European Journal of Therapeutics
pISSN: 2564-7784
eISSN: 2564-7040

Eur J Ther. 2026;32(4):496–505.
https://doi.org/10.58600/eurjther3191

Original Research

Association Between Vitamin D Levels and Fatigue in Patients with Spinal Cord Injury

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Received: 2026–06–02 **Accepted:** 2026–08–09 **Published Online:** 2026–08–14

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ABSTRACT

Objective: Fatigue frequently occurs after spinal cord injury (SCI) and can markedly diminish quality of life. Studies involving different patient groups have reported links between deficient vitamin D status, fatigue, and compromised neuromuscular performance. Accordingly, we evaluated the association of circulating 25-hydroxyvitamin D [25(OH) D] with fatigue among individuals with SCI.

Methods: A single-center, cross-sectional design was used to compare 25 individuals with SCI with 25 healthy participants matched for age and sex. Serum 25(OH) D was assayed to characterize vitamin D status. The Chalder Fatigue Scale (CFS) was used to quantify fatigue, whereas the Functional Independence Measure (FIM) provided the measure of functional independence. Correlations of serum 25(OH) D with CFS scores were calculated within the SCI cohort.

Results: Compared with controls, participants with SCI showed reduced serum 25(OH) D concentrations (19.82 ± 10.69 vs. 29.20 ± 14.83 ng/mL, $p = 0.014$) and elevated physical, mental, and total fatigue scores (all $p < 0.001$). In the SCI group, serum vitamin D was inversely related to total fatigue (rs = −0.899, $p < 0.001$) and physical fatigue (rs=−0.955, $p < 0.001$); the inverse relation with mental fatigue was moderate (rs = −0.479, $p = 0.015$). Its association with the FIM motor score was not statistically significant. After adjustment for time since injury, AIS grade, and injury level, the inverse associations with physical and total fatigue persisted (partial rs = −0.945 and −0.882, respectively; both $p < 0.001$).

Conclusion: Low vitamin D status was frequent among individuals with SCI and was accompanied by greater fatigue, most notably in the physical domain. Serum vitamin D was inversely associated with fatigue in this population; however, the cross-sectional design precludes causal inference, and shared determinants such as immobility and reduced sun exposure may partly explain this relationship. Larger prospective and interventional studies are required to define this relationship more clearly.

Keywords: fatigue, serum 25(OH) D level, spinal cord injury, vitamin D

INTRODUCTION

SCI interrupts the neural pathways responsible for motor, sensory, and autonomic functions and constitutes a major neurological disorder. Beyond the primary neurological deficit, it carries substantial morbidity and can markedly diminish quality of life [1]. Secondary consequences are not limited to physical disability; chronic pain, fatigue, and psychological problems may also occur and may complicate rehabilitation and daily functioning [2].

Fatigue is one of the frequently reported complaints among individuals with SCI and may substantially restrict participation and quality of life [3]. In this population, fatigue is considered a multidimensional symptom that may reflect reduced physical capacity, inflammatory mechanisms, sleep problems, pain, and psychological factors [4]. Identifying potentially modifiable contributors to fatigue is therefore clinically important. Vitamin D has received growing attention not only for its role in bone metabolism but also for its effects on neuroimmune and neuromuscular function [5]. Because vitamin D receptors are distributed across numerous tissues, including neural structures, its physiological actions are thought to extend beyond bone [6]. Suboptimal vitamin D concentrations have been related to muscle weakness, heightened inflammatory activity, and neurological impairment [6,7]. Among people with SCI, inadequate vitamin D status is frequently observed. Prior investigations indicate that low concentrations are common in this population and could adversely influence rehabilitation and functional recovery [8].

Main Points

- Serum 25(OH)D levels were found to be significantly lower in patients with spinal cord injury compared to healthy controls.
- In the spinal cord injury group, a strong negative correlation was observed between serum vitamin D levels and total fatigue and physical fatigue, whilst a moderate negative correlation was found with mental fatigue.
- Vitamin D deficiency may be a modifiable factor associated with physical fatigue in particular among patients with spinal cord injury
- Prospective studies are required to clarify the causality between low vitamin D levels and fatigue in patients with spinal cord injury.

They have also been associated with complications that arise after SCI [9]. Recent attention has focused on possible links between vitamin D deficiency and pain, including neuropathic pain [9,10]. Findings from neurological populations indicate that lower vitamin D concentrations may accompany a heavier symptom burden [11]. Although links between vitamin D and fatigue have been explored in several clinical conditions, SCI-specific evidence remains scarce.

Few studies have directly related circulating 25-hydroxyvitamin D [25(OH) D] to fatigue after SCI. We therefore assessed whether serum 25(OH) D concentration was associated with fatigue severity in individuals with SCI and explored the clinical importance of this association. To our knowledge, this is among the first studies to examine the relationship between serum 25(OH) D and fatigue specifically in SCI while analysing the physical and mental fatigue domains separately against an age- and sex-matched control group, thereby addressing a gap left by earlier work that focused on vitamin D deficiency and its skeletal or prognostic correlates rather than on fatigue.

MATERIALS AND METHODS

Study Design and Participants

A single-center cross-sectional approach was adopted to investigate serum 25(OH) D in relation to fatigue among patients with SCI. Data collection took place at the Department of Physical Medicine and Rehabilitation within the Faculty of Medicine at Sivas Cumhuriyet University. A total of 25 patients with SCI who were at least one month beyond the injury were enrolled, together with 25 healthy controls matched by age and sex. Individuals who had received vitamin D supplementation within the preceding six months were excluded, and all blood samples were obtained during the autumn season to limit seasonal variation in 25(OH) D.

Ethical Approval

Ethics clearance was granted by the Non-Interventional Clinical Research Ethics Committee of Sivas Cumhuriyet University (Decision No: 2023-07/07; Date: July 20, 2023). Every participant provided written informed consent before entering the study. Study procedures were implemented in accordance with the Declaration of Helsinki.

Inclusion and Exclusion Criteria

Eligibility for the SCI cohort required a diagnosis of SCI, a post-injury interval of at least one month, an age of 18 years or

older, willingness to participate, and adequate cognitive ability to complete the assessments. The control group consisted of adults aged 18 years or older without a history of SCI or any central nervous system disorder, with a similar age and sex distribution in the SCI group. Participants were excluded if they had a traumatic brain injury, electrolyte imbalance, thyroid dysfunction, iron deficiency anemia, a known psychiatric disorder, a systemic disease that could affect vitamin D metabolism, or if they declined participation.

Data Collection

Age and sex were recorded, while height and body weight were obtained by measurement. Body mass index (BMI) was computed as body weight in kilograms divided by height in meters squared (kg/m²). For participants with SCI, the neurological level and completeness of injury were determined by a physiatrist using a standardized International Standards for Neurological Classification of Spinal Cord Injury (ISNCSCI) examination, from which the AIS grade and the classification as tetraplegia or paraplegia were derived; time since injury (months) and injury etiology were recorded from the ISNCSCI assessment and verified against the medical records. The Chalder Fatigue Scale and the Functional Independence Measure were administered face-to-face by a single trained physiatrist who was blinded to participants' serum 25(OH) D results, which were obtained separately as routine central-laboratory tests.

Assessment of Vitamin D Levels

Serum 25(OH) D concentration served as the measure of vitamin D status. Serum 25(OH) D was quantified in the hospital's central biochemistry laboratory as part of routine clinical testing on a Roche cobas e 802 immunoassay module (Roche Diagnostics GmbH, Mannheim, Germany) using an electrochemiluminescence immunoassay (ECLIA); the inter-assay coefficient of variation was 4.7%. Because this biomarker reflects vitamin D derived from dietary sources as well as endogenous synthesis, it is considered an appropriate indicator of overall vitamin D status [12]. Thresholds specified in the Endocrine Society clinical practice guideline were applied: values <20 ng/mL indicated deficiency, ≥20 to <30 ng/mL indicated insufficiency, and ≥30 ng/mL indicated sufficiency [13].

Evaluation of Fatigue

Fatigue severity was assessed using the Chalder Fatigue Scale (CFS). The scale includes 11 items that assess physical and mental fatigue and are widely used in clinical and community-based studies [14]. Each item receives a score between 0 and 3; higher scores correspond to greater fatigue severity [15]. The scale comprises seven physical-fatigue items (subscale range 0–21) and four mental-fatigue items (subscale range 0–12), giving a total score of 0–33. All items are anchored in the same direction so that higher values consistently indicate greater fatigue, and Likert scoring (0–3 per item) was applied exactly as specified for the validated Turkish version [16]. Validity and reliability have been confirmed for the Turkish adaptation [16].

Evaluation of Function

The Functional Independence Measure (FIM) provided the assessment of functional ability. This 18-item instrument comprises 13 motor items (self-care, sphincter management, transfers, and locomotion; motor subscore range 13–91) and 5 cognitive items (communication and social cognition; cognitive subscore range 5–35), and is an established, reliable rehabilitation outcome measure; higher scores indicate better functional independence [17–19]. Because the present study focused on physical function and its relationship with fatigue and vitamin D, only the motor subscore (the sum of the 13 motor items) was analysed. The cognitive subscore was not examined, as adequate cognition was an inclusion requirement and cognitive scores showed a pronounced ceiling effect with minimal variability in this cohort.

Statistical Analysis

Analyses were performed with IBM SPSS Statistics 22.0 (IBM Corp., Armonk, NY, USA). The sample size was determined a priori for the primary endpoint, namely the between-group difference in serum 25(OH) D concentration. Assuming a large effect size (Cohen's d ≈ 0.94), consistent with earlier reports of substantially lower vitamin D status in individuals with SCI, a 2-sided alpha of 0.05 and a target power of 0.90 required 25 participants per group; the calculation yielded a power of 0.904. The Shapiro-Wilk test assessed whether continuous variables followed a normal distribution. Normally distributed variables are summarized using the mean and standard deviation; variables with non-normal distributions are given as median with minimum and maximum values. Age, height, weight, and body mass index were normally distributed, whereas serum 25(OH) D and the Chalder Fatigue Scale scores departed from normality; these were therefore compared with the Mann-Whitney *U* test and correlated using Spearman's rank coefficient. Two-group comparisons used the independent-samples t-test when its assumptions were fulfilled; otherwise, the Mann-Whitney *U*

test was applied. Categorical variables were evaluated with the Chi-square test. Within the SCI cohort, associations of serum 25(OH) D with the total CFS score and the physical and mental subscale scores were examined by Spearman's rank correlation. To address potential confounding, partial Spearman correlations between serum 25(OH) D and physical and total fatigue were additionally computed, adjusting for time since injury, AIS grade, and injury level (tetraplegia vs. paraplegia). For non-normally distributed variables, medians with minimum-maximum values and the rank-biserial correlation (as a rank-based effect size) are reported alongside the Mann-Whitney *U* test, whereas Cohen's d is reported only for normally distributed variables. Results with $p < 0.050$ were accepted as statistically significant.

RESULTS

A total of 25 individuals with SCI and 25 healthy controls formed the study sample. Within the SCI group, 9 participants (36%) had tetraplegia and 16 (64%) had paraplegia; American Spinal Injury Association Impairment Scale (AIS) grades were A in 2, C in 10, and D in 13. The injury was traumatic in 17 participants (68%) and non-traumatic in 8 (32%). The median time since injury was 24 months (interquartile range 6–48; range 2–372), with 11 participants (44%) classified as subacute (under 12 months) and 14 (56%) as chronic (12 months or longer). All participants were wheelchair-dependent for ambulation. Age, sex, height, weight, and BMI did not differ significantly between the groups (all $p > 0.05$) (Table 1).

The SCI group had a lower mean serum 25(OH) D concentration than the control group (19.82 ± 10.69 ng/mL vs. 29.20 ± 14.83 ng/mL, $p = 0.014$). According to the Endocrine Society thresholds, 14 of the 25 participants with SCI (56%) were vitamin D deficient (<20 ng/mL), 8 (32%) were insufficient (≥20 to <30 ng/mL), and 3 (12%) were sufficient (≥30 ng/mL).

Fatigue was greater among participants with SCI. Their mean physical fatigue score was 13.48 ± 2.54, compared with 4.48 ± 2.00 in controls ($p < 0.001$), while the corresponding mental fatigue scores were 5.68 ± 1.44 and 1.96 ± 1.46 ($p < 0.001$). Total CFS scores were likewise higher in the SCI group (19.16 ± 3.41 vs. 6.44 ± 3.25, $p < 0.001$) (Table 2).

Table 1. Demographic and clinical characteristics of the study groups

Variable	SCI (n = 25)	Control (n = 25)	p
Age (years)	44.36 ± 18.25	45.48 ± 19.62	0.835
Height (cm)	173.24 ± 6.49	173.56 ± 7.62	0.874
Weight (kg)	76.36 ± 10.17	73.88 ± 10.91	0.410
BMI (kg/m²)	25.39 ± 2.67	24.45 ± 2.57	0.208
Male, n (%)	23 (92)	23 (92)	1.000
Female, n (%)	2 (8)	2 (8)	1.000
Clinical characteristics (SCI group)			
Injury type — Tetraplegia, n (%)	9 (36)	–	–
Paraplegia, n (%)	16 (64)	–	–
AIS grade — A / C / D, n	2 / 10 / 13	–	–
Etiology — Traumatic, n (%)	17 (68)	–	–
Non-traumatic, n (%)	8 (32)	–	–
Time since injury (months), median (IQR)	24 (6–48; range 2–372)	–	–
Subacute (<12 mo) / Chronic (≥12 mo), n	11 / 14	–	–
Ambulation — Wheelchair-dependent, n (%)	25 (100)	–	–

Data are mean ± SD unless otherwise stated. p from independent-samples t-test (continuous variables) or chi-square test (categorical variables). Clinical variables apply to the SCI group only. AIS, American Spinal Injury Association Impairment Scale; BMI, body mass index; IQR, interquartile range; SCI, spinal cord injury; –, not applicable.

An inverse association was observed between serum vitamin D concentration and total CFS score (rs = −0.899, $p < 0.001$). The inverse relation with the physical fatigue subscale was also strong (rs = −0.955, $p < 0.001$), whereas a moderate inverse relation was detected for the mental fatigue subscale (rs = −0.479, $p = 0.015$) (Figure 1). The 95% confidence intervals for these coefficients were −0.955 to −0.782 for total fatigue, −0.980 to −0.900 for physical fatigue, and −0.735 to −0.103 for mental fatigue; all coefficients with their confidence intervals are also presented in Table 3.

These associations persisted after adjustment for potential confounders. In partial Spearman correlations controlling for time since injury, AIS grade, and injury level (tetraplegia vs. paraplegia), the inverse relationship of serum 25(OH) D remained strong for physical fatigue (partial rs = −0.945, $p < 0.001$) and for total fatigue (partial rs = −0.882, $p < 0.001$), indicating that the association was not explained by these clinical characteristics.

Vitamin D level showed a positive but statistically non-significant correlation with the FIM motor score (rs = 0.371, $p = 0.068$) (Table 3). This near-threshold result should be interpreted with caution, as the modest sample (n = 25) may have limited the statistical power to detect an association of this magnitude.

Table 2. Serum 25(OH)D and Chalder Fatigue Scale scores by group

Variable	SCI (n = 25) mean ± SD	Control (n = 25) mean ± SD	SCI median (min–max)	Control median (min–max)	p	Rank-biserial r	Cohen's d (95% CI)
Serum 25(OH)D (ng/mL)	19.82 ± 10.69	29.20 ± 14.83	19.0 (5.7–53.0)	25.0 (12.0–62.0)	0.014	0.41	−0.73 (−1.30, −0.15)
CFS physical (0–21)	13.48 ± 2.54	4.48 ± 2.00	13 (7–17)	4 (0–7)	<0.001	0.99	3.94 (2.99, 4.89)
CFS mental (0–12)	5.68 ± 1.44	1.96 ± 1.46	6 (3–8)	2 (0–4)	<0.001	0.94	2.57 (1.82, 3.32)
CFS total (0–33)	19.16 ± 3.41	6.44 ± 3.25	18 (11–25)	6 (1–11)	<0.001	0.99	3.82 (2.88, 4.75)

Data are mean ± SD and median (minimum–maximum). The Chalder Fatigue Scale was scored 0–3 per item in accordance with the validated Turkish version (physical 0–21, mental 0–12, total 0–33). p from Mann–Whitney U test; because these variables were non-normally distributed, the rank-biserial correlation is reported as the primary, rank-based effect size, with Cohen's d provided for reference. Exact p-values for the fatigue comparisons were <0.001 (physical 1.7×10^{-9}, mental 1.1×10^{-8}, total 1.5×10^{-9}). CFS, Chalder Fatigue Scale; CI, confidence interval; SCI, spinal cord injury; 25(OH)D, 25-hydroxyvitamin D.

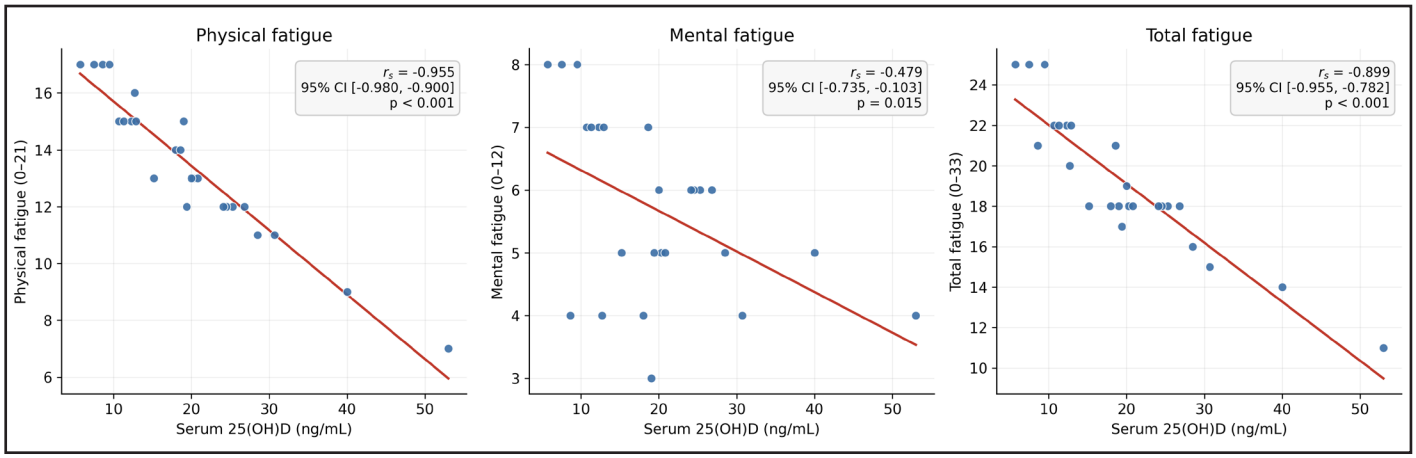


Figure 1. Correlations between serum 25(OH) D and Chalder Fatigue Scale scores in the SCI group (n = 25). Scatterplots with fitted regression lines for physical, mental, and total fatigue. Each panel shows the Spearman rank correlation coefficient (rs), its 95% confidence interval, and the corresponding *p*-value. CFS, Chalder Fatigue Scale; SCI, spinal cord injury; 25(OH) D, 25-hydroxyvitamin D. The straight lines are ordinary least-squares fits shown for visual guidance only and do not represent the analysed rank-based (Spearman) model.

Table 3. Correlations of serum 25(OH)D with fatigue and function in the SCI group

Association	rs	95% CI	p
Unadjusted (zero-order) correlations			
Serum 25(OH)D – CFS total	−0.899	−0.955 to −0.782	<0.001
Serum 25(OH)D – CFS physical	−0.955	−0.980 to −0.900	<0.001
Serum 25(OH)D – CFS mental	−0.479	−0.735 to −0.103	0.015
Serum 25(OH)D – FIM motor	0.371	−0.028 to 0.668	0.068
Partial correlations (adjusted for time since injury, AIS grade, and injury level [tetraplegia vs. paraplegia])			
Serum 25(OH)D – CFS physical (adjusted)	−0.945	−0.98 to −0.87	<0.001
Serum 25(OH)D – CFS total (adjusted)	−0.882	−0.95 to −0.73	<0.001

rs, Spearman rank correlation coefficient; zero-order 95% CIs derived by Fisher z-transformation; confidence intervals for the partial coefficients were obtained by the same transformation with the standard error adjusted for the number of covariates (degrees of freedom n − 3 − k, where k is the number of variables partialled out). Partial correlations are partial Spearman coefficients (n = 25) adjusting simultaneously for time since injury, AIS grade, and injury level; the inverse associations with physical and total fatigue remained strong after adjustment. CFS, Chalder Fatigue Scale; CI, confidence interval; FIM, Functional Independence Measure; SCI, spinal cord injury.

DISCUSSION

Relative to matched healthy controls, participants with SCI showed reduced serum 25(OH) D concentrations and greater fatigue. Within the SCI cohort, lower vitamin D concentrations accompanied higher fatigue scores, and this association was most pronounced for physical fatigue. These observations indicate that inadequate vitamin D status may have clinical relevance to fatigue after SCI.

Fatigue after SCI is a complex symptom that may arise from physical deconditioning, inflammatory processes, pain, sleep disturbance, and psychological factors [4,20]. Previous literature indicates that fatigue is common in SCI and may impair quality of life and functional independence [21]. The present results are consistent with these observations, as patients with SCI had markedly higher CFS scores than controls.

Vitamin D has been studied extensively because its effects extend beyond skeletal metabolism. Vitamin D receptors are widely expressed in muscle and nervous tissue, supporting a role in neuromuscular function [22,23]. Vitamin D insufficiency has been associated with muscle weakness, mitochondrial dysfunction, and increased inflammatory response [24,25]. Mechanistically, vitamin D supports skeletal-muscle contractile performance and calcium handling, modulates neuroinflammatory signalling, and contributes to mitochondrial oxidative capacity, providing plausible pathways by which deficiency could heighten physical fatigue. These mechanisms may contribute to fatigue, particularly in chronic neurological conditions. However, several of these mechanistic findings derive from non-SCI and non-neurological models, including studies in athletes, obese pregnant women, and in vitro or animal muscle preparations, so their extrapolation to SCI remains hypothesis-generating.

Previous work has documented a substantial burden of vitamin D insufficiency among individuals with SCI [26]. Restricted mobility, reduced sunlight exposure, and coexisting chronic health problems could help explain the low vitamin D concentrations in this population [27]. In our sample, 25(OH) D concentrations in the SCI group were significantly below those of the controls. The inverse association with vitamin D was most evident for the physical component of fatigue. The mean 25(OH) D of the control group (29.20 ng/mL) itself lay within the insufficiency range, reflecting the high background prevalence of vitamin D inadequacy in this setting and possibly attenuating the between-group difference. The strength of the observed correlation, particularly for physical fatigue (rs=−0.955), is unusually high for a biological association and warrants cautious interpretation. Because reduced mobility and limited sun exposure can simultaneously lower 25(OH) D and increase physical fatigue, these shared determinants, rather than a direct causal effect of vitamin D, may substantially account for the magnitude of the association; the relationship nonetheless persisted after adjustment for time since injury, AIS grade, and injury level. Part of this very strong physical-fatigue association may also reflect construct overlap rather than confounding

alone. Because the physical-fatigue subscale is closely linked to physical disability and immobility, and immobility itself lowers 25(OH) D, the physical-fatigue items and vitamin D status may share variance at the level of measurement.

This pattern may be related to the contribution of vitamin D to muscle performance and physical function. Earlier studies have linked insufficient vitamin D status to poorer muscle performance and diminished physical capacity [28,29].

Vitamin D and fatigue have also been investigated outside the SCI population. A placebo-controlled randomized study of vitamin D-deficient individuals found that vitamin D3 supplementation lowered self-reported fatigue [30]. In contrast, a recent randomized, double-blind, placebo-controlled trial in individuals with chronic SCI reported no discernible effect of vitamin D3 supplementation on secondary health outcomes, including fatigue [31]; the present cross-sectional association should therefore be interpreted cautiously and does not establish that supplementation reduces fatigue. Our finding that lower vitamin D concentrations accompanied higher fatigue scores suggests that a clinically relevant relationship may also be present in SCI.

The weaker correlation between vitamin D and mental fatigue may reflect the multifactorial nature of cognitive or mental fatigue, which may be more strongly influenced by psychological, sleep-related and neurological variables.

This study also has notable strengths. Few investigations have addressed vitamin D status in relation to fatigue among patients with SCI while separately analyzing total, physical, and mental fatigue. Comparisons were also strengthened by the inclusion of a control group matched for age and sex.

Limitations

Several methodological limitations should be considered. Because the design was single-center and cross-sectional, the relationship between serum 25(OH) D concentration and fatigue can be identified as an association but cannot be interpreted as causal. Both study groups were predominantly male (92%), and the sample size was relatively small, which limits generalizability to women and reduces the statistical power of the findings. The small sample also restricted detailed subgroup analyses based on variables that reflect the heterogeneous nature of spinal cord injury, such as etiology, injury level, complete/incomplete injury status, duration of illness, mobility level, and rehabilitation intensity.

Fatigue is a multidimensional symptom, yet several potential confounders were not comprehensively evaluated, including pain intensity, sleep quality, depression and anxiety, physical activity, nutritional status, sun exposure, seasonal variability, vitamin D supplementation, and medication use. In particular, because reduced mobility and limited sun exposure can simultaneously lower 25(OH) D and increase fatigue, part of the observed association may reflect these shared determinants rather than a direct effect of vitamin D; although uniform autumn sampling removed seasonal variation, mobility and sun exposure were not quantified. The current findings therefore require validation in larger, multicenter, prospective studies. Because the sample was modest (n = 25) and three covariates were adjusted for simultaneously, the partial correlations should be regarded as exploratory, since such estimates can be unstable when the number of observations per adjusted variable is limited.

CONCLUSION

Low vitamin D status occurred frequently in the SCI group and was accompanied by higher fatigue, particularly in the physical domain. These results raise the possibility that vitamin D status is associated with fatigue; because the design was cross-sectional, a causal or directly “modifiable” role cannot be inferred and requires confirmation in interventional studies among individuals with SCI. Furthermore, shared determinants such as immobility and reduced sun exposure may contribute to both low vitamin D and greater fatigue, so vitamin D may represent a marker rather than a direct cause of fatigue in this setting.

Confirmation requires larger prospective studies, including interventional designs, to establish the nature of this association and assess whether restoring vitamin D sufficiency alleviates fatigue in this population.

Acknowledgments: The authors have reviewed and edited the output and take full responsibility for the content of this publication.

Funding: This research received no external funding.

Conflict of Interest: The authors declare no conflicts of interest.

Informed Consent: There is an informed consent form.

Informed consent was obtained from all participants.

Data Availability Statement: We respect the importance of transparency and reproducibility in research, but we are committed to the privacy of the participants involved in our study. Therefore, raw data are protected and cannot be publicly disclosed. However, we offer a comprehensive guide within the sections detailing our methodology and statistical analysis. This thorough explanation aims to enable other researchers to replicate our methods and compare their findings with ours.

Ethical Approval: Approval was obtained from the Non-Interventional Clinical Research Ethics Committee of Sivas Cumhuriyet University (Decision No: 2023-07/07; Date: 20.07.2023). Written informed consent was obtained from all participants before enrollment. The study was carried out in accordance with the principles of the Declaration of Helsinki.

Author Contributions: Conception: MA, CDS; Design: MA, CDS; Supervision: MA, CDS; Materials: CDS; Data Collection and/or Processing: CDS; Analysis and/or Interpretation: CDS; Literature: CDS; Review: CDS; Writing: MA; Critical Review: MA, CDS.

Author Statement Regarding the Use of Artificial Intelligence-Enhanced Tools: The authors used an artificial intelligence-assisted language tool (ChatGPT, OpenAI) solely for language editing, grammar checking, and improving the readability of the manuscript. The AI tool was not used for data collection, data analysis, interpretation of results, generation of scientific content, or decision-making. All scientific content, analyses, conclusions, and final manuscript revisions were reviewed and approved by the authors, who take full responsibility for the integrity and accuracy of the work.

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How to Cite;

Atas M, Ceyhan Dogan S (2026) Association Between Vitamin D Levels and Fatigue in Patients with Spinal Cord Injury. Eur J Ther. 32(4):496–505. https://doi.org/10.58600/eurjther3191