Original Article

Relationship of vitamin D deficiency with motor functions of Parkinson's disease

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ABSTRACT

Background: *Parkinson's disease (PD), a neurodegenerative disorder, is associated with substantial public health and economic burdens. Low levels of vitamin D are a common finding in patients of PD. This study was conducted to assess the serum vitamin D level in PD patients and to investigate the relationship of the vitamin D level with motor functions of PD.*

Methods: *This cross-sectional study was conducted in Department of Neurology, BIRDEM General Hospital, Dhaka from 1st July, 2022 to 30th June, 2023. A total of 120 participants, 60 patients with PD and 60 healthy controls were enrolled and informed written consent was taken. Healthy controls were the attendants of the cases who gave informed written consent for the study. Information on socio-demographic characteristics, clinical features, laboratory parameters and neurological examinations were assessed. A semi-structured questionnaire was used for data collection and data was analyzed with Statistical Package for Social Science (SPSS) version 24.0.*

Results: *Mean vitamin D level was significantly lower among the patients with PD compared to controls (25.97±3.44 ng/ml vs 38.47±5.08 ng/ml, p<0.01). Among all the cases of PD, 90% had bradykinesia, 85% had tremor, 71.7% had rigidity and 70% had postural instability. Modified Hoehn and Yahr score (H&Y) has* been used for the staging of the motor disability associated with PD. *According to Modified H &Y score, 53.3% patients were in stage 1-2, 26.7% in stage 2-3 and 20% in stage >3. The mean vitamin D level was 28.43±2.43, 24.06±1.57 and 21.92±1.62 in stage 1-2, stage 2.5-3 and stage >3 respectively and vitamin D level decreased significantly with advancement in stages of PD (p<0.01).*

Conclusion: *Patients who had low vitamin D level was associated with more advanced stage of PD.*

Key words: *Parkinson's disease, motor symptoms, vitamin D level.*

BIRDEM Med J 2024; 14(2): 75-80
DOI: https://doi.org/10.3329/birdem.v14i2.73305

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Received: October 25, 2023
Revision received: April 15, 2024
Accepted: April 30, 2024

INTRODUCTION

Parkinson's disease (PD) is the second most common neurodegenerative disease; it affects 1–2/1000 population. The prevalence of PD increases with age; it affects 1% of the population over the age of 60.[1] PD also known as Paralysis Agitans is a common disease, known from ancient times, first described by James Parkinson in 1817. Movement Disorder Society Clinical Diagnostic Criteria for Parkinson's disease (MDS-PD) criteria is the diagnosis of Parkinsonism, which is based on three cardinal motor manifestations and defined Parkinsonism as bradykinesia, in combination with either rest tremor, rigidity, or both. In Bangladesh, among various symptoms of PD, the prominent symptoms were voice disorders (96%), slowness of movement (90%), mask-like face expression (86%), tremor (80%), sensory

and sleep difficulties (78%), excessive sweating (60%) and insomnia (56%).[2]

Several epidemiologic studies have suggested an inverse relationship between circulating vitamin D levels and the risk of PD. Serum level of vitamin D is significantly lower in patients with PD compared to healthy controls[3-5]. In a meta-analysis on the relationship between the vitamin D level and PD that included 20 studies (1 interventional, 14 observational, and 5 rodent studies), serum levels of 25(OH)D in PD patients were lower than in controls and higher levels of vitamin D were associated with better motor functions in most of the included studies.[6] Moreover, higher levels of vitamin D in PD patients were associated with better mood and cognitive function.[7] Vitamin D is proposed to alter cholinergic, dopaminergic, and noradrenergic neurotransmitter pathways in the central nervous system (CNS). Furthermore, vitamin D may play a role in neuronal plasticity and axogenesis.Several studies demonstrated that vitamin D ameliorates synthesis of neurotrophic factors and detoxification pathways which protect the integrity and structure of neurons.[8] Furthermore, vitamin D was assumed to have a neuroprotective effect on dopaminergic pathways in the CNS. Accumulating studies reported that the distribution of vitamin D receptors (VDR) in the substantia nigra is altered in patients with Parkinson's disease.[9] It has been demonstrated that vitamin D plays a role in dopamine synthesis through regulation of tyrosine hydroxylase gene expression.[10] Despite the accumulating biological and epidemiological data which revealed that vitamin D deficiency contributes in the development of Parkinson's disease, it is a debate if this relation is a direct effect or that patients suffering from Parkinson's disease mostly have decreased ambulation and sun exposure and, as a sequence, higher prevalence of vitamin D deficiency.[9,11]

Parkinson's disease is associated with substantial public health and economic burdens, which are expected to increase in the future with a rapidly growing older population. Identification of modifiable risk factors may therefore have important public health implications. Multiple epidemiological studies have shown that relative to controls, PD cases have lower serum/plasma levels of 25-hydroxyvitamin D (25(OH) D). Several studies concluded that, higher level of vitamin D in patients of Parkinson's disease were associated with better motor function.[3-7] The aims of this study are to assess the serum vitamin D level in patients with Parkinson's disease and to investigate the possible relationship between the serum vitamin D level and motor symptoms in PD.

METHODS

Study design

This cross-sectional study was conducted in the Department of Neurology, BIRDEM General Hospital from 1st July, 2022 to 30th June, 2023. The adultpatients who attended neurology OPD or admitted in neurology department were recruited for the study. Convenient sampling method was used. Sixty patients with PD were taken and 60 age and sex matched sample of healthy controls from the attendant of respective patients were taken. Patients who fulfilled the criteria for diagnosis of idiopathic PD based on the British Brain Bank criteria[12], age matched control group and who gave consent for the study were recruited. Patients with visual impairment or hearing loss affecting their ability to complete the tests, patients with secondary Parkinsonism, Parkinson's plus syndrome, clinically overt dementia, history of alcohol intake or drug abuse, major psychiatric disorders, structural brain lesions in an Magnetic Resonance Imaging/Computed Tomography (MRI/CT) scan study, patients on vitamin D supplements or medications that affect the vitamin D level, chronic kidney disease, malabsorption syndromewere excluded.

Study procedure

All collected data was checked very carefully to identify any error in collecting data. Data processing work consisted of registration of schedules, editing, coding-recoding and computerization, preparation of dummy tables, analysis and matching data. The technical matter of editing, encoding and computerization was followed up by investigator. Before commencement of the study, formal ethical approval was taken from the Institutional Review Board (IRB) of BIRDEM General Hospital, Dhaka. Face to face interview was conducted by using a semi-structured questionnaire containing socio-demographic parameters, clinical presentations and relevant information was collected from all the participants, reports of certain investigations including vitamin D level was collected from participant's clinical records. Clinical neurological examination including H&Y staging was performed and the findings were recorded for each PD cases.

Statistical analysis

Results were expressed by appropriate tables, figures. Data was compiled and analyzed by using SPSS version 24.0 (SPSS Inc., Chicago, IL, USA). Continuous variables were expressed as mean (standard deviation) and categorical variables as frequencies and percentages. Comparison were done by Chi-Square (χ^2) test and Fisher Exact test for categorical variable and independent student t-test and one-way ANOVA and Post-Hoc analysis for continuous variable where necessary. A probability (p) value of < 0.05 ($p<0.05$) was considered statistically significant.

RESULTS

A total of 120 patients were enrolled in the study. Among them 60 patients with PD were in case group and 60 age and sex matched sample was healthy controls. Majority of the patients were aged between 61 to 80 years in both case (66.7%) and control (70%) groups. Mean age of the cases and controls was 67.98±10.4 years and 69.43±10.1 years respectively. No significant difference in age was observed between two groups ($p>0.05$). Among all, in case group 56.7% (n=34) were male and in controls group 61.7% (n=37) were male. Regarding gender, no significant difference was observed between two groups (p=0.577). In both case and control group, most of the patients were married, completed higher secondary examination, and from a medium income group (Table I).

Table I. Distribution of the study participants according to the sociodemographic profile (N=120).

Variables	Case-group (N=60) N (%)	Control-group (N=60) N (%)	P value
Marital status			
Married	48 (80)	46 (76.7)	0.658*
Widow	12 (20)	14 (23.3)	
Educational status			
Illiterate	5 (8.3)	7 (11.7)	0.887*
Primary education	7 (11.7)	5 (8.3)	
SSC	21 (35)	18 (30)	
HSC	19 (31.7)	21 (33.3)	
Graduation and above	8 (13.3)	10 (16.7)	
Occupation			
Service-holder	8 (13.3)	6 (10)	0.697**
Business	3 (5)	4 (6.7)	
Housewife	21 (35)	18 (30)	
Labor	3 (5)	7 (11.7)	
Unemployed	25 (41.7)	25 (41.7)	
Socio-economic status[13]			
Low income (d"20,600) ref	12 (20)	18 (30)	0.091*
Medium income(20600-51,600)	36 (60)	24 (40)	
High income(>51,600)	12 (20)	18 (30)	
Cases group: PD patients.			
Control group: Healthy controls.			

p-value was determined by *Chi-square test and **Fisher Exact test. Data Expressed in column.

Regarding comorbidities, no significant difference was observed between two groups (p>0.05).28.3% and 25% of the case and controls had HTN respectively. Family history of PD was 31.7% and 11.7% in PD patients and healthy controls respectively (p=0.007).

Mean serum 25 hydroxy vitamin D level in cases was 25.97±3.44 ng/ml and in controlswas 38.47±5.08 ng/ml. Mean vitamin D level was significantly lower among the patients with PD compared to controls (p<0.01). Vitamin D deficiency and insufficiency was significantly associated with PD (p<0.01), 5% and 78.3% of the patients had vitamin D deficiency and insufficiency compared to 1.7% in healthy controls respectively (Table II).

Table II. Distribution of the study participants according to vitamin D level (N=120)

Serum 25 hydroxy vitamin D level (ng/ml)	Case-group (N=60) N (%)	Control-group (N=60) N (%)	p-value
Deficient (<20)	3(5)	1(1.7)	<0.01
Insufficient (20-30)	47(78.3)	1(1.7)	
Sufficient (30-100)	10(16.7)	58(96.7)	

*p-value obtained by chi-square test.

Among all the cases of PD, 90% had bradykinesia, 85% had tremor, 71.7% had rigidity and 70% had Postural instability (Table III). Majority had duration of disease <5 years (58.3%). According to Modified Hoehn and Yahr score 53.3% patients were in stage 1-2, 26.7% in stage 2.5-3 and 20% in stage >3.

Table III. Clinical presentation of patients with PD (N=60)

Clinical presentation	Frequency	Percentage
Cardinal features of disease		
Tremor	51	85
Rigidity	43	71.7
Bradykinesia	54	90
Postural instability	42	70
Duration of the disease		
<5	35	58.3
5-10	22	36.7
>10	3	5
Modified Hoehn andYahr score		
1-2	32	53.3
2.5-3	12	26.7
>3	16	20

Vitamin D level significantly decreased with the advancing stage of Parkinson's disease patients (p<0.01), the mean vitamin-D level was 28.43±2.43, 24.06±1.57 and 21.92±1.62 in stage 1-2, stage 2.5-3 and stage>3 respectively (Table IV).

Table IV. Association of serum 25 hydroxy vitamin D level with different stages of Parkinson's disease patients (N=60)

Variable	Serum 25-hydroxy vitamin D level((ng/ml)
Stage 1-2Mean±SD	28.43±2.43
Stage 2.5 to 3Mean±SD	24.06±1.57#
Stage >3Mean±SD	21.92±1.62
p-value*	<0.01

*p-value was determined by one-way ANOVA.

#denotes significant difference between stage 1-2 vs stage 2.5 to 3 and stage >3 and @denotes significant difference between stage 2.5 to 3 vs stage >3, determined by Post-Hoc analysis of Bonferroni test.

DISCUSSION

PDis a progressive neurological condition characterized by resting tremor, rigidity, bradykinesia and postural instability. Neurotransmission in dopaminergic neural circuits is one biological activity in the central nervous system that is significantly impacted by vitamin D. Vitamin D levels in PD patients were shown to be lower than in healthy controls in a number of studies.[14]

Majority of the patients were aged between 61 to 80 years in both case (66.7%) and control (70%) groups. Majority of the cases and controls were male.Another study also found older age and male predominant among the PD patients. Ageing remains the biggest risk factor for developing Parkinson's disease.[15]

Mean serum 25 hydroxy vitamin D levels in cases was 25.97±3.44 ng/ml and in controls 38.47±5.08 ng/ml. Mean vitamin D level was significantly lower among the Case groups.Similar study revealed a strong association between hypovitaminosis D and PD.[14] Another study described that mean serum 25(OH)D concentrations were lower in PD than control participants (44.1±21.7 vs. 52.2±22.1 nmol/L, p < 0.05).A study also revealed that vitamin D has a significant impact on Parkinson's

disease.[16] Beyond regulating calcium homeostasis and bone metabolism, vitamin D has extensive impacts on a wide range of systems and tissues, including the CNS. There are accumulating evidences supporting the role of vitamin D deficiency in the pathogenesis of PD. Long-standing low vitamin D levels may lead to chronic loss of dopaminergic neurons in the central nervous system and, as a consequence, the development of Parkinson's disease.[17]

Among all the cases, 90% hadBradykinesia, 85% had tremor, 71.7% had rigidity and 70% had Postural instability.According to Modified Hoehn and Yahr score 53.3% patients were in stage 1-2 followed by stage 2.5-3 (26.7%) and stage >3 (20%). A similar study revealed that, most of the patients presented in Hoehn and Yahr stages 1 (37.5%) and 2 (42.8%); there were fewer patients in stages 3–5 (19.7%).In another study, majority of patients were in H&Y stages 3 and 4 (37.1% and 14.4%, respectively); 3.5% of the patients were in H&Y stage 5.Stages of PD depends on the enrolled patients during the study period.[18]

Current study revealed that Vitamin D level significantly decreases with the increased stage of Parkinson's disease patients which was similar to a previous study.[19]A relevant study also revealed that Vitamin D deficiency seems to be related to disease severity and disease progression.[7]It was observed in another study that Vitamin D deficiency was significantly associated with disease severity of PD.[14]

Conclusion

In summary, this study results showed that patients who have had more advance stage of PD had lower serum vitamin D levels. These study findings provide evidence to evaluate the role of vitamin D in the progression of PD. Importance should also be given for recognition and management of motor symptoms in PD patients, since these symptoms have an impact of patient's quality of life. Furthermore, multicenter study is recommended to understand the role of vitamin D level in the progression of PD.

Authors' contribution: MSKH, MRI, JUA planned the study. MSHK drafted manuscript. All authors approved final version.

Funding: None

Conflicts of interest: Nothing to declare.

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