



(RESEARCH ARTICLE)



## Effects of vitamin D on motor symptoms and cognitive functions in people with Parkinson's disease

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### Abstract

**Aim of the study:** Parkinson's disease is the second most common neurodegenerative disorder. The present study investigates the role of vitamin D deficiency thought to be one of the etiopathological and modifying factors in Parkinson's disease that is known to be multifactorial.

**Materials and Methods:** Designed as a retrospective review of medical records, this study compares the serum vitamin D levels of the idiopathic Parkinson's disease patients with and without dementia to those of the healthy individuals with no metabolic/degenerative disorders. It also investigates the relationship between the patients' Standardized Mini-Mental State Examination (SMMSE) and the Unified Parkinson's Disease Rating Scale (UPDRS) scores and serum vitamin D levels to show the effects of vitamin D on motor symptoms and cognitive functions.

**Results:** In this study, we compared the serum vitamin D levels of 40 Parkinson's disease patients and 15 Parkinson's disease patients with dementia to those of the control group comprising 30 healthy individuals. Vitamin D levels were  $21,4 \pm 15,9$  ng/mL in the control group;  $16,5 \pm 6,4$  ng/mL in Parkinson's disease patients and  $13,8 \pm 4,5$  ng/mL in Parkinson's disease patients with dementia. All the patient groups had significantly lower vitamin D levels than the control group ( $p < 0,005$ ). Within the Parkinson's disease group, furthermore, the dementia group had lower vitamin D levels than the non-dementia group. Having examined the relationship between the SMMSE scores and serum vitamin D levels, we found a significant difference in the Parkinson's disease dementia group ( $p: 0,020$ ), as well as a relationship of 59,4% in the same direction. On the other hand, there was no significant difference in either patient group in the scores of UPDRS evaluating clinical disability.

**Conclusion:** Consistent with the literature, the present study found that people with Parkinson's disease had lower mean values of serum vitamin D levels than the control group and showed that serum vitamin D levels were correlated with the cognitive performance. However, the study could not find a relationship between the serum vitamin D levels and the motor performance.

**Keywords:** Parkinson's disease; Dementia; Vitamin D; Cognition; Motor symptom

### 1. Introduction

Parkinson's disease (PD) is the second most common neurodegenerative disorder affecting 2-3% of the people aged 65 or above. The neural loss in the substantia nigra resulting in striatal dopamine deficiency and the intracellular inclusions with aggregates of  $\alpha$ -Synuclein are neuropathological characteristics of the Parkinson's disease [1]. While the prevalence of dementia throughout the course of PD varies from 20% to 40%, the risk increases with age [2]. The

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Diagnostic and Statistical Manual of Mental Disorders (DSM-V) defines the Parkinson's disease dementia (PDD) as a cognitive disorder involving decrements in cognitive and motor performance, executive dysfunction, and impaired memory retrieval [3].

Vitamin D is a steroid hormone synthesized photochemically in the epidermis [4]. Serum levels above 30 ng/mL are considered adequate (the preferred range being 40-60 ng/mL) [5]. It was found that vitamin D can affect the brain development and functions. In vivo and in vitro experiments have shown that, as with other steroid hormones signaling through nuclear receptors, vitamin D plays an important role in the regulation and differentiation of the proliferative brain cells in addition to several other roles such as downregulating the L-type voltage-gated calcium channels, providing trophic support for developing and mature neurons, protecting against reactive oxygen species (ROS), and contributing to the viability and connectivity of individual neurons [6].

A meta-analysis reviewing 26 observational studies found that reduced serum vitamin D levels and cognitive decline were related, and serum vitamin D levels had a bigger effect on the general cognition, mental speed and visuospatial abilities in particular than on the memory [7]. It was found that the risk of cognitive impairment increased up to fourfold in people with a serum vitamin D level of 25 nmol/L compared to those with a serum vitamin D level of 75 nmol/L [8].

Our study investigates the relationship between neurodegeneration and the deficiency of vitamin D, which has such important functions in neuronal development.

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## 2. Materials and Methods

The present study was designed to include patients who were followed up by the Movement Disorders Outpatient Clinic of the Neurology Department of Istanbul Health Sciences University Haydarpaşa Numune Teaching Hospital for diagnosed idiopathic Parkinson's disease (IPH), took the Standardized Mini-Mental State Examination (SMMSE) and the Unified Parkinson's Disease Rating Scale (UPDRS) during their routine blood tests which also measured their serum vitamin D levels, had no metabolic disorders that could change their serum vitamin D levels, and had not taken and vitamin supplements for the last three months.

Accordingly, the study included 40 people with Parkinson's disease meeting the above criteria, 15 people with Parkinson's disease dementia diagnosed in accordance with the DSM-V, and a control group of 30 healthy individuals within the same age range as the Parkinson's disease group, who had their serum vitamin D levels measured, had no history of neurodegenerative disorders or any metabolic disorders that could change their serum vitamin D levels, and had not taken any vitamin supplements for the last three months.

In the present study, we compared the serum vitamin D levels of the three groups. We examined the relationship between the serum vitamin D levels and SMMSE scores in the patient group to show the effect of serum vitamin D levels on cognitive performance. We also investigated in the same group whether there was a correlation between the UPDRS scores and serum vitamin D levels.

IBM SPSS Statistics 22 software was used for data analysis. In addition to descriptive statistics, one-sample t-test was used for the comparisons between the patient and control groups, independent-samples t-test was used for the patient group, Pearson's correlation coefficient was used for correlation, and the value  $p < 0,05$  was taken as the threshold for statistical significance.

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## 3. Results

The present study included 40 people with Parkinson's disease of whom 17 were women and 23 were men (mean age  $68,5 \pm 12,2$  years), and 15 people with Parkinson's disease dementia of whom 4 were women and 11 were men (mean age  $76,6 \pm 4,4$  years). The control group comprised 30 people (19 women and 11 men with a mean age of  $71,1 \pm 8,7$  years) (Table 1).

**Table 1** Age and sex distribution of the groups.

|                        | Age     |         |      |                    | Sex    |      |
|------------------------|---------|---------|------|--------------------|--------|------|
|                        | Minimum | Maximum | Mean | Standard Deviation | Female | Male |
| Parkinson's            | 32      | 87      | 68,5 | 12,2               | 17     | 23   |
| Parkinson's + dementia | 68      | 84      | 76,6 | 4,4                | 4      | 11   |
| Control                | 56      | 90      | 71,1 | 8,7                | 19     | 11   |

While the mean serum vitamin D levels were  $16,5 \pm 6,4$  ng/mL in the Parkinson's disease group and  $13,8 \pm 4,5$  ng/mL in the Parkinson's disease dementia group, this value was  $21,4 \pm 15,9$  ng/mL in the control group. Considering the difference among the serum vitamin D levels of all the three groups, both patient groups had significantly lower levels than the control group ( $p: 0,000$ ). As for the difference between only the two patient groups, the Parkinson's disease dementia group had significantly lower serum vitamin D levels than the Parkinson's disease group ( $p: 0,012$ ) (Table 2).

**Table 2** Serum vitamin D levels of the groups.

|                        | Serum vitamin D level (ng/mL) |         |      |                    |       |
|------------------------|-------------------------------|---------|------|--------------------|-------|
|                        | Minimum                       | Maximum | Mean | Standard Deviation | p     |
| Control                | 6,5                           | 88,1    | 21,4 | 15,9               |       |
| Parkinson's            | 4                             | 27      | 16,5 | 6,4                | 0,000 |
| Parkinson's + dementia | 5,4                           | 21,8    | 13,8 | 4,5                | 0,000 |

Both patient groups were given the SMMSE to determine their cognitive states where the Parkinson's disease group scored  $23,8 \pm 3,2$  on average while the Parkinson's disease dementia group showed a deterioration with a score of  $19,4 \pm 4,8$  on average. It was found that the UPDRS scores evaluating the motor findings in particular ranged from 10 to 96 in the Parkinson's disease group while the Parkinson's disease dementia group had higher mean values of those scores (Table 3).

**Table 3** Distribution of the SMMSE and UPDRS scores in the patient groups.

|                    | Parkinson's |       | Parkinson's + dementia |       |
|--------------------|-------------|-------|------------------------|-------|
|                    | SMMSE       | UPDRS | SMMSE                  | UPDRS |
| Minimum            | 17          | 10    | 10                     | 33    |
| Maximum            | 29          | 96    | 26                     | 86    |
| Mean               | 23,8        | 32,4  | 19,4                   | 51,1  |
| Standard deviation | 3,2         | 18,6  | 4,8                    | 16,9  |

Having examined the relationship between the Standardized Mini-Mental State Examination (SMMSE) scores and serum Vitamin D levels, we found no significant difference in the Parkinson's disease group, whereas we detected a significant difference in the Parkinson's disease dementia group ( $p: 0,020$ ), as well as a relationship of 59,4% in the same direction. That is to say, the SMMSE scores rose as the serum vitamin D levels increased. On the other hand, there was no significant difference in either patient group in the Unified Parkinson's Disease Rating Scale (UPDRS) scores.

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#### 4. Discussion

A common cause of disability in the elderly population, Parkinson's disease is a movement disorder that is characterized by tremor, rigidity, akinesia, and loss of postural reflexes, and causes immobility and frequent falls [9]. Considering the relationship between the diet and Parkinson's disease with a multifactorial etiology comprising genetic and environmental factors, it was found that a Mediterranean diet, caffeine, and the vitamins B6 and E were associated with a lower risk of developing Parkinson's disease (PD) while hyperhomocysteinemia deteriorated the prognosis of the disease owing to its neurotoxic effect, but did not increase the risk of developing the disease [10, 11].

A Finnish follow-up study with 50 patients spanning over 29 years and aiming to show the effects of vitamin D on the development of Parkinson's disease found that a serum vitamin D level of 50 nmol/L minimum was associated with a 65% lower risk of developing Parkinson's disease [12]. Another study with a much larger sample size, however, reported that vitamin D levels did not affect the risk of developing Parkinson's disease [13].

Even though serum vitamin D level was reported not to affect the risk of developing Parkinson's disease, there are many studies relating to its effects on the prognosis of the disease. An article presented as a systematic review of a total of 20 studies, 14 of which being observational studies, reported that eight of the observational studies had found that the Parkinson's disease group had serum vitamin D levels significantly lower than those of the control group consisting of healthy individuals, and there was a positive correlation between the vitamin D concentration and the automatic postural responses such as the sit-to-stand test and walk and turn test [14]. Another review study showed that vitamin D could modify the Parkinson's disease, could be related with the motor and non-motor symptoms such as the risk of falling, mood changes, orthostatic hypotension, and olfactory impairment, and could also be correlated with verbal fluency and verbal memory [15]. The first randomized, double-blind, placebo-controlled trial aiming to show the effects of vitamin D on Parkinson's disease reported that the Parkinson's disease group assigned to receive vitamin D supplement showed no changes in the modified Hoehn and Yahr (HY) stage, the UPDRS Part II scores, and the scores of the Parkinson's Disease Questionnaire-39 (PDQ-39) sections investigating the daily life activities and mood while the group assigned not to receive vitamin D supplement showed a worsening of those results. Furthermore, as with our study, there were no significant differences in the UPDRS total scores and SMMSE scores [16].

It was shown that when the concentration of vitamin D, whose relationship with cognition is better clarified now, goes below 50 nmol/L in particular, the risk of Alzheimer's disease and other forms of dementia increases considerably [17]. A study with adult mice found that postnatal prolonged vitamin D deficiency or overdose impairs the development and physiology of the hippocampus in particular, with accompanying impairments in various brain functions including especially learning and memory [18]. The same study also showed that mice born with vitamin D deficiency had thinner cortices and enlarged lateral ventricles. Human studies, too, reported no difference in the brain volume, but showed larger lateral ventricles, and several non-randomized controlled studies found that a vitamin D supplementation of 1 to 15 months resulted in an improved cognition [19]. Supporting those studies, our study also found that people with lower vitamin D levels in the Parkinson's disease dementia group had worse cognitive performances. Although there are fewer studies reporting the opposite, a study in the patients with newly diagnosed Parkinson's disease showed a significant correlation between vitamin D levels and the deterioration of motor symptoms while it did not find any relationship between vitamin D levels and falling and cognition [20].

Many studies investigating the effects of vitamin D levels on motor symptoms reported a relationship between vitamin D levels and motor symptoms, and found that patients with lower vitamin D levels showed poorer motor performance [21]. This was also given a different explanation that rather than the direct effect of vitamin D, mobility of patients decreased as the severity of the disease increased, which resulted in a lower exposure to sunlight and thus detection of lower vitamin D levels in the advanced stages of the disease [15]. Another study investigating the relationship between the Hoehn and Yahr (HY) scores and vitamin D levels found that serum ionized calcium levels were positively correlated with the HY stage while vitamin D levels showed a negative correlation, which was explained by the immobility-induced hypercalcemia's inhibition of the vitamin D production [22]. However, another study including, similarly to our study, more middle-to-late stage patients found no correlation between motor symptoms and vitamin D levels [23].

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#### 5. Conclusion

Although having been conducted in a small patient population, our study found, consistently with the literature, that the patient group had lower serum vitamin D levels than the control group and vitamin D levels had a positive correlation with the cognitive performance in the patient group. Thus, it seems best to note that Parkinson's disease may be accompanied by vitamin D deficiency and measure the vitamin D levels during patient follow-ups to prevent

cognitive decline in particular, and supplement vitamin D in case of a deficiency. Even though our study found no relationship between serum vitamin D levels and motor performance, we believe that studies with larger patient groups in the earlier stages of Parkinson's disease may show the effects of vitamin D levels on motor performance more clearly.

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## Compliance with ethical standards

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### *Disclosure of conflict of interest*

There is no conflict of interest.

### *Statement of ethical approval*

Ethics committee approval received from Haydarpaşa Training and Research Hospital with decision number E-62977267-000-2760 in 23.02.2021.

### *Statement of informed consent*

Informed consent was obtained from all individual participants included in the study.

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