96.25/3.75

Table(6) Frequency of each symptom according to NMSQuest

Non motor symptoms	Yes (n, %)	No (n, %)
1-Dribbling saliva during the daytime.	33(31.7%)	79(55.8%)
2-Loss or change in your ability to taste or smell.	11(9.8%)	101(90.1%)
3-Difficulty swallowing food or drink or problems with chocking.	27(24.1%)	85 (75.9%)
4-Vomiting or feelings of sickness (nausea).	12(10.7%)	90(89.3%)
5- Constipation (less than 3 bowel movements a week) or having to strain to pass a stool (feces).	58(51.8%)	54(48.2%)
6- Bowel (fecal) incontinence.	5(4.5%)	107(95.5%)
7-Feeling that your bowel emptying is incomplete after having been to the toilet.	18(16.1%)	94(83.9%)
8- A sense of urgency to pass urine that makes rush to the toilet.	61(54.5%)	51(45.5%)
9-Getting up regularly at night to pass urine.	67(59.8%)	45(40.2%)
10- Unexplained pains (not due to known conditions such as arthritis).	49(47.1%)	53(52.9%)
11- Unexplained change in weight (due to change in diet).	37 (33 %)	75 (67%)
12-Problems remembering things that have happened recently, or forgetting to do things.	34(30.36%)	78(69.6%)
13- Loss of interest in what is happening around you or in doing things.	43(38.39%)	69(61.61%)
14- Seeing or hearing things that you know or told are not there.	15(13.4%)	97(86.6%)
15- Difficulty concentrating or staying focused.	47(41.96%)	65(58.04%)
16- Feeling sad, "low or blue".	53(47.3%)	59(52.68%)
17- Feeling anxious, frightened or panicky.	68(60.7%)	44(39.3%)
18- Feeling less interested in sex or more interested in sex.	52(46.4%)	60(53.6%)
19- Finding it difficult to have sex when you try.	48(42.9%)	64(57.1%)
20- Feeling lightheaded, dizzy or weak when standing from sitting or lying.	60(53.6%)	52(46.4%)
21- Falling.	44(39.3%)	68(60.7%)
22- Finding it difficult to stay awake during activities such as working, driving or eating.	44(39.3%)	68(60.7%)
23- Difficulty getting to sleep at night or staying asleep at night.	52(46.4%)	60(53.6%)
24- Intense, vivid dreams or frightening dreams.	31**(27.7%)**	81(72.3%)
25- Talking or moving about in your sleep as if you are 'acting out' a dream.	17(15.2%)	95(84.8%)
26- Unpleasant sensations in your legs at night or while resting, and a feeling that you need to move.	17(15.2%)	95(84.8%)
27- Swelling of your legs.	20(17.9%)	92(82.1%)
28- Excessive sweating.	24(21.4%)	88(88.6%)
29- Double vision.	8 (7.1%)	104 (92.9%)
30- Believing things are happening to you that other people say are not true.	11(9.8%)	101(97.1%)

Table 7: The correlation between age, UPDRS , duration, stage, on one hand and diffenet scales used in this study score

Item	Age r(p value)	Duration r(p value)	UPDRS part 3 (motor score) r(p value)	Stage Hoehn and Yahr scale r (p value)
Hamilton anxiety scale	0.05 (0.57)	0.35(0.0001)	0.57(0.0001)	0.52(0.0001)
Hamilton depression scale (HAM-D)	9.1(0.23)	0.33(0.0001)	0.53(0.0001)	0.48(0.0001)
Mini mental state examination score(MMSE)	-0.24(0.009)	-0.19(0.04)	-0.27(0.003)	-0.29(0.003)
Non motor symptoms Questionnaire score (NMSQuest)	0.02(0.84)	0.22(0.01)	0.25(0.006)	0.18(0.52)
Total score of Non motor symptoms assessment scale (NMSS)	0.07(0.411)	0.23(0.01)	0.30(0.001)	0.71(0.066)
cardiovascular domain	0.09(0.33)	0.12(0.19)	0.18(0.055)	0.07(0.44)
sleep/ fatigue domain	0.04(0.67)	0.29(0.002)	0.33(0.0001)	0.27(0.004)
mood/cognition domain	0.13(0.156)	0.16(0.288)	0.31(0.001)	0.26(0.005)
Perceptual problems/ hallucination domain	0.08(0.382)	0.52(0.000)	-.04(0.679)	-0.12(0.208)
attention/ memory domain	0.12(0.198)	0.29(0.002)	0.35(0.0001)	0.21(0.02)
gastrointestinal domaind	0.02(0.78)	0.02(0.82)	0.15(0.10)	0.01(0.990)
urinary domain	0.06(0.53)	0.17(0.06)	0.07(0.45)	0.04(0.65)
sexual domain	-0.01(0.95)	0.09(0.95)	0.07(0.4)	0.045(0.650)
miscellaneous domain	0.13(0.167)	-0.15(0.32)	0.15(0.108)	0.02(0.815)

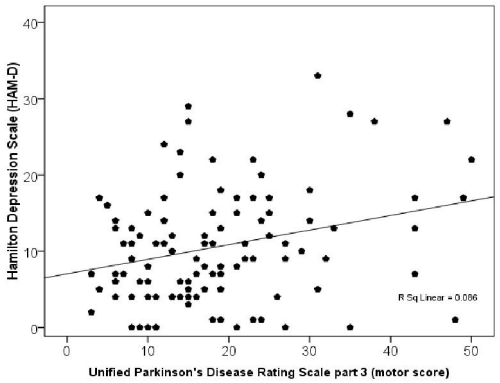
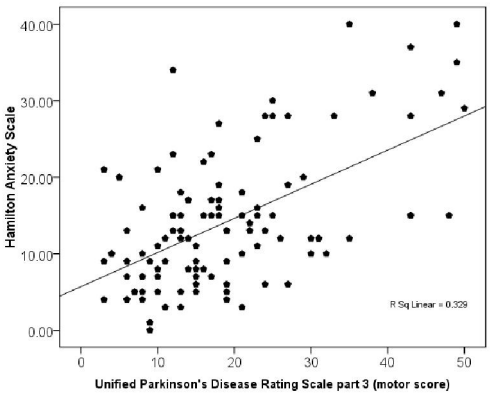


Figure: 1A



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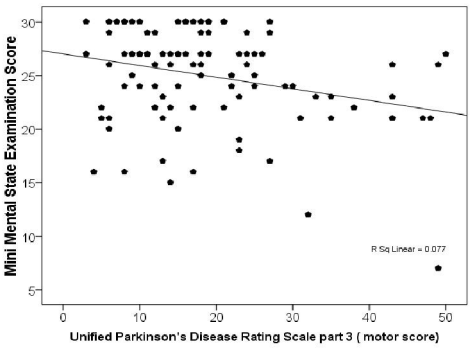

Figure: 1C

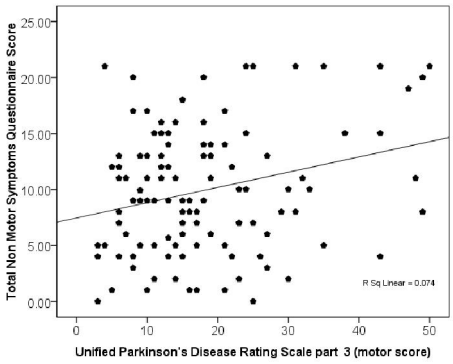

Figure 2.

4. Discussion

NMS of PD have received relatively little attention, despite diverse presentations of these conditions and their impact on the quality of life. It is increasingly clear that non-motor symptoms have a dramatic effect on the lives of both PD patients and caregivers [7]. NMS of PD are not well recognized in clinical practice, either in primary and secondary care. Some physicians have devoted significant attention to the NMS of PD [2, 19].

Depression, anxiety, fatigue and sleep disturbance are among the most troubling symptoms for PD patients, but during routine consultations, **Shulman *et al.*** [20] reported that patients with these symptoms are not identified by neurologists in over 50% of consultations and sleep disturbance in particular is not recognized in over 40% of patients. These efforts induced the Movement Disorder Society to modify the existing UPDRS to include an independent subpart to measure NMS [21].

To our knowledge, this is the first report of prevalence of non-motor symptoms among a large sample of Egyptian PD patients. Our study population included all stages of **Hoehn and Yahr** Scale [13] from 1 to 5, probably as a consequence of study participants being recruited from the outpatient clinic of Assiut University Hospital. Tremor (95.5%), rigidity (85.7%), and bradykinesia (82.1%), were the dominant motor symptoms in the present study.

In the present study the overall rate of NMS that occurred not only during the off period, but during other periods as well was 96.25% (at least one domain of NMSS), and only 3.75% had criteria of PD without any NMS. All of them seen as early as stage I of **Hoehn and Yahr**[13]. Previous studies that focused on NMS reported a wide range of prevalence, between 17% and 100%, of NMS among PD patients showing motor fluctuations. **Hillen and Sage** [22] reported that only 17% of patients with fluctuating PD had NMS. They used a single question with an open answer and likely to have underestimated the prevalence of NMS. On the other hand, **Witjas *et al.*** [23] reported that all patients had at least one type of NMS, most of which were associated with the off state. The wide variation in the prevalence for NMS may be related to severity, staging, time of assessment (off or on period) as well as tasks used to diagnose NMS.

Shulman *et al.* [20], **Sullivan *et al.*** [24] reported a low detection rate of NMS. In one study, **Sullivan *et al.*** [24] depression, anxiety, and constipation were addressed and treated in only 50% of patients, with even lower detection rates for other NMS such as fatigue (6%), memory (9%), somnolence (16%), insomnia (30%), incontinence (35%), and pain (35%). Another study, **Shulman *et al.*** [20] found a lower diagnostic accuracy for fatigue (25%), depression

(35%), anxiety (42%), and sleep disturbance (60%) by physician's interview compared to patients' response using a screening questionnaire.

Depression:

As domain Mood/cognition was the most common domain recorded in the present study 87.5% but because this domain including only 6 items concerning in NMSS depression and Anxiety we tried to apply HAM-D and HAM-A scales to assess not only the symptoms and degree of depression and Anxiety.

Depression in PD is the main factor impacting quality of life [25, 26, 27]. The actual rate of depression in persons with PD is unknown but reported rates vary from 7 to 76%. This may be due to the different criteria used to diagnose depression and to the different characteristics of the population to be screened. Higher rates are observed in subjects of outpatient neurologic clinics when compared to community setting studies [4]. **In the present study** depression was recorded in 53.6%, with variable degree of depression. The high prevalence of depression reported in this study is consistent with **Schrag *et al.*** [28] and **Kummer and Teixeira**, [29]; **Dobkin *et al.*** [30] and it may be attributable to sociocultural factors including poor social support in Egypt and the high cost of PD treatment. The significant correlation between UPDRS with Hamilton depression in the studied patients means that increasing the severity of PD associated with more depression.

Some authors claimed that depression in PD would be mild to moderate, seldom fulfilling diagnostic criteria for a major depressive disorder. However, the frequency of major depression, minor depression and dysthymia is now estimated to be 17%, 22% e 13%, respectively [31]. In the present study 18.8%, 19.6% and 15.2% had mild, moderate and severe degree of depression respectively. Age and sex had no relation with the depression while the potential risk factors for depression in PD include, comorbidity with anxiety, increased severity of the disease.

A problem regarding depression in PD is the fact that the somatic symptoms following depression may superimpose symptoms from PD itself and other co morbidities. Psychomotor slowness, decreased initiative, and blunted affect are depressive symptoms which may be confounded with bradykynesia, stooped posture and hypomania in PD. Our results showed that depressed PD patients had higher UPDRS-3 and HY scores when compared to non-depressed PD patients. There are conflicting studies on the association between depression and PD severity but the majority of them report a positive association [32, 33].

Psychiatric symptoms (hallucinations perceptual problems) were the least recorded symptoms (9.9%) among Egyptian PK patients. **Gallagher *et al.*** [34] reported that cognitive and neuropsychiatric complications of PD were generally well documented: hallucinations (82%), and delusional thought disorder (64%). The difference may be related to the use of anti-cholenergic drugs anti-parkisonian drugs.

Anxiety

The precise frequency of anxiety in PD is still uncertain. Nevertheless it is recognized that anxiety in PD is extremely common. It has been estimated that the prevalence rate of anxiety disorder in patients with PD was variable ranging from 3.6% to 40% [35,36]. It is feasible that the most frequent anxiety disorder in PD is social anxiety disorder, as nearly 50% of PD patients can be diagnosed with social phobia [37]. In the present study, the highest prevalence of the non-motor manifestations among PD patients was the anxiety. It was recorded in 77.7%, mild degree of anxiety was the commonest (52.7%), while only 15.2% had severe anxiety. The high prevalence of depression and anxiety observed in our study indicates that this problem should be addressed by clinicians managing PD patients.

We did not find any significant differences in prevalence of anxiety or depression between males and females, in contrast with the general population in which women have a higher prevalence of anxiety disorders than men [5,38, 39] . This result supports the hypothesis that anxiety and depression disorders are uniquely associated with PD, and may differ from anxiety disorders in the general population.

Comorbid depression with anxiety was observed in 53.6% of our patients. The severity and the duration of PD were also positively related to anxiety and depression. **Menza *et al.*** [38] reported 26% comorbidity, while **Nuti *et al.*** [5] reported 19% comorbidity. It is possible that anxiety worsens motor signs, which can reciprocally determine further depression.

This high prevalence of anxiety disturbances in PD underscores its prominence as a significant psychiatric co-morbidity in PD. Previous estimates have ranged from 28%- 40% [5, 40, 41, 38, 42, 43, 44] which was lower than observed in our study. This difference may be related to methodological assess, severity and staging.

Cognitive impairment and dementia

According to the NMSS the domain of attention/memory including only 3 items, the prevalence of this domain was 72.3%. However this domain didn't allowing to measure dementia and the degree of cognitive important. So we applied MMSE as screening test to measure the prevalence of dementia among our patients.

The prevalence of dementia in PD vary between 24 to 31% [45]. In the present study dementia was recorded in 22.3% of PD patients most of them had

mild degree of dementia. One of the risk factor of dementia is the educational factor which may be relevant since 62.5 % of our sample were illiterate and 11.6% were educated for less than 6 years. It is worth mentioning that patients with low educational level are particularly susceptible to the deleterious effect of depression on cognition [46].

However the prevalence of dementia among our patients was lower than that recorded in the previous study it may be attributed to many factors such as ; young age group (the mean was 60.96), shorter disease duration (the mean = 6 years), severity of motor signs as 90 patients presented in stage 1, 1.5 and 2. Anxiety and depression were also presented as risk factors for dementia in PD patients, as MMSE were correlated with the age, duration, UPDRS, depression and anxiety.

The recorded cardiovascular domain included experience light-headedness, dizziness, weakness on standing from sitting or lying positions and falling secondary to fainting or blacking out. In the present study, cardiovascular symptoms domain recorded in 70.5% of patients with PD. Dizziness was the commonest cardiovascular symptom in PD, with prevalence rate up to 58%[47]. Similar to our result, **Gallagher *et al.*** [34] recorded CV domain in 64%.

Sleep Disorders

In the present study sleep/fatigue domain was the second most prevalent non-motor symptoms in PD after anxiety. Nearly 78.6% of PD patients have one or more type of sleep disorders. The commonest type of sleep disturbances in the form of difficulty getting to sleep at night or staying asleep at night that was recorded in 46.4%. In the previous studies, 80 to 90% of PD patients have some type of sleep difficulty [6], and virtually all patients with PD will experience a sleep disorder during the course of the disease [2]. Sleep disorders may be caused by a series of factors including degeneration of sleep regulatory centers in the brainstem and thalamo-cortical pathways, or due to PD symptoms affecting the normal sleep, such as the motor impairment, depressive and anxiety disorders, and bladder incontinency.

Sleep fragmentation is the earliest and most common sleep disorder in PD, and it gradually worsens with disease progression [6]. Vivid dreaming nightmares and night terrors (27.7%), were also common in this study that nearly similar to the results reported by **Sharf *et al.*** [48].Thirty one patients vocalize during sleep recorded in our study. The vocalization content may vary from incomprehensible sounds to detailed conversations, laughing, cursing or screaming as recorded by Friedman and **Millman**,[49]. PD patients were also more prone to other sleep disorders such as restless legs syndrome, periodic limb movements that was recorded in 15% in the present study. Sleep disorders in PD are seldom diagnosed and treated.

In the present study gastrointestinal domain was also common that were recorded in 76.8% in studied patients, constipation (51.8%) and dribbling saliva (31.7%) during the daytime were the commonest symptoms. Our findings were consistent with results of **Gallagher *et al.*** [34] who reported that hyper salivation and constipation in 48% PD patients. However, the less common GIT symptoms in the present study, was that difficulty of swallowing or chocking problems with drinking (24.1%), feeling of incomplete bowel emptying after toilet (16.1%),vomiting or nausea (10.7%), loss or change in taste or smell ability (9.8%), and fecal incontinence (4.5%). Although salivary production is reduced in PD, drooling occurs partly due to reduced swallowing which may reflect involvement of cranial autonomic ganglia or brainstem salivatory nuclei [50]

These recorded GIT symptoms were partially consistent with recording data of **Sakakibara *et al.*** [51] who reported that patients with PD $\geq$ 50% report lower GIT symptoms such as constipation, diarrhea and fecal incontinence. Because in PD ; constipation occurs from decreased colonic transport and disturbed defecation as in 80% of PD patients; clonic transport time is increased and most patients cannot defecate completely [52]. However, **Cersosimo and Benarroch**, [50] stated that upper GIT symptoms including drooling, esophageal dysmotility and delayed reduced gastric emptying is secondary to involvement of cranial autonomic ganglia or brainstem salivatory nuclei .

Urinary domain

The reported prevalence of lower urinary tract symptoms (LUTS) in patients with PD ranges from 38 to 71% [53, 54, 55, 56]. However, it has been difficult to determine to what extent PD contributes to LUTS. This is because not only PD patients, but also men older than 60 years of age may have an obstruction component to their urinary symptoms brought about by benign prostate hyperplasia. Among our studied patients urinary symptoms were recorded in 76.8% including nocturia (59.8%) and urgency (54.5 %) that were consistent with findings of **Gallagher *et al.*** [34] and **Sakakibara *et al.*** [51] study. **Araki and Kuno**, [57] have shown a correlation between bladder dysfunction in patients with PD and neurological disability.

Sexual dysfunctions:

Only few previous studies have looked at sexual symptoms in PD and control subjects. The reported prevalence of sexual symptoms in patients with PD ranges from 37 to 65% [58, 59, 60, 61, 62, 63, 64]. In the present study sexual dysfunction domain was recorded in more than half percent of patients (73.2%),

either feeling less interested in sex or more interested in sex (46.4%) or difficult to have sex in 48 patients (42.9%). Our findings are nearly similar to finding of **Gallagher *et al.*** [34] study who recorded libido changed in 45% among PD patients.

Miscellaneous domain included pain, change in taste, weight and excess sweating. This domain was recorded in 64.3% in the present study. Sweating problems in PD is considered one of non motor symptoms and autonomic dysfunctions in PD [3]. **Schestatsky *et al.*** [65] study reported hyperhidrosis in PD. In the present study, we recorded excessive sweating in 21.4% of studied PD patients. It has been postulated that excessive sweating in PD may occur as a compensatory reaction to lower sympathetic function in the extremities [55].

Unlike previous studies (**Witjas *et al.*** [23]; **Hillen and Sage**, [22] ;**Raudino**, [66]; **Gunal *et al.***[67]), diffuse pain was frequent (47.1%) in our study. These discrepancies may be attributed to methodological differences for assessment of pain. Our study counted NMS occurring during off and on periods.

In this study, we found that NMS were very common in Egyptian patients with PD, with a prevalence of the whole spectrum of NMS being 96.3%, and the similarities with international studies strongly suggests the results are reliable but larger confirmatory studies may be needed.

In conclusion, neuropsychiatric and NMS are common in PD, but not frequently recognized by clinicians. The assessment of these conditions must be routinely conducted due to their impact on the motor signs and on the quality of life of patients and caregivers. The results of this study further indicated that Egyptian doctors should increase their recognition capabilities of NMS in PD. Future studies must focus on elucidating their pathophysiology these syndromes.

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