

## ORIGINAL ARTICLES

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# Association of Serum testosterone Level with Depression in Parkinson's Disease

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### Abstract:

**Background:** Depression is a non-motor symptom in Parkinson's disease (PD) as well as elderly population due to testosterone deficiency (TD). Because of similarity between depression in PD and for testosterone deficiency, clinician may fail to recognize and treat TD in patients with PD. Objectives: Our aim was to find out the association between serum total testosterone level and depression in men with Parkinson disease.

**Methods:** This was a case control study carried out in the OPD of department of Neurology, Department of Psychiatry and Department of Biochemistry, Bangabandhu Sheikh Mujib Medical University (BSMMU) on total of 64 subjects where 34 were cases and 30 were controls age ranging from 40 to 85 years of age. **Results:** This analysis showed serum testosterone levels were significantly low in PD patients with depression compared to controls (4.90±1.86 ng/ml in cases and 6.66±1.18 ng/ml in control group with Odds ratio is 2.071; 95% CI 1.587-2.704). Significantly (P <0.05) low levels of serum testosterone were noted in case suffering from depression more than one year (4.56±1.82 ng/ml vs 6.18±1.50 ng/ml). Serum testosterone level was significantly (<0.001) low in stage III PD patients with depression compared to control (4.96±1.41 ng/ml vs 7.30±1.23 ng/ml). **Conclusion:** Low serum testosterone level is an important factor causing depression in PD patients. Also progression of PD and duration of depression showed strong correlation with serum testosterone level in this study.

**Key words:** Testosterone, depression, Parkinson's disease

**Abbreviation:** PD (Parkinson's disease), TD (testosterone deficiency), OPD (Out patient department).

### Introduction:

Parkinson's disease is a chronic, progressive and degenerative disease of the nervous system affecting the basal ganglia which presents with various motor and non-motor problems. The cardinal motor symptoms are resting tremor, bradykinesia, rigidity and postural instability<sup>1</sup>. The non-motor symptoms of Parkinson's disease are depression, apathy, anxiety, emotional changes, fatigue with loss of energy, pain, memory difficulties with slow thinking, sleep disturbances hyposmia or anosmia and some autonomic disturbances<sup>1,2,3</sup>. Each

person with Parkinson's disease will experiences these symptoms differently.

Parkinson's disease begins between 40 and 70 years of age. Incidences of the disease increases with age. Below 40 years of age the incidence is 3-4/100,000 population while above 70 years it is about 500/100,000 population. Males are more affected than females (M: F=3:2)<sup>3</sup>.

Depression is a common problem which may appear early in the disease, even before other symptoms are noticed. Depression occurs for long periods of

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time in approximately 40% of persons with Parkinson disease and it can also occur for short bouts<sup>4</sup>. Though mechanism of depression is poorly known, an interaction among biological and psychological factors with genetic predisposition and life history may play an important role. Patients with depression were reported to have faster cognitive and functional decline, a faster progression along the Hoehn and Yahr stages of the illness and an increased need for antiparkinsonian therapy compared with age and gender comparable Parkinson disease patients without depression<sup>5</sup>.

Testosterone, the principal hormone of the testes, is a C19 steroid. It is synthesized from cholesterol in leydig cells and formed from androstenedione secreted by the adrenal cortex. The main functions of this hormone are to develop and maintain the male secondary sex characteristics, exert an important protein-anabolic, growth promoting effect, maintenance of spermatogenesis and to exert an inhibitory feedback effect on pituitary LH secretion<sup>6</sup>.

Testosterone deficiency occurs in various testicular disorders, disease of brain and some external factors like acute critical illness, burns, major trauma or surgery, use of some drugs like steroids, chronic disease and its treatment, alcohol abuse, and ageing. The commonest cause of testosterone deficiency is ageing. It is the androgen deficiency in adult male that is the largest under diagnosed group of all testosterone deficient individuals<sup>7</sup>.

Testosterone deficiency due to ageing affects 20% to 25% of males over the age of 60 years in the general population. Whether due to testicular or brain or ageing, the signs and symptoms as a result of the androgen deficiency are similar. Individuals may exhibit some or all of the features like; changes in mood (fatigue, depression, anger), lethargy, decreased lean body mass, decreased muscle strength, sleep disturbances, decreased body hair (feminization), decreased bone mineral density, decreased enjoyment in life, deterioration in work performance, decreased libido and erectile quality and low or zero sperm in the semen<sup>7</sup>.

So male Parkinson disease patients, who have testosterone deficiency, may have features resembling non-motor Parkinsonian symptoms.

Because of the similarity between the non-motor symptoms of Parkinson disease and the symptoms of testosterone deficiency, clinicians may fail to recognize and treat testosterone deficiency in patients with Parkinson disease. The identification of testosterone deficiency may have a significant impact on the long term course of the disease.

This study is therefore planned to assess how common undiagnosed symptomatic testosterone deficiency is in our Parkinson disease population and how they correlate with depressive manifestations.

## **Materials and Methods:**

### **Study population:**

This was a case control study done in the out patient department of neurology, Department of Psychiatry and Department of Biochemistry, Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka. Study population was 40 to 85 years of age male patient of idiopathic Parkinson disease with depression as case. Age and sex matched patients of idiopathic Parkinson disease without depression was considered as control. Data were collected by filling up a semi-structured questionnaire by the investigator and also by a self reported questionnaire by the subjects. Serum total testosterone level was measured subsequently of all the subjects to evaluate the association between serum total testosterone level and depression in male Parkinson disease patients.

### **Statistical analysis:**

All data were recorded systematically in preformed data collection form and quantitative data were expressed as mean and standard deviation and qualitative data as frequency distribution and percentage. Statistical analysis was performed by using SPSS for windows version 10.0. 95% confidence limit was taken. Probability value <0.05 was considered as level of significance and <0.001 was considered as level of highly significant.

### **Results and observations:**

A total 64 male subjects were studied. Of them 34 were idiopathic PD with depression and 30 were idiopathic PD without depression. Thirty seven subjects were below 60 years of age (57.81%) and

27 were above 60 years of age (42.19%). The mean age was 59.09±9.45 years in cases and 58.37±10.49 years in control. This is shown in table-I

**Table-I**  
*Age distribution of the study subjects*

Age (years)	Case (n=34)		Control (n=30)		P value
	No.	(%)	No.	(%)	
<60	20	(58.8)	17	(56.7)	>0.862 <sup>ns</sup>
>60	14	(41.2)	13	(43.3)	
Mean±SD	59.09±9.45		58.37±10.49		>0.50 <sup>ns</sup>
Range	41-85		40-80		

Case: Parkinson disease with depression  
Control: Parkinson disease without depression  
Chi square test/Unpaired Student's 't' test  
ns = Not significant

In the case group 20.6% of subjects had been suffering from PD for less than one year and 79.4%

were more than one year. In the control group 63.3% have their disease <1 year while rest (36.7%) were suffering for more than one year. This variation is statistically highly significant (p<0.001). The Odds ratio is 6.67 which signifies high incidence of depression in the longer duration (>1 yr) group. The mean duration of disease in case group is 2.48±1.38 years while in the control group it is 1.28±0.96 years. This is also statistically highly significant (p<0.001). This is shown in table-II.

In the case group 41.2%, 29.4% and 29.4% were in stage II, III, IV respectively. In the control group 60%, 33.3% and 6.7% were in stage II, III, IV respectively. No patient was found in stage I status in both groups. This is shown in table-III.

Mean serum total testosterone level in case group was 4.90±1.86ng/ml and in control group is 6.66±1.18 ng/ml. This is statistically highly (<0.001)

**Table-II**  
*Duration of Parkinson disease*

Duration (years)	Case (n=34)		Control (n=30)		P value	Odds ratio	95% CI
	No.	(%)	No.	(%)			
>1	27	(79.4)	11	(36.7)	<0.001 <sup>***</sup>	6.67	0.049 0.458
?1	7	(20.6)	19	(63.3)			
Mean±SD	2.48±1.38		1.28±0.96		<0.001 <sup>***</sup>		
Range	0.17 5.00		0.17 3.00				

Chi square test/Unpaired Student's 't' test  
\*\*\* = Significant

**Table-III**  
*Clinical stage of Parkinson disease (Hoehn & Yahr rating)*

Stage	Case (n=34)		Control (n=30)		P value
	No.	(%)	No.	(%)	
I	0	(0)	0	(0)	>0.05 <sup>ns</sup>
II	14	(41.2)	18	(60.0)	
III	10	(29.4)	10	(33.3)	
IV	10	(29.4)	2	(6.7)	

Chi square test  
ns = Not significant

significant. So Parkinson disease patients with depression have significantly lower mean serum total testosterone level than those with Parkinson disease without depression. Also 17.6% cases had serum total testosterone level below the normal ( $<3$  ng/ml) biochemical range, while in the control group none was found in this range. This is also statistically significant finding ( $p < 0.05$ ). The Odds ratio is 2.071. This is shown in table-IV.

Mean serum total testosterone level in the case group who suffered for less than 1 year is  $6.18 \pm 1.50$  ng/ml and in those who suffered for more than 1 year is  $4.56 \pm 1.82$  ng/ml. This finding is statistically significant. The mean serum total testosterone level in the control group who suffered for less than 1 year is  $6.60 \pm 1.09$  ng/ml and in them who suffered for more than 1 year is  $6.76 \pm 1.36$  ng/ml. This finding is statistically not significant. On the other hand, below 1 years of disease duration, mean serum

total testosterone level in the case group is  $6.18 \pm 1.50$  ng/ml and in the control group is  $6.60 \pm 1.09$  ng/ml. This finding is also statistically not significant. Above 1 years of disease duration, mean serum total testosterone level in the case group is  $4.56 \pm 1.82$  ng/ml while that in the control group is  $6.76 \pm 1.36$  ng/ml. This finding is statistically highly significant. This is shown in table-V.

The mean serum total testosterone level in the stage-II PD patients is  $6.17 \pm 1.39$  ng/ml in case group and  $6.44 \pm 1.05$  ng/ml in control group. This variation is not significant statistically. The mean serum total testosterone level in the stage-III PD patients is  $4.96 \pm 1.41$  ng/ml in case group and  $7.30 \pm 1.23$  ng/ml in control group. This variation is significant statistically. The mean serum total testosterone level in the stage-IV of PD patients is  $3.06 \pm 1.28$  ng/ml in case group and  $5.49 \pm 0.35$  ng/ml in control group. This variation is not significant statistically. This is shown in table-VI.

**Table IV**  
*Status of serum total testosterone level*

Serum total testosterone (ng/ml)	Case (n=34)		Control (n=30)		P value	Odds ratio	95% CI
	No.	(%)	No.	(%)			
<3 (low)	6	(17.6)	0		<0.05*	2.071	1.587 2.704
3 (normal)	28	(82.4)	30	(100.0)			
Mean±SD	4.90±1.86		6.66±1.18			<0.001***	
Range	0.14 8.22		4.53 9.27				

Chi square test/Unpaired Student's 't' test ; \*/\*\*\* = Significant

**Table-V**  
*Effect of duration of Parkinson disease on serum total testosterone level*

Duration of Parkinson disease	Serum total testosterone (ng/ml) level		P value
	Case (n=7)	Control (n=19)	
<1 year			>0.10 <sup>ns</sup>
Mean±SD	6.18±1.50	6.60±1.09	
Range	3.35 7.47	4.53 8.77	
>1 year			<0.001***
Mean±SD	4.56±1.82	6.76±1.36	
Range	0.14 8.22	5.24 9.27	
P value	<0.05*	>0.50 <sup>ns</sup>	

Unpaired Student's 't' test

ns = Not significant, \*/\*\*\* = Significant

**Table-VI**  
*Effect of clinical stage of Parkinson disease on serum total testosterone level*

Clinical stage of Parkinson disease	Serum total testosterone (ng/ml) level		P value
	Case (n=14)	Control (n=18)	
Stage II			
Mean±SD	6.17±1.39	6.44±1.05	>0.50 <sup>ns</sup>
Range	4.11 8.22	4.53 8.77	
Stage III	(n=10)	(n=10)	
Mean±SD	4.96±1.41	7.30±1.23	<0.001 <sup>***</sup>
Range	2.79 7.28	5.93 9.27	
Stage IV	(n=10)	(n=2)	
Mean±SD	3.06±1.28	5.49±0.35	<0.05 <sup>*</sup>
Range	0.14 4.96	5.24 5.73	
P value	P value		
Stage II vs III	<0.05 <sup>*</sup>	>0.05 <sup>ns</sup>	
Stage II vs IV	<0.001 <sup>***</sup>	>0.10 <sup>ns</sup>	
Stage III vs IV	<0.01 <sup>**</sup>	>0.05 <sup>ns</sup>	

Unpaired Student's 't' test  
ns = Not significant, \*/\*\*/\*\* = Significant

Comparing the mean serum total testosterone level between Stage-II and Stage-III of Parkinson disease patients in the case group shows significant variation while that in the control group has not varied significantly. The mean serum total testosterone level between Stage-II and Stage-IV of Parkinson disease patients in the case group have differed highly significantly, while that in the control group have not varied significantly. Comparison of mean serum total testosterone level between Stage-III and Stage-IV of Parkinson disease patients shows significant variation in the case group while that in the control group the variation is not significant statistically.

**Discussion:**

This study was carried out in the outpatient department of Neurology, BSMMU, Dhaka. A total 64 patients were studied. Among them 34 subjects was Parkinson disease with depression and the other 30 subjects were Parkinson disease without depression. The aim of this study was to detect the association of serum testosterone concentration with depression in male Parkinson disease patients.

The mean age of the cases is 59.09±9.45 years while that of the controls is 58.37±10.49 years. This difference is statistically insignificant. So case and control groups are age matched. In a community

study in Sweden, among 1, 47,777 inhabitants, data was analyzed of 170 Parkinson disease cases where mean age of onset was at 65.5 years <sup>8</sup>, but that difference disclose the fact of more life expectancy in western countries from balanced nutrition and better health care facilities which likely delayed the later age of onset of Parkinson disease. But our finding is in harmony with another study who found the mean age of his subjects with Parkinson disease was 52.6±14 years <sup>9</sup>.

But from this study it would be hard to make any final comment regarding age, as this is a hospital based study (rather than a population based data) where many patients cannot reach or come, female patients were not included and the patients below 40 years of age are excluded.

The duration of illness has affected the patients significantly. Our findings point out that patients who had been suffering from Parkinson disease for prolong period (>1 year) were more likely to suffer from depression than those who had the disease for shorter period (<1 year). The Odds ratio was 6.67 which signifies high incidence of depression in the longer duration (>1 yr) group. So Parkinson disease patients who are prolong (>1 yr) sufferers develop depression 6.67 times more than those who have

been suffering for shorter (<1 yr) period. This result is consistent with a study who found that the frequency and severity of major depression were higher in Parkinson disease patients<sup>10</sup>. Longer duration of Parkinson disease is significantly associated with major depression. This may have several reasons. Early in the disease the motor features respond well to anti-Parkinsonian drugs. But as time progresses, the efficacy of the drugs gradually decay. Also in the advanced stage patients understand that this is an incurable disease which will deteriorate progressively. Economic involvement due to functional loss, disease burden, cost of the medications and a hopeless future may all contribute to the occurrence of depression especially in them who are prolong sufferer. Also depression can occur as part of disease per se. Those who have the longer disease course are more vulnerable to suffer from depression.

No significant difference noted in staging of Parkinson disease between the case and control groups. So the case and control groups are matched on this ground also.

This study revealed an inverse relation with mean serum total testosterone level and severity of depression. The more is the deficiency of serum total testosterone, the more severe depression the person suffers from. The Odds ratio is 2.071 which signify depression took place twice more frequently in PD patients with testosterone deficiency than those who do not have. This finding is consistent with one study where he investigates 3987 men, aged 71 to 89 years over a period of 4 years. He found men with testosterone deficiency had three times the Odds in favor of depression compared to men with normal/ highest level of serum testosterone<sup>11</sup>.

Increased duration (>1 yr) of Parkinson disease causes decreasing level of serum total testosterone which is significantly present in Parkinson disease patients with depression. So depression in Parkinson disease may be due to lower levels of serum total testosterone.

It is evident that patients in advanced stage of Parkinson disease have decreasing level of serum total testosterone, which is significantly present in

those have depression (i.e. case group). So severity of Parkinson disease is associated with decreasing level of serum total testosterone concentration. This result is steady with the findings of Gomula A (2004) who observed testosterone deficient PD patients in advanced stage and after correction of their testosterone level, their symptoms and signs of depression improved significantly. Decreasing level of serum total testosterone concentration appears to be responsible for the depression as in the control group testosterone concentration has not decreased significantly even with disease severity, keep them out of depression.

Overall 17.6% of Parkinson disease patients with depression had low serum total testosterone level. 5.4% below 60 year age group and 23.5% above 60 year age had testosterone deficiency. Thus this study yields a potentially association between testosterone deficiency and depression.

#### **Conclusion:**

Low serum total testosterone concentration is vital for development of depression in PD patients. Duration of disease, advanced stage of PD is also important contributory factor for depression in Parkinson disease patients.

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