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Relationship between 25-Hydroxyvitamin D, bone density, and Parkinson's disease symptoms

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Objectives: Vitamin D deficiency is widespread in patients with Parkinson's disease (PD). Our aim was to determine whether serum vitamin D levels correlated with bone mineral density (BMD) and non-motor symptoms in patients with PD.

Materials & Methods: A consecutive series of 182 patients with PD and 185 healthy controls were included. Serum 25-hydroxyvitamin D (25[OH]D) levels were measured by immunoassay, while BMD of the lumbar spine and femoral neck was measured by dual-energy X-ray absorptiometry. Associations between serum vitamin D levels and clinical data were evaluated using partial correlation analysis.

Results: Patients with PD had significantly lower serum 25(OH)D levels relative to healthy controls (49.75 ± 14.11 vs 43.40 ± 16.51, $P < 0.001$). Furthermore, PD patients with lower vitamin D levels had a significantly higher frequency of falls ($P = 0.033$) and insomnia ($P = 0.015$). They also had significantly higher scores for the Pittsburgh Sleep Quality Index (PSQI; $P = 0.014$), depression ($P = 0.020$), and anxiety ($P = 0.009$). Finally, patients with PD also had a significantly lower mean BMD of the lumbar spine ($P = 0.011$) and femoral neck ($P < 0.001$). After adjusting for age, sex, and body mass index, vitamin D levels significantly correlated with falls, insomnia, and scores for the PSQI, depression, and anxiety.

Conclusions: In patients with PD, vitamin D levels significantly correlated with falls and some non-motor symptoms. However, no associations were found between BMD and the serum 25(OH)D levels in patients with PD. Thus, vitamin D supplementation is a potential therapeutic for non-motor PD symptoms.

KEYWORDS
bone mass density, non-motor symptoms, Parkinson's disease, vitamin D

1 | INTRODUCTION

The importance of vitamin D deficiency in Parkinson's disease (PD) patients and bone health was explored by several studies. The vitamin D levels and bone mass of patients with PD were reduced relative to healthy controls.[1,2] And Newmark proposed that a lack of vitamin D might affect PD pathogenesis.[3]

Vitamin D levels are commonly defined as deficient at <20 ng/mL, insufficient at 20-30 ng/mL, and sufficient at >30 ng/mL.[4] Importantly, vitamin D deficiency is widespread in patients with PD. Indeed, Evatt et al previously showed that vitamin D insufficiency occurs in 55% of patients with PD, 41% of Alzheimer's Disease (AD) patients, and in only 36% of a control population, suggesting that patients with PD have a higher incidence of vitamin D insufficiency.[1] Although epidemiological studies have investigated the relationship between PD progression and vitamin D levels, the results have been controversial.

Hui-Jun Zhang and Jin-Ru Zhang equally contributed to this manuscript.

Some case-control studies have reported a higher prevalence of vitamin D deficiency in patients with PD than in controls.[1,5,6] Furthermore, Suzuki's study found that vitamin D3 supplementation may stabilize PD with the Hoehn & Yahr stage (H&Y) and UPDRS scores for a short period.[7] Alternatively, Evatt et al found that vitamin D levels and PD progression did not correlate after an 18-month follow-up.[5] To be more important, in a prospective study, no significant association between serum 25(OH)D and PD risk was found among those participants identified as PD and non-PD during 17-year follow-up.[8]

Furthermore, these previous studies only focused on one or two aspects of PD and did not include facets such as non-motor symptoms. Importantly, non-motor symptoms in patients with PD can seriously limit quality of life. Vitamin D has a vital role in bone metabolism, and a lack of vitamin D is correlated with an increased risk of falls and fractures,[4] which can increase hospitalization, and even fatal disability rate in patients with PD.[9] Severe vitamin D deficiency may contribute to this reduced bone mineral density (BMD) by causing osteomalacia and secondary hyperparathyroidism, which increase bone turnover and bone loss.[4] Studies have also shown that vitamin D levels are associated with cognition and mood in patients with PD.[10] Finally, recent studies have found that vitamin D levels are associated with gastrointestinal dysfunction, mainly delayed gastric emptying time.[11]

Thus, while there is potential for vitamin D deficiency to affect several clinical symptoms of PD, the relationship between these variables remains unclear. Here, we sought to determine the relationship between vitamin D levels and the non-motor symptoms of PD by performing extensive clinical evaluations and vitamin D measurements in patients with PD.

2 | MATERIALS & METHODS

2.1 | Participants

Patients were consecutively recruited from the Department of Neurology at the Second Affiliated Hospital of Soochow University from March 2014 to December 2017. A total of 381 subjects, comprised of 193 patients with PD and 188 age- and sex-matched healthy controls (HC), were recruited. All patients with PD were diagnosed according to the United Kingdom PD Society Brain Bank clinical diagnosis criteria. Patients with secondary parkinsonism syndrome, atypical parkinsonian syndrome, and other diseases based on the Diagnostic Statistical Manual-IV criteria were excluded. Subjects taking vitamin D supplements were also excluded. This resulted in a total of 182 patients with PD and 185 HC. This study was approved by the Ethics Committee of the Second Affiliated Hospital of Soochow University. All subjects signed written informed consent prior to participation.

2.2 | Clinical assessment

Demographic information and clinical characteristics were collected from all patients, including age at onset, sex, disease duration, medical history, and medications. Motor manifestations were evaluated by UPDRS total and part III scores in the "off" state. Patients with PD (LEDD) were calculated according to Tomlinson et al[12] Patients were asked to record if they had experienced falls in the previous month. To evaluate the non-motor symptoms of PD, cognition was assessed by the Mini-Mental State Examination (MMSE) and the Montreal Cognitive Assessment (MoCA). Depression and anxiety were assessed using the Hamilton Depression Rating Scale (HAM-D) and the Hamilton Anxiety Rating Scale (HAM-A), respectively. Quality of sleep was assessed using the Pittsburgh Sleep Quality Index (PSQI). The Fatigue Severity Scale and Parkinson's Disease Questionnaire-39 (PDQ-39) were used to evaluate fatigue and quality of life, respectively. Rapid eye movement (REM) sleep behavior disorder (RBD) was diagnosed using the RBD-Screening Questionnaire (RBDSQ), with a cutoff score of 7.

2.3 | 25(OH)D measurements

Serum levels of 25 hydroxyvitamin D3 (25[OH]D) were quantified using an electrochemiluminescence immunoassay (Cobas-Roche) according to the manufacturer's instructions. Levels of 25(OH)D were divided into tertiles: 1st tertile, <35.0 nmol/L; 2nd tertile, 35.0-47.5 nmol/L; and 3rd tertile, >47.5 nmol/L. Because seasonality can affect 25 hydroxyvitamin D3 levels, we recorded the season for every sample and divided these into two groups defined as Jan-Jun and Jul-Dec.

2.4 | Bone mass measurements

Bone mineral density of the lumbar spine and the femoral neck were measured using dual-energy X-ray absorptiometry (DXA; Lunar Inc). Results were expressed as T-scores and Z-scores. BMD was analyzed in units of g/cm^2, which the instrument then converted to T- and Z-scores. The difference between an individual's BMD and the mean for a reference population was expressed in standard deviation (SD) units. T-scores were the SD of the individual BMD relative to the mean BMD in a young healthy population. Z-scores were compared to a similar sex-, age-, weight-, and height-matched population. The diagnostic criteria for osteoporosis were according to World Health Organization recommendations, as normal ($T \geq -1$), osteopenic ($-2.5 < T \leq -1$), or osteoporotic ($T \leq -2.5$). Height and weight were registered, and body mass index (BMI) was calculated.

2.5 | Statistical analysis

Data were analyzed using SPSS software version 19.0. Visual inspection of histograms was used to confirm data normality. Continuous variables were represented as the mean ± standard deviation (SD) or median (interquartile range [IQR]). Comparisons were performed using independent Student's *t* tests or chi-square tests for comparisons between groups. For the non-normal distribution variants, Mann-Whitney test was used for comparisons between groups.

Analysis of variance (ANOVA) or chi-square tests was used for comparisons of continuous and categorical data, respectively. Pearson and Spearman correlation analyses were used to analyze the correlations between 25(OH)D levels and clinical symptoms. All *P*-values were two-tailed, and a significance level of 0.05 was used.

3 | RESULTS

Serum 25(OH)D levels and BMD were available for 367 subjects, which included 182 patients with PD and 185 HC. Subject demographic information is shown in Table 1. Patients with PD had significantly lower BMI (24.51 ± 3.00 vs 23.29 ± 3.19, $P < 0.001$) and serum 25(OH)D levels (49.75 ± 14.11 vs 43.40 ± 16.51, $P < 0.001$) relative to HC. In terms of the group distribution of 25(OH)D levels, both groups had a similar percentage of participants with moderately low 25(OH)D levels (<75 nmol/L). However, patients with PD had a significantly higher percentage of individuals with low 25(OH)D (<50 nmol/L) levels relative to HC (68.68% vs 54.05%, $P = 0.004$).

3.1 | Clinical characteristics for serum 25(OH)D level tertiles

Demographic information and clinical features of the 25(OH)D level tertiles are presented in Table 2. The tertiles did not differ based on disease duration, motor symptoms, and cognitive function. However, PD patients with lower serum 25(OH)D levels had a significantly higher frequency of falls ($P = 0.033$), insomnia ($P = 0.015$) and higher mean scores for the PSQI ($P = 0.014$), HAM-A ($P = 0.009$), and HAM-D ($P = 0.020$) among three groups. The 1st tertile group also had a significantly higher frequency of falls ($P = 0.011$), insomnia ($P = 0.005$) and had significantly higher mean scores for the PSQI ($P = 0.008$), depression ($P = 0.005$), and anxiety ($P = 0.006$) compare with the 3rd tertile. The 2nd tertile group had a higher mean anxiety score compare with the 3rd tertile. Finally, the frequency of hyposmia, constipation, pain, and RBD was comparable between PD and HC.

TABLE 1 Demographics and 25(OH)D levels in PD patients and HC

	PD (n = 182)	HC (n = 185)	*P*
Age, y	65.38 ± 10.16	64.75 ± 6.15	0.468
Sex, M (%)	90 (49.45)	98 (52.97)	0.500
BMI, kg/m^2	23.29 ± 3.19	24.51 ± 3.00	**<0.001**
Season (Jan-Jun), n (%)	108 (59.34)	119 (64.32)	0.326
25(OH)D, nmol/L	43.40 ± 16.51	49.75 ± 14.11	**<0.001**
<50 nmol/L, n (%)	125 (68.68)	100 (54.05)	**0.004**
<75 nmol/L, n (%)	173 (95.05)	176 (95.14)	0.972

Data are mean ± standard deviation or median (interquartile range).
Abbreviations: BMI, body mass index; HC, healthy controls; M, male; PD, Parkinson's disease; y, year.
Significant differences ($P < 0.05$) are represented in bold.

3.2 | Bone mass comparisons between HC and PD patients by 25(OH)D levels

Table 3 shows the mean BMD of the lumbar spine and femoral neck for patients with PD and HC. Relative to HC, patients with PD had a significantly lower mean BMD in the lumbar spine ($P = 0.007$) and femoral neck ($P < 0.001$). L Z-score was not significant among the two groups ($P = 0.085$). However, there were no differences in BMD among the 25(OH)D tertiles of patients with PD.

3.3 | Correlation between serum 25(OH)D levels and clinical characteristics in PD patients

We next evaluated the correlations between serum 25(OH)D levels and clinical characteristics in patients with PD. As shown in Table 4, after adjusting for age, sex, and BMI, serum 25(OH)D levels significantly correlated with falls ($r = -0.187$, $P = 0.011$). Additionally, serum 25(OH)D levels negatively correlated with insomnia ($r = -0.230$, $P = 0.002$) and scores for the PSQI ($r = -0.195$, $P = 0.045$), HAM-D ($r = -0.244$, $P = 0.007$), and HAM-A ($r = -0.255$, $P = 0.012$). No significant difference was found about the association between 25(OH)D level and disease duration or UPDRS scores.

4 | DISCUSSION

Among patients with PD, vitamin D deficiency is widespread and is thought to contribute to PD pathogenesis. While previous studies have evaluated the relationship between vitamin D and various PD symptoms,[13-16] these studies focused on only one or two aspects of PD. Furthermore, the results of these studies were controversial. Here, we clearly identified associations between serum vitamin D levels and some non-motor symptoms in patients with PD. Specifically, our three primary findings were as follows: (a) patients with PD had lower serum 25(OH)D levels compared to HC; (b) PD patients with low serum 25(OH)D levels had a higher frequency of falls, sleep problems, depression, and anxiety; and (c) patients with PD had a significantly lower mean BMD in the lumbar spine and femoral neck relative to HC. Together, these results indicate that vitamin D deficiency may play a role in PD pathogenesis, while vitamin D supplementation may be used to treat the non-motor symptoms of PD.

Considering the possible neuroprotection action of vitamin D, we revised the discussion as follows. Epidemiological studies suggested that vitamin D deficiency is common in PD. Some mechanisms may underline the role of vitamin D in the pathogenesis of PD. As vitamin D exerts its biological functions by binding with vitamin D receptor (VDR), studies found VDR genetic variants impact bioactivities of vitamin D and also involved in the development of PD.[17] Recent studies found vitamin D3 deficiency can provoke development of neurological consequences by changing glutamate/GABA

TABLE 2 Clinical characteristics of PD patients by serum 25(OH)D level tertiles

	Level of 25(OH)D			
	1st tertile (<35.0 nmol/L)	2nd tertile (35.0-47.5 nmol/L)	3rd tertile (>47.5 nmol/L)	*P*
Age (y)	67.97 ± 11.14	64.41 ± 9.67	63.77 ± 9.32	**0.049**
Sex, M (%)	36 (59.00)	25 (40.98)	29 (96.67)	0.134
BMI, kg/m^2	23.18 ± 2.95	23.24 ± 3.40	23.46 ± 3.27	0.884
Season (Jan-Jun), n (%)	34 (55.73)	38 (62.30)	36 (60.00)	0.756
Disease duration (y)	5.20 ± 3.39	4.93 ± 3.91	4.70 ± 2.83	0.725
25(OH)D	26.42 ± 4.28	41.84 ± 3.23	61.58 ± 12.14	**<0.001**
LEDD	350.0 (200.0-512.5)	300.0 (150.0-493.8)	300.0 (200.0-539.06)	0.365
UPDRS III	24.64 ± 13.62	23.05 ± 11.55	23.13 ± 11.45	0.723
UPDRS total	41.44 ± 20.37	39.41 ± 16.67	39.55 ± 17.72	0.792
Falls, n (%)	30 (49.18)	21 (34.43)	16 (26.67)	**0.033****
H & Y	2.5 (2.0-3.0)	2.00 (2.0-2.5)	2.0 (1.5-2.5)	0.500
MMSE	24.50 ± 4.04	24.68 ± 4.96	25.48 ± 4.73	0.486
MoCA	20.68 ± 4.03	20.89 ± 5.70	21.85 ± 5.75	0.480
FSS	2.89 (1.00-4.00)	2.38 (2.00-3.59)	2.00 (1.10-4.00)	0.439
PSQI	7.00 (4.00-12.00)	7.00 (4.00-10.00)	4.00 (3.00-6.00)	**0.014***
HAM-D	10.00 (6.00-16.00)	8.00 (4.00-12.00)	5.50 (2.25-12.00)	**0.020***
HAM-A	9.00 (3.25-13.00)	7.00 (4.00-11.00)	5.00 (2.00-7.50)	**0.009*,****
PDQ-39	28.50 (12.25-35.75)	25.00 (8.00-35.00)	23.00 (7.00-37.50)	0.586
Hyposmia, n (%)	35 (57.38)	31 (50.82)	29 (48.33)	0.588
Constipation, n (%)	34 (55.74)	33 (54.10)	30 (50.00)	0.809
Pain, n (%)	24 (39.34)	24 (39.34)	23 (38.33)	0.991
RBD, n (%)	34 (55.74)	33 (54.10)	30 (50.00)	0.809
Insomnia, n (%)	29 (47.54)	26 (42.62)	14 (23.33)	**0.015***

Data are mean ± standard deviation or median (interquartile range).
Abbreviations: BMI, body mass index; FSS, Fatigue Severity Scale; H & Y, Hoehn-Yahr scale; HAM-A, Hamilton Anxiety Rating Scale; HAM-D, Hamilton Depression Rating Scale; LEDD, levodopa equivalent daily dose; M, male; MMSE, Mini-Mental State Examination; MoCA, Montreal Cognitive Assessment; PD, Parkinson's disease; PDQ-39, Parkinson's Disease Questionnaire-39; PSQI, Pittsburgh Sleep Quality Index; RBD, rapid eye movement sleep behavior disorder; UPDRS, Unified Parkinson's Disease Rating Scale; y, year.
Significant differences ($P < 0.05$) are represented in bold.
*$P < 0.016$ after Bonferroni correction compared with the 1st and 3rd tertile.
**$P < 0.016$ after Bonferroni correction compared with the 2st and 3rd tertile.

transporter expressions and excitation/inhibition balance.[18] A meta-analysis study[19] found, in rodent models of PD, vitamin D treatment could protect dopaminergic neurons in the substantia nigra by attenuating neuroinflammation and anti-oxidative stress.[20,21] However, the pathogenic role of vitamin D deficiency is far from certain. Some studies insisted no difference in the striatal dopamine levels and other markers of cell death after lesioning in vitamin D-depleted mice.[22,23]

Several studies have investigated the relationship between low vitamin D levels and the risk of PD onset. For example, reduced vitamin D levels can occur in the early stages of disease, even prior to disease onset. Evatt et al found that vitamin D deficiency is present in patients with early and untreated PD.[5] Furthermore, the risk of PD significantly increases as vitamin D levels decrease.[24] Importantly, this phenomenon is complex and can be affected by intake of vitamin D-rich foods[25] and sunlight exposure at different latitudes, longitudes, and skin colors.[26-29]

In this study, patients with PD had significantly lower serum 25(OH)D levels and mean BMD relative to HC. However, serum 25(OH)D levels and BMD in patients with PD did not significantly correlate. Indeed, the relationship between vitamin D levels and BMD is controversial. While some studies have demonstrated that

TABLE 3 Comparisons of bone mineral density between HC and PD patients by serum 25(OH)D level tertiles

				PD			
	HC	PD	*P*	1st tertile (<35.0 nmol/L)	2nd tertile (35.0-47.5 nmol/L)	3rd tertile (>47.5 nmol/L)	*P'*
LBMD, g/cm^2	1.06 ± 0.18	1.00 ± 0.20	**0.007**	1.05 ± 0.22	0.96 ± 0.18	0.99 ± 0.20	0.200
L T score	−0.50 (−1.40,0.80)	−1.00 (−2.25,0.55)	**0.010**	−0.40 (−2.20,0.90)	−1.50 (−2.40,0.10)	−1.10 (−1.85,0.30)	0.239
L Z-score	0.80 (0.00,1.50)	0.40 (−0.30,1.40)	0.085	0.90 (−0.15,2.05)	0.30 (−0.90,1.40)	0.30 (−0.20,1.18)	0.130
FBMD, g/cm^2	0.89 ± 0.14	0.81 ± 0.14	**<0.001**	0.81 ± 0.13	0.82 ± 0.14	0.80 ± 0.16	0.932
F T-score	−0.70 (−1.30,0.20)	−1.30 (−1.90,0.50)	**<0.001**	−1.30 (−1.75,0.75)	−1.10 (−2.10, −0.30)	−1.30 (−2.10, −0.45)	0.901
F Z score	0.50 (0.00,1.10)	0.20 (−0.40,0.80)	**<0.001**	0.30 (−0.30,0.75)	0.20 (−0.53,0.83)	0.15 (−0.38,0.85)	0.809

Data are mean ± standard deviation or median (interquartile range).
P comparison between PD and HC groups; *P'* comparison among tertiles of PD patients.
Abbreviations: F T-score, femoral neck T-score; F Z score, femoral neck Z-score; FBMD, femoral neck bone mineral density; HC, healthy controls; L T score, lumbar spine T-score; L Z-score, lumbar spine Z-score; LBMD, lumbar spine bone mineral density; PD, Parkinson's disease.
Significant differences ($P < 0.05$) are represented in bold.

TABLE 4 Correlation coefficients between serum 25(OH)D levels and clinical characteristics in PD patients

	Level of 25(OH)D	
	Coefficient	*P*
Age	−0.177	0.017
Sex	0.083	0.263
Disease duration	−0.073	0.327
UPDRS III	−0.034	0.649
UPDRS total	−0.035	0.635
LEDD	0.045	0.546
Fall	−0.187	**0.011**
H & Y	0.275	0.182
MMSE	0.152	0.050
MoCA	0.109	0.185
FSS	−0.100	0.367
PSQI	−0.195	**0.045**
HAM-D	−0.244	**0.007**
HAM-A	−0.255	**0.012**
PDQ-39	−0.149	0.172
Hyposmia	−0.117	0.115
Constipation	−0.066	0.373
Pain	−0.029	0.700
RBD	−0.045	0.544
Insomnia	−0.230	**0.002**

Abbreviations: BMI, body mass index; FSS, Fatigue Severity Scale; H & Y, Hoehn-Yahr scale; HAM-A, Hamilton Anxiety Rating Scale; HAM-D, Hamilton Depression Rating Scale; LEDD, levodopa equivalent daily dose; MMSE, Mini-Mental State Examination; MoCA, Montreal Cognitive Assessment; PD, Parkinson's disease; PDQ-39, Parkinson's Disease Questionnaire-39; PSQI, Pittsburgh Sleep Quality Index; RBD, rapid eye movement sleep behavior disorder; UPDRS, Unified Parkinson's Disease Rating Scale.
Significant differences ($P < 0.05$) are represented in bold.

BMD positively correlates with serum 25(OH)D status,[30,31] others report no correlation,[32,33] even in the middle-aged and older Chinese populations living in Asia.[34]

Several factors may underlie the decreased bone density in patients with PD. For example, PD can lead to malnutrition, weight loss, and decreased muscle strength, all of which may lower BMD[35]; in addition, hyperhomocysteinaemia due to levodopa intake is common in PD and is associated with fracture risk and a low BMD.[36] Previous studies have also reported that physical performance may be related to bone density in ambulatory patients with PD.[37] Bone density is reflected by lower extremity strength and gait. PD patients with lower BMD are also at a higher risk of fractures.[38] Here, we found that PD patients with lower vitamin D levels had a higher percentage of falls. Few studies have evaluated the relationship between vitamin D levels and balance, cognition, and emotion. Importantly, Peterson et al showed that balance control negatively correlated with vitamin D levels.[13] A study in Iran also found that reduced vitamin D levels are associated with more severe postural instability, freezing gait, and postural abnormalities.[39] It is interesting that, in our results, the incidence of falls was higher in patients with lower vitamin D levels, while the scores of UPDRS and H&Y were not significant. The most commonly cited theory for the connection between falls and vitamin D levels is related to reduced muscle mass and strength.[35] According to the previous studies and our results, it is indicated that vitamin D concentrations did not decline during progression of PD but patients with lower 25(OH)D levels might had higher prevalence of falls, and some non-motor symptoms.[5,40] And further studies with larger sample size might find the difference of UPDRS and H&Y scores between the three PD groups with different 25(OH)D levels. Here, we evaluated the relationship between vitamin D levels, BMD, and prevalence of falls in patients with PD. However, more replications are needed to confirm pathogenesis.

Mood disorders are common non-motor symptoms in patients with PD. Such disorders can impair patient quality of life. In our

study, patients with lower vitamin D levels had significantly higher scores on the PSQI, HAM-D, and HAM-A. A previous study evaluating neuropsychological function in patients with PD found that vitamin D levels positively correlated with verbal fluency and verbal memory, but negatively correlated with depression.[10] This negative correlation between vitamin D levels and anxiety in patients with PD is novel. However, several studies have previously reported that vitamin D status is associated with depression and anxiety in healthy adults.[41,42] Though the association between vitamin D and mood is clear, the underlying mechanism and causality remains unknown. Therefore, future research is needed to better define this relationship. The connection between vitamin D and sleep disorders is also controversial. McCarty et al observed lower vitamin D levels in PD patients with sleep disorders, which is consistent with our results.[43] This suggests that sleep latency and duration could be improved by vitamin D supplementation.[44] The vitamin D receptor (VDR) and the enzyme associated with synthesis of the active form of the hormone 1α-hydroxylase have been mapped in the human brain. These molecules may be involved in sleep regulation.[45]

Our study had several limitations. First, there are different sources of vitamin D, so different forms of vitamin D could potentially be detected. In this study, we only evaluated 25(OH)D levels. Second, our study had a relatively small sample size and was cross-sectional. We did not test the serum calcium, phosphate, or parathyroid hormone levels. Future studies with a larger sample size tested those blood parameters may be needed to better understand the role of vitamin D levels in patients with PD. Third, pair-test in the PD and controls should be performed to improve the reliability, and more replications with pair-test are needed to explain the association between 25(OH)D levels and PD risk. Overall, these data support further study of vitamin D supplementation for its possible benefits on both the clinical symptoms and quality of life of patients with PD.

In conclusion, vitamin D levels and clinical symptoms were correlated in patients with PD, suggesting that vitamin D plays an important role in PD pathogenesis.

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CONFLICT OF INTERESTS

There is no conflict of interest to be disclosed.

DATA AVAILABILITY

The data used to support the findings of this study are available from the corresponding author upon request.

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