

## Clinical Association of Depression in a Group of Iraqi Patients with Parkinson's Disease

Zaki N Hasan<sup>1</sup> MBChB FICMS, Hasan A Al-Hamadani<sup>2</sup> MBChB FICMS, Farah I Al-Saffar<sup>3</sup> MPH

<sup>1</sup>Section of Neurology, Dept. of Medicine, Al-Kindi College of Medicine, Baghdad University, <sup>2</sup>Section of Neurology, Dept. of Medicine, College of Medicine, Al-Nahrain University, Baghdad, Iraq, <sup>3</sup>Epidemiology & biostatistics 2012, school of rural public health, Texas A&M Health science center, college station, Texas, USA.

### Abstract

- Introduction** Parkinson's disease (PD) is the second most common form of a group of progressive neurodegenerative disorders. Depression is more common in Parkinson's disease than in the general population.
- Objective** To evaluate the depressive features that accompanies Parkinson's disease and its relation to different parameter of this disease.
- Methods** This cross sectional study examined 30 patients with idiopathic Parkinson's disease neurologically and psychiatrically, searching for depression and its association with different features of idiopathic Parkinson's disease. The American diagnostic and statistical manual (DSM-IV) and the international classification of the disease (ICD10) were used for diagnosis of depression.
- Results** 53% of Parkinson's disease patients were found to be depressed and their depression significantly correlated with autonomic system infliction, dysphagia and insomnia. This finding was not correlated with duration or severity of the Parkinson's disease or the late complications of the disease.
- Conclusion** We found depression to be very common among Parkinson's disease patients; however, no specific type of depression could be identified in those patients. There is significant association between depression and autonomic involvement, insomnia and dysphagia in Parkinson's disease. Depression in Parkinson's disease was not found to be related to the age of onset or to the duration of the disease.
- Keywords** Parkinson, Depression

### Introduction

Parkinson's disease (PD) is the second most common neurologic degenerative disorder after Alzheimer's disease. Pathophysiologically there is neuronal loss within the substantia nigra of the midbrain and the neocortex <sup>(1)</sup>. Parkinson's disease is a variety of Parkinsonism occurs without obvious cause this idiopathic form is called Parkinson's disease or paralysis agitans <sup>(2)</sup>. This common disease, known since ancient times, was first cogently described by James Parkinson in 1817 <sup>(3)</sup>. The disease is of unknown etiology, but loss of Dopaminergic

neuron at the substantia nigra is the primary pathological process that leads to upsetting the normal balance between inhibitory dopamine effects and the excitatory acetylcholine effects on the motor neuron in the motor cortical area <sup>(2)</sup>.

Depression is more common in Parkinson's disease than in the general population, ranging from 10% to 25% in epidemiological studies to 40% in clinics specialized in movement disorders <sup>(4)</sup>. Serotonergic, noradrenergic, and dopaminergic mechanisms are all involved in its onset <sup>(5)</sup>.

The diversity of etiological factors had led to different classification systems including endogenous-reactive, primary- secondary and unipolar- bipolar and so on. In order to avoid this classification confusion most researchers use the American diagnostic and statistical manual (DSM-IV) and the international classification of the disease (ICD10) for diagnosis of depression<sup>(6)</sup>. Depression symptoms are defined as those that impair social, occupational, or other important areas of functioning<sup>(7)</sup>. The aim of this study is to evaluate the depressive features that accompany the Parkinson’s disease and its relation to different parameter of this disease.

**Methods**

In our cross-sectional study, thirty patients with Parkinson’s disease attending consultation clinic at Al-Kindy Teaching Hospital between September 2005 and April 2006 were included. Twenty five were males and five were females; the diagnosis of Parkinson’s disease fulfilled the

UK Parkinson's disease society brain bank clinical diagnostic criteria<sup>(1)</sup>. Patients with secondary Parkinsonism, patients with chronic medical disease and patients with Parkinson plus diseases were excluded from this study. The patients were asked about sleep, sphincter control, postural dizziness and swallowing deficit. Each patient was examined medically and neurologically by a neurologist.

The patients assessed by a psychiatrist, the DSM4 criteria for major depression was applied on the patients to diagnose depressive illness (Table 1).

The diagnosis of minor depression is based on the same symptoms, but only requires presence of two to five symptoms in the DSM IV-TR classification, and dysthymia requires that depressed mood has been present on most days for at least two years with at least two out of six other symptoms<sup>(8)</sup>.

**Table 1. DSM – 4 criteria for diagnosis of major depression<sup>(6)</sup>**

<b>A</b>	<b>Five or more of following present during the same 2 weeks (at least one of the symptom is either 1 or 2)</b>
1	Depressed mood most or the day, every day
2	Diminished interest or pleasure in all or almost all activities most of the day, nearly every day
3	Significant weight loss when not dieting or weight gain or decrease or increase appetite nearly every day
4	Insomnia or hypersomnia nearly every day
5	Psychomotor retardation or agitation nearly every day
6	Fatigue or loss of energy nearly every day
7	Feelings of worthlessness or excessive or inappropriate guilt nearly every day
8	Diminished ability to think or concentrate nearly every day
9	Recurrent thoughts of death, recurrent suicidal idea and suicidal attempt
<b>B</b>	<b>symptoms do not meet criteria for mixed episode</b>
<b>C</b>	<b>the symptom cause clinically significant distress or impairment in social, occupational, or other areas of functioning</b>
<b>D</b>	<b>the symptoms are not due to drug or general medical disease</b>
<b>E</b>	<b>the symptom are not better accounted for by bereavement</b>

**Results**

Out of the 30 patients with Parkinson’s disease, 16 were proved to have depression according to (DSM 4). Out of those 16 patients, 12 were males and four were females. Four females out of 5(80%) Parkinson’s disease patients had depression; while 12 males out of 25 (48%) were

having depression (Table 2). Six of the patients were between 50-59 years, six between 60-69 years and four between 70-79 years. We did not have any patient developing depression that was above 80 years and below 50 years (table3). The duration of Parkinson’s disease of one year was recorded in three patients out of the 16 who

have depression. Moreover, two years duration were in three patients, three years duration in two patients, four years duration in four patients and finally, five years duration in were in four patients (Table 4) .

All patients with depression reported some autonomic involvement, insomnia and dysphagia. Five patients out of the 16 had on – off phenomena and only one patient was bed bound state. All the patients between 60-79 years showed severe depression, while only 50% of those between 50- 59 years and 33% of those between 60-69 years, in total 62% were having severe depression. Anxiety/agitation was prevalent among 75% of patients, while stressful life events were seen among 62.5% of patients; both symptoms demonstrating female predominance. The prevalence of the low mood and loss of interest were in 10 out of the 16 patients (62.5%) as shown in Table 5.

**Table 2. Parkinson’s disease patients who have depression**

Patients		Male	Female	Total
Depression	<b>Yes</b>	12	4	16
	<b>No</b>	13	1	14
Total		25	5	30

**Table 3. Age distribution of Parkinson’s disease patients who have depression**

Patients	Age (years)			Total
	50-59	60-69	70-79	
Females	4	5	3	12
Males	2	1	1	4
Total	6	6	4	16

**Table 4. Duration of Parkinson’s disease patients who have depression**

No. of Patients	Duration (Years)					Total
	1	2	3	4	5	
	3	3	2	4	4	16

**Table 5. Different characteristics of the study group distributed across age categories**

Character		Age group (years)			Total
		50-59	60-69	70-79	
Depression	Severe	3	2	4	9
	Mild				
Anxiety/Agitation	Males	1	0	1	2
	Females	3	3	4	
Stress	Males	1	1	1	3
	Female	2	2	3	
Depressive Features	Low mood	3	3	4	10
	Guilt feeling	3	1	1	
	Suicidal thoughts	1	0	1	

**Discussion**

When James Parkinson’s wrote his monograph describing the shaking palsy (as he termed) in 1817; he mentioned that the disease process left the senses and intellect uninjured. This opinion was repeatedly analyzed by other neurologist and researchers; until 1923 when Lewy proved that mental disturbances are so common in Parkinson’s disease<sup>(9)</sup>. In a textbook published in 1996 it was postulated the depression occurring in association with Parkinson disease could be a reaction to the disease and its disabilities or could be an intrinsic feature of the Parkinson’s disease<sup>(10)</sup>.

Our study showed that 53% of the enrolled Parkinson’s disease patients had depression. This was very close to the 51% prevalence seen in Reiff<sup>(7)</sup>, and in old literature of Sano et al clinic /hospital based study<sup>(11)</sup>. Marsden mentioned in many review articles that one third of the Parkinson’s disease patients have depression<sup>(2)</sup>. This is the same rate in the Harding series<sup>(12)</sup>. Brown et al, found depression in 40% in their series of Parkinson’s disease patients<sup>(13)</sup>. A review of literature reveals prevalence rate of depression from (12-90%)<sup>(14)</sup>. This wide range differences among all these studies could be due to using different methodological scales for diagnosis of depression. Sano et al had used Hamilton criteria for depression diagnosis while the present study used the DSM 4 criteria which are more widely used at the present time to diagnose the depression, and considered the most sensitive and precise depression diagnostic scale<sup>(6)</sup>.

The present study showed that 80% of the Parkinson's disease females had depressive features and only 50% of the Parkinson's disease males had depressive features. These different gender rates of depression with higher female percentage in the present study were in consistent with those of previous studies which found that women with Parkinson's disease reported lower levels of quality of life, another index of social functioning, and more depression than men<sup>(14-19)</sup>. These finding disagree with old literatures of Horn<sup>(9)</sup> and Majons<sup>(20)</sup> who found no sex difference in the depression rate. The differences between the old and newer literatures may be related to better understanding of numerous correlates or possible risk factors for depression in Parkinson's disease, including female sex and psychiatric comorbidity<sup>(21)</sup>. One possible source of differences in cognition, and a growing area of research, is the effect of estrogen on dopaminergic neurons and pathways in the brain<sup>(15)</sup>.

The study showed a high correlation with history of stressful life events. Thus the depression can be reactive to Parkinson's disease consequences and to the life events as well. Nevertheless the stressful life events were unrelated to the anxiety. These results support the fact that the depression not seems to correlate with disease duration or disease severity, would support the argument that depression is intrinsic feature of the disease<sup>(22)</sup>.

We found no relation or specific pattern between depression and the duration of the Parkinson's disease. This was in agreement with Reichmann's findings who found no correlation with the severity of motor impairment<sup>(23)</sup> as well as Horn<sup>(9)</sup>, and Sano<sup>(11)</sup>. Shiba<sup>(24)</sup> found that depression may precede motor symptoms by years. The apparent lack of relation of depression to disease duration supports the opinion that classifies depression in Parkinson's disease as an intrinsic feature of the Parkinson's disease and not as a reaction to the disease and its disabilities. The study showed that all patients with depression were having autonomic

involvement, insomnia, and dysphagia. Five patients out of the 16 had on-off phenomena and only one patient was bed bound state. It cannot be excluded that depression in Parkinson's reflects more advanced and widespread neuro-degeneration<sup>(25)</sup> rather than severity of the disease<sup>(26)</sup>.

We could not find any Parkinson's disease patient who was below 50 and above 80 years of age with depression. This may be a result of the small sample of this study. We could not see a pattern relating the age of the Parkinson's patients and the development of depression. This result was agreeing Sano<sup>(11)</sup>, Mjons<sup>(20)</sup> and Horn<sup>(9)</sup> studies, but not Brown's study. Brown found depression to be more common before age of 58 years. This suggests that the disease threat of disability and loss of social status may become relevant for many people as adaptation to the disease results which leads to return to normal mood. The results agreed with this suggestion as we noted no significant difference of affection by depression with the duration of the disease.

The present study found more severe symptoms of depression in late ages and in those between 50-59 years. These results agreed with Brown<sup>(13)</sup>, Sano<sup>(11)</sup> and Horn<sup>(9)</sup>. The depression of intrinsic factor, disabilities and the complications of the Parkinson's disease can be the possible causes for the more severe depression in Parkinson's disease in older patients. We also identified high prevalence anxiety and agitation in depressed Parkinson patients; but no clear evidence of its importance. These results need to be compared to the isolated depression to confirm whether they are significant or not.

There is inconsistent evidence that depression of Parkinson's disease is distinct from non-Parkinson's disease depression, with some studies reporting higher rates of anxiety, pessimism, suicide ideation without suicidal behavior, and less guilt and self-reproach<sup>(27)</sup>. Our study showed very low incidence of suicidal thoughts. This was in agreement with the Burn<sup>(28)</sup> who found depression is mostly of mild to

moderate intensity and suicide is very rare in Parkinson's disease.

In conclusion, depression to be very common among Parkinson's disease patients; however, no specific type of depression could be identified in those patients. There is an association between depression and autonomic involvement, insomnia and dysphagia in Parkinson's disease. In our study, depression in Parkinson's disease was not found to be related to the age of onset or to the duration of the disease. The strength of our study was mainly that only few previous studies assessed depression as an intrinsic feature of Parkinson's disease, as opposed to simply assuming depression to be reactive to Parkinson's disease. Our findings that the prevalence was not correlated with the duration of the disease were evidence that supports this theory.

Limitations of our study can be that we used the cross-sectional design. This is mainly because in Iraq, we are faced with many challenges when conducting studies on patients, as many will refuse to be followed up, or to repeatedly appear at the hospital for security reasons. Also, we could not identify comparable controls. Gives rise to many potential confounding factors that may have obscured our vision. For example, females are known to have higher prevalence of depression. Moreover, socioeconomic status, life style, medications, and comorbidities might all have played a role in over or underestimating the prevalence of depression on those patients. We would therefore recommend future studies to compare a large sample of Parkinson patients to controls that are matched for age, gender, stage of Parkinson's disease, comorbidities, and medication use. This can yield results that are potentially less biased. Finally, study designs like cohort or case control can aid strengthen future research. It would also be interesting to conduct research investigating the effect of antidepressant medications use on depression in Parkinson's disease.

## References

1. Davie CA. A review of Parkinson's disease. *Br Med Bull.* 2008; 86(1): 109-127.

2. Simon RP, Greenberg DA, Aminof MJ. *Clinical neurology.* New York: Lange medical books; 2006. P. 241.
3. Ropper AH, Samuels MA. *Adams and Vectors principles of neurology, Part 4.* New-York: McGraw Hill press; 2009. P. 915-25.
4. Martinez-Castrillo JC, Vela L, Del Val J, et al. Non-motor disorders and their correlation with dopamine can they be treated by currently available methods? *The Neurologist.* 2011; 17: S9-S17.
5. Remy P, Doder M, Lees A, et al. Depression in Parkinson's disease: loss of dopamine and noradrenaline innervations in the limbic system. *Brain.* 2005; 128: 1314-22.
6. American Psychiatry Association. *Diagnostic and statistical manual of mental disease.* 4<sup>th</sup> ed. Test review for major depressive episode, 2001. p. 335.
7. Reiff J, Schmidt N, Riebe B, et al. Subthreshold depression in Parkinson's disease. *Mov Disord.* 2011; 26(9): 1741-4.
8. Aarsland D, Marsh L, and Schrag A. Neuropsychiatric symptoms in Parkinson's disease. *Mov Disord.* 2009; 24(15): 2175-86.
9. Horn S. Some psychological factors in Parkinson. *J Neurol Neurosurg Psychiatr.* 1974; 37: 27-31.
10. Sano M, Marder K, Doorcef G. Basal ganglia disorder. In: Schiffer R, Fogel B. eds. *Neuropsychiatry.* Baltimore: William and Wilkins; 1996. P. 807.
11. Sano M, William J, Rosenstein B. Coexisting dementia and depression in Parkinson. *Arch Neurol.* 1989; 46: 1284-6.
12. Harding A. Movement disorders. In: Walton J. ed. *Brain's diseases of the nervous system.* 10<sup>th</sup> ed. New York: Oxford Press; 1993. P. 399.
13. Brown R, Jahanshahi M. Depression and Parkinson disease (psychological view). *Adv Neurol.* 1995; 65: 61-84.
14. Warburton J. Depressive symptom in Parkinson disease. *J Neurol Neurosurg Psychiatr.* 1994; 30: 368-70.
15. Scott B, Borgman A, Engler H, et al. Gender differences in Parkinson's disease symptom profile. *Acta Neurol Scand.* 2000; 102: 37-43.
16. Baba Y, Putzke JD, Whaley NR, et al. Gender and the Parkinson's disease phenotype. *J Neurol* 2005; 252: 1201-1205.
17. Fernandez HH, Lapane KL, Ott BR, et al. Gender differences in the frequency and treatment of behavior problems in Parkinson's disease. *SAGE Study Group. Systematic Assessment and Geriatric drug use via Epidemiology. Mov Disord.* 2000; 15: 490-6.
18. Riedel O, Klotsche J, Spottke A, et al. Cognitive impairment in 873 patients with idiopathic Parkinson's disease. Results from the German study on Epidemiology of Parkinson's Disease with Dementia (GEPAD). *J Neurol.* 2008; 255: 255-64.
19. Miller IN, Cronin-Golomb A. Gender differences in Parkinson's disease: Clinical characteristics and

- cognition movement disorders. *Mov Disord.* 2010; 25(16): 2695-703.
20. Mjones H. Paralysis agitans. A clinical and genetic study. *Acta Psychiatrica et Neurologica. Scandinavica.* 1949; Suppl. 54. 1-195.
  21. Weintraub D, Burn DJ. Parkinson's disease: The quintessential neuropsychiatric disorder. *Mov Disord.* 2011; 26(6): 1022-31.
  22. Robert JK. Glossaries. In: Robert JK. *Differential diagnosis in neuropsychiatry.* New York: Willy publication; 1984. p. 333.
  23. Reichmann H, Schneider C, Lohle M. Non-motor features of Parkinson's disease: depression and dementia. *Parkin Relat Disord.* 2009; 15S3: S87-S92.
  24. Shiba M, Bower JH, Maraganore DM, et al. Anxiety disorders and depressive disorders preceding Parkinson's disease: a case-control study. *Mov Disord.* 2000; 15(4): 669-77.
  25. Palhagen SE, Carlsson M, Curman E, et al. Depressive illness in Parkinsons disease indication of a more advanced and widespread neurodegenerative process? *Acta Neurol Scand.* 2008; 117: 295-304.
  26. Manor Y, Balas M, Giladi N, et al. Anxiety, depression and swallowing disorders in patients with Parkinson's disease. *Parkin Relat Disord.* 2009; 15: 453-6.
  27. Leentjens AF. Depression in Parkinson's disease: conceptual issues and clinical challenges. *J Geriatr Psychiatry Neurol.* 2004; 17: 120-6.
  28. Burn D. Beyond the iron mark: towards better recognition and treatment of depression associated with Parkinson's disease. *Mov Disord.* 2002; 17: 445-54.

---

**Correspondences to: Dr. Hasan A Al-Hamadani**  
**E-mail: hah\_hamdani@yahoo.com**  
**Received 15<sup>th</sup> Jan. 2012: Accepted 24<sup>th</sup> Jun. 2012**