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Research

Association of Baseline Vitamin B12 and Vitamin D Levels with Clinical Response to Paraffin Therapy in Patients with Hand Symptoms

El Semptomları Olan Hastalarda Başlangıç Vitamin B12 ve D Vitamini Düzeyleri ile Parafin Tedavisine Klinik Yanıt Arasındaki İlişki

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ABSTRACT

Objective: Paraffin bath therapy is commonly used in rehabilitation for hand and wrist symptoms, but clinical response varies among patients. This study evaluated whether baseline vitamin B12 and 25-hydroxyvitamin D [25(OH)D] levels were associated with short-term clinical response after paraffin therapy in patients with hand pain and/or numbness.

Methods: This single-center, retrospective, observational study included 128 adults who completed a 10-session paraffin therapy program. Pain, numbness, and hand-related function were assessed before treatment and after the 10th session, using the visual analogue scale (VAS) scores and the patient-rated wrist/hand evaluation (PRWHE). Clinical response was defined as either a ≥30% improvement in PRWHE total score or a ≥2-point reduction in VAS numbness score. Serum vitamin B12 and 25(OH)D levels, obtained before treatment, were analyzed both as continuous and as categorical variables.

Results: Significant improvements were observed in VAS pain, VAS numbness, PRWHE total score, and appearance-related discomfort after therapy (all p<0.001). Overall, 63 patients (49.2%) were classified as responders. Responders had higher baseline vitamin B12 and 25(OH)D levels than non-responders. Patients with 25(OH)D levels ≥30 ng/mL had a higher response rate than those with lower levels (74.4% vs. 38.2%, p<0.001). Vitamin B12 ≥300 pg/mL was also associated with response in categorical analysis, but not after adjustment. In multivariable logistic regression analysis, 25(OH)D ≥30 ng/mL was independently associated with clinical response (odds ratio: 4.48, 95% confidence interval: 1.66-12.05, p=0.003).

Conclusion: Baseline vitamin D status was independently associated with the short-term clinical response to paraffin therapy in patients with hand pain and/or numbness. Further prospective, controlled studies are needed.

Keywords: Paraffin therapy, vitamin D, vitamin B12, hand pain, numbness, rehabilitation, patient-rated wrist/hand evaluation

ÖZ

Amaç: Parafin banyosu tedavisi el ve el bileği semptomlarında rehabilitasyon pratiğinde sık kullanılan bir yöntemdir; ancak klinik yanıt hastalar arasında değişkenlik gösterebilir. Bu çalışmada, el ağrısı ve/veya uyuşma yakınması olan hastalarda parafin tedavisi sonrası kısa dönem klinik yanıtın başlangıç vitamin B12 ve 25-hidroksivitamin D [25(OH)D] düzeyleri ile ilişkisi değerlendirildi.

Gereç ve Yöntem: Bu tek merkezli retrospektif gözlemsel çalışmaya, el ağrısı, uyuşma veya parestezi nedeniyle 10 seans parafin tedavisini tamamlayan 128 erişkin hasta dahil edildi. Ağrı, uyuşma ve el ile ilişkili fonksiyonel durum tedavi öncesinde ve 10. seans sonrasında görsel analog skala (VAS) ve hasta bildirimli el bileği/el değerlendirme ölçeği (PRWHE) ile değerlendirildi. Klinik yanıt, PRWHE toplam skorunda ≥%30 iyileşme veya VAS uyuşma skorunda ≥2 puan azalma olarak tanımlandı. Tedavi öncesi serum vitamin B12 ve 25(OH)D düzeyleri sürekli ve kategorik değişkenler olarak analiz edildi.

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ÖZ

Bulgular: Tedavi sonrası VAS ağrı, VAS uyuşma, PRWHE toplam skoru ve görünümle ilişkili rahatsızlık skorlarında anlamlı iyileşme saptandı (tümü p<0,001). Toplam 63 hasta (%49,2) yanıt veren olarak sınıflandırıldı. Yanıt verenlerde başlangıç vitamin B12 ve 25(OH)D düzeyleri daha yüksekti. 25(OH)D düzeyi ≥30 ng/mL olanlarda klinik yanıt oranı daha yüksekti (%74,4 vs. %38,2; p<0,001). Vitamin B12 ≥300 pg/mL kategorik analizde yanıtla ilişkiliydi; ancak düzeltme sonrası anlamlılığını korumadı. Çok değişkenli lojistik regresyonda yalnızca 25(OH)D ≥30 ng/mL klinik yanıtla bağımsız ilişkili bulundu (olasılık oranı: 4,48; %95 güven aralığı: 1,66-12,05; p=0,003).

Sonuç: Başlangıç D vitamini durumu, el ağrısı ve/veya uyuşma yakınması olan hastalarda parafin tedavisi sonrası kısa dönem klinik yanıtla bağımsız olarak ilişkili bulundu. Prospektif kontrollü çalışmalara ihtiyaç vardır.

Anahtar Kelimeler: Parafin tedavisi, D vitamini, vitamin B12, el ağrısı, uyuşma, rehabilitasyon, hasta bildirimli el bileği/el değerlendirme ölçeği

INTRODUCTION

Hand and wrist pain, stiffness, numbness, and functional limitations are common complaints in physical medicine and rehabilitation practice. These symptoms may occur in various conditions, including hand osteoarthritis, carpal tunnel syndrome (CTS), tenosynovitis, trigger finger, soft-tissue pain, and neuropathic symptoms of cervical origin. Although the underlying etiology may differ, many patients experience overlapping problems such as impairment of daily activities, reduced grip performance, nocturnal paresthesia, and pain aggravated by hand use.

Paraffin bath therapy is a superficial heat modality that has been used for many years in the management of hand and wrist disorders. It is commonly applied for hand osteoarthritis and painful soft-tissue conditions to reduce pain, to increase tissue extensibility, and to prepare the hand for therapeutic exercises. Previous studies have reported that paraffin therapy may provide short-term benefits in pain, stiffness, and functional limitation in patients with hand osteoarthritis (1,2). However, paraffin therapy is usually delivered as part of a multimodal rehabilitation program, and the degree of clinical response may vary considerably between patients. This variation makes it important to investigate patient-related factors that may influence treatment response.

Vitamin D is frequently evaluated in rehabilitation practice because of its potential relationship with muscle function, neuromuscular performance, and musculoskeletal pain. Although vitamin D deficiency has been associated with muscle weakness, diffuse musculoskeletal pain, and impaired functional capacity, this relationship is not consistent across studies (3,4). Therefore, vitamin D status may be better considered a patient-related factor that could influence rehabilitation outcomes rather than a direct cause of pain. Vitamin B12 is another important factor for peripheral nervous system function. Deficiency or borderline-low levels may be associated with paresthesia, numbness, burning sensations, and peripheral neuropathy-like symptoms (5). Because these symptoms may overlap with local compressive neuropathies or mechanical hand disorders, evaluating the association between vitamin B12 levels and post-treatment changes in symptoms represents a practical clinical question.

The existing literature has mainly focused on the short-term symptomatic effects of paraffin therapy, particularly in hand osteoarthritis and other hand disorders (1,2). However, whether baseline vitamin B12 and vitamin D levels are associated with clinical response to paraffin therapy has not been adequately investigated. In routine practice, patients who complete the same treatment protocol may show markedly different degrees of improvement. This variability may not be explained solely by diagnosis, age, or baseline symptom severity; metabolic and neuromuscular factors may also contribute.

The aim of this study was to evaluate the association of baseline serum vitamin B12 and 25-hydroxyvitamin D [25(OH)D] levels with changes in pain, numbness, and hand function after standard paraffin therapy in patients with hand pain and/or numbness. The study was designed to identify patient-related factors that may influence treatment response in routine physical medicine and rehabilitation practice, rather than to prove the efficacy of paraffin therapy itself.

METHODS

Study Design and Ethical Approval

This single-center, retrospective, observational cohort study was based on the medical records of patients who were evaluated in the physical medicine and rehabilitation outpatient clinic for hand pain and/or numbness and who subsequently received paraffin therapy. Ethical approval was obtained from the University of Health Sciences Türkiye, Bakırköy Dr. Sadi Konuk Training and Research Hospital Clinical Research Ethics Committee (approval no: 2026-10-02, date: 22.04.2026).

Patient Selection

Patients aged 18 years or older who presented with pain, numbness, or paresthesia involving the hand and/or wrist who were scheduled for paraffin therapy based on clinical

judgment and who completed a 10-session treatment program were included in the study. To be eligible for analysis, patients were required to have pre- and post-treatment patient-rated wrist/hand evaluation (PRWHE), and visual analogue scale (VAS) assessments available, as well as recorded serum vitamin B12 and 25(OH)D levels obtained before treatment initiation.

Patients who did not complete the paraffin therapy program, who received paraffin therapy for conditions unrelated to the hand or wrist, who had incomplete clinical assessment forms, or who had missing laboratory data were excluded. Patients with severe neurological disorders that could influence treatment response and patients who had recently received vitamin B12 or vitamin D supplementation were also excluded from the analysis.

Age, sex, height, weight, body mass index (BMI), diagnostic group, comorbidities, history of diabetes mellitus, serum vitamin B12 level, and serum 25(OH)D level were recorded. Diagnoses were classified according to the medical records, clinical examination findings, imaging results, and, when available, electrophysiological assessments. Patients were grouped as having hand osteoarthritis, CTS, tenosynovitis or trigger finger, or other causes of hand pain, paresthesia, or both. CTS was diagnosed based on clinical findings and electrophysiological assessment.

Paraffin Therapy

All patients received the standard paraffin bath protocol used in our clinic. Paraffin therapy was applied as a superficial heat modality targeting the hand and wrist region. During the procedure, the hand was dipped repeatedly into heated paraffin to create a paraffin layer and was then wrapped in a plastic covering and a towel to retain heat. Each session lasted approximately 20 minutes, and the treatment was completed in 10 sessions. No additional study-specific intervention was applied.

Clinical Assessment

Clinical assessments were performed before the start of paraffin therapy and after the 10th session. Pain and functional status were evaluated using the PRWHE, a patient-reported measure of pain and functional limitation in hand and wrist disorders. Higher scores indicate greater pain and functional impairment. The original and Turkish validity and reliability studies were reported by MacDermid et al. (6) and Öke Topcu and İkbali Afşar (7), respectively. Appearance-related discomfort was recorded using a 0-10 numeric rating scale, and the perceived importance of hand appearance was categorized as very important, somewhat important, or not important.

Pain and/or numbness severity was assessed using a 0-10 VAS, where higher scores indicated more severe symptoms (8). The primary outcome was a clinical response to paraffin therapy. Because there is no universally accepted responder definition for paraffin therapy in heterogeneous hand disorders, clinical response was defined a priori using clinically meaningful change thresholds derived from the hand/wrist and pain outcome literature. Clinical response was defined as either a ≥30% improvement in PRWHE total score or a ≥2-point reduction in VAS numbness score after treatment (9-11). Patients meeting at least one of these criteria were classified as the "clinical response" group, whereas those meeting neither criterion were classified as the "no clinical response" group. This composite definition was chosen because the cohort included patients with both pain-dominant and sensory symptom-dominant presentations. Improvement in PRWHE was used to reflect clinically meaningful recovery in hand-related pain and function, whereas improvement in VAS numbness was used to capture sensory symptom relief that may be particularly relevant to CTS and neuropathic-like hand symptoms.

Laboratory Assessment

Serum vitamin B12 and 25(OH)D levels, measured as part of routine clinical evaluation before treatment, were recorded. No additional laboratory testing was performed for the purposes of this study. Serum 25(OH)D level was analyzed both as a continuous and a categorical variable. For the primary categorical analysis, 25(OH)D <20 ng/mL was defined as vitamin D deficiency; an additional analysis was performed using the <30 ng/mL threshold. Serum vitamin B12 level was also evaluated both as a continuous and as a categorical variable. In the primary analysis, vitamin B12 levels <300 pg/mL were considered low or borderline-low, while the conventional deficiency threshold of <200 pg/mL was used for additional analysis.

Sample Size

Sample size estimation was performed using G*Power software version 3.1.9.7 (Heinrich Heine University Düsseldorf, Düsseldorf, Germany). The calculation was based on a comparison of PRWHE total score improvements between two independent groups defined by baseline vitamin status. Because previous studies on paraffin therapy did not provide directly comparable data on response groups defined by vitamin levels, a moderate effect size was assumed for the expected between-group difference in PRWHE improvement. Using a two-tailed independent-samples t-test with Cohen's d=0.50, an alpha error probability of 0.05, an allocation ratio of 1:1, and a statistical power of 80%, the minimum required total sample

size was estimated to be approximately 128 patients. Accordingly, the final study cohort of 128 patients was considered sufficient for detecting a moderate between-group difference, although subgroup analyses by diagnosis were not separately powered (7,12).

Statistical Analysis

Statistical analyses were performed using appropriate statistical software. Continuous variables were summarized as mean±standard deviation and median (minimum-maximum), while categorical variables were presented as numbers and percentages. The distributions of continuous variables were assessed using visual methods and normality tests.

Because the main clinical outcome variables were not normally distributed, pre- and post-treatment scores for VAS pain, VAS numbness, PRWHE total, and appearance-related discomfort were compared using the Wilcoxon signed-rank test. Comparisons between responders and non-responders were performed using the Mann-Whitney U test for continuous variables. Categorical variables, including sex, diagnostic categories, diabetes mellitus, night awakening, vitamin D categories, and vitamin B12 categories, were compared using Pearson's chi-square test or Fisher's exact test when expected cell counts were low.

Vitamin D and Vitamin B12 levels were analyzed as both continuous and categorical variables. For vitamin D, 25(OH) D levels were categorized using thresholds of <20 ng/mL and <30 ng/mL. For vitamin B12, values <300 pg/mL were considered low or borderline-low, and values <200 pg/mL were used as the conventional deficiency threshold. Correlations between serum vitamin levels and clinical improvement, measured by PRWHE and VAS numbness scores, were evaluated using Spearman's rank correlation analysis.

Binary logistic regression analysis was performed to identify factors independently associated with clinical response. Variables with clinical relevance and/or with $p<0.10$ in univariable analyses were entered into the multivariable model. To reduce the risk of overfitting, a parsimonious model was constructed considering the number of clinical response events. The final model included baseline VAS numbness score, night awakening due to symptoms, hand appearance importance, vitamin B12 status (≥300 pg/mL), and vitamin D status (≥30 ng/mL). Odds ratios (ORs) with 95% confidence intervals (CIs) were reported. Model performance was assessed using the Omnibus test, Nagelkerke R^2, and overall classification accuracy. A p-value <0.05 was considered statistically significant.

RESULTS

Participant Characteristics

A total of 128 patients were included in the study. The mean age was 55.94±11.90 years, and 107 participants (83.6%) were female. The mean BMI was 29.19±5.28 kg/m^2. The most common diagnosis was hand osteoarthritis (53.9%), followed by CTS (23.4%). Diabetes mellitus was present in 27.3% of the participants, and 50.0% reported night awakening due to hand symptoms. Mean serum vitamin B12 and 25(OH)D levels were 465.47±254.59 pg/mL and 27.04±16.70 ng/mL, respectively. Baseline mean VAS pain, VAS numbness, and PRWHE scores were 5.22±2.27, 4.07±3.88, and 59.16±21.44, respectively (Table 1).

Changes in Clinical Outcomes Following Paraffin Therapy

Significant improvements were observed in all clinical outcome measures following paraffin therapy. Mean VAS pain scores decreased from 5.22±2.27 to 3.77±2.11 ($p<0.001$), while VAS numbness scores decreased from 4.07±3.88 to 2.70±3.23 ($p<0.001$). Similarly, PRWHE scores improved significantly, decreasing from 59.16±21.44 to 46.73±22.57 ($p<0.001$). Appearance-related discomfort scores also showed a significant reduction from 5.14±3.44 to 4.38±3.25 ($p<0.001$) (Table 2).

Comparison of Responders and Non-Responders

According to the predefined response criteria, 63 patients (49.2%) were classified as responders and 65 patients (50.8%) as non-responders.

Responders had significantly higher baseline serum vitamin B12 levels (513.98±217.76 vs. 418.46±279.50 pg/mL, $p=0.001$) and 25(OH)D levels (30.25±15.10 vs. 23.94±17.67 ng/mL, $p=0.001$) compared with non-responders. Baseline VAS numbness scores were also significantly higher in responders (5.19±3.58 vs. 2.98±3.88, $p=0.002$). In addition, responders more frequently reported night awakening due to symptoms (60.3% vs. 40.0%, $p=0.022$) and had higher appearance discomfort scores (5.95±3.10 vs. 4.35±3.59, $p=0.009$).

No significant differences were observed between responders and non-responders with respect to age, BMI, sex distribution, smoking status, alcohol consumption, diabetes mellitus, diagnosis, baseline pain severity, or baseline PRWHE scores (all $p>0.05$) (Table 3).

When vitamin levels were analyzed categorically, patients with 25(OH)D levels ≥20 ng/mL had a higher clinical response rate than those with levels <20 ng/mL (60.8% vs. 30.6%, $p=0.001$). Similarly, the response rate was higher in patients with 25(OH)D levels ≥30 ng/mL compared with those below this threshold (74.4% vs. 38.2%, $p<0.001$). Patients with vitamin

B12 levels ≥300 pg/mL also had a higher response rate than those with levels <300 pg/mL (62.5% vs. 35.9%, p=0.003). However, the conventional deficiency threshold of 200 pg/mL was not associated with treatment response (p=0.182).

Multivariable Logistic Regression Analysis

A multivariable logistic regression model was constructed including baseline numbness severity, night awakening, hand appearance importance, vitamin B12 status (≥300 pg/mL), and vitamin D status (≥30 ng/mL). The overall model was significant (Omnibus test, p<0.001) with a Nagelkerke R^2 of 0.262 and an overall classification accuracy of 75.8%.

Table 1. Baseline demographic, clinical, and laboratory characteristics of the study population (n=128)

Variable	Value
Demographic characteristics	
Age (years)	55.94±11.90
Female sex, n (%)	107 (83.6)
Height (cm)	160.38±9.46
Weight (kg)	74.85±13.72
Body mass index (kg/m^2)	29.19±5.28
Smoking, n (%)	23 (18.0)
Alcohol use, n (%)	6 (4.7)
Clinical characteristics	
Diabetes mellitus, n (%)	35 (27.3)
Other comorbidity, n (%)	32 (25.0)
No comorbidity, n (%)	61 (47.7)
Night awakening due to symptoms, n (%)	64 (50.0)
Appearance discomfort score (0-10)	5.14±3.44
Diagnostic categories	
Hand osteoarthritis	69 (53.9)
Carpal tunnel syndrome	30 (23.4)
Tenosynovitis/trigger finger	14 (10.9)
Other diagnoses	15 (11.7)
Importance of hand appearance	
Very important	66 (51.6)
Somewhat important	47 (36.7)
Not important	15 (11.7)
Laboratory parameters	
Vitamin B12 (pg/mL)	465.47±254.59
25(OH)D (ng/mL)	27.04±16.70
Baseline symptom severity	
VAS pain score (0-10)	5.22±2.27
VAS numbness score (0-10)	4.07±3.88
PRWHE total score (0-100)	59.16±21.44

Values are presented as mean±standard deviation or n (%)
BMI: Body mass index, PRWHE: Patient-rated wrist/hand evaluation, VAS: Visual analogue scale, 25(OH)D: 25-hydroxyvitamin D

Among the variables entered into the model, serum 25(OH)D levels ≥30 ng/mL emerged as the only independent predictor of clinical response (OR: 4.48, 95% CI: 1.66-12.05, p=0.003). Baseline numbness severity showed a borderline association with treatment response (OR: 1.17, 95% CI: 0.99-1.39, p=0.061). Vitamin B12 status (OR: 1.84, 95% CI: 0.81-4.16, p=0.144), night awakening (OR: 0.98, 95% CI: 0.28-3.40, p=0.973), and importance of hand appearance were not independently associated with treatment response (Table 4).

Correlation Analyses

Serum vitamin B12 and 25(OH)D levels were moderately correlated (r_s=0.460, p<0.001). Higher serum vitamin B12 levels were associated with greater improvements in PRWHE scores (r_s=0.282, p=0.001) and VAS numbness scores (r_s=0.347, p<0.001). Similarly, higher serum 25(OH)D levels were positively correlated with improvements in PRWHE scores (r_s=0.355, p<0.001) and VAS numbness scores (r_s=0.260, p=0.003) (Table 5).

DISCUSSION

The present study evaluated whether baseline vitamin B12 and 25(OH)D status were associated with short-term clinical response to standard paraffin therapy in patients with hand pain and/or numbness. The main finding was that serum 25(OH)D ≥30 ng/mL was independently associated with clinically meaningful response after adjustment for baseline numbness, night awakening, hand appearance importance, and vitamin B12 status. Although higher vitamin B12 levels were associated with greater improvement in PRWHE and VAS numbness scores in univariable and correlation analyses, vitamin B12 status did not remain an independent predictor.

The short-term improvements observed after paraffin therapy are consistent with previous studies evaluating superficial heat modalities in hand disorders. In symptomatic hand osteoarthritis, paraffin therapy combined with exercise or compared with other physical modalities has been reported to improve pain, hand function, grip strength, and quality of life, although the magnitude of benefit varies across studies (12-15). In CTS, paraffin therapy combined with wrist orthosis has also been associated with symptom improvement, although ultrasound with orthosis may provide greater functional benefit in some patients (16). A recent systematic review and meta-analysis similarly reported that paraffin bath therapy may reduce pain and improve hand function, grip strength, and pinch strength in various hand diseases, but emphasized the limited number and heterogeneity of available trials (2). Overall, current

Table 2. Changes in clinical outcomes after paraffin therapy (n=128)

Outcome	Baseline	Post-treatment	p-value
VAS pain (0-10)	5.22±2.27, median: 6 (0-9)	3.77±2.11, median: 4 (0-9)	<0.001
VAS numbness (0-10)	4.07±3.88, median: 5 (0-10)	2.70±3.23, median: 1 (0-10)	<0.001
PRWHE total score (0-100)	59.16±21.44, median: 62.25 (7-99)	46.73±22.57, median: 45.00 (1-98)	<0.001
Appearance discomfort score (0-10)	5.14±3.44, median: 5 (0-10)	4.38±3.25, median: 5 (0-10)	<0.001

Values are presented as mean±standard deviation and median (minimum-maximum). Comparisons between baseline and post-treatment measurements were performed using the Wilcoxon signed-rank test
PRWHE: Patient-rated wrist/hand evaluation, VAS: Visual analogue scale

evidence supports paraffin as a symptomatic modality in selected hand conditions while highlighting variability in treatment response across patients and diagnoses (17).

The diagnostic heterogeneity of the cohort should also be considered when interpreting the relationship between vitamin D status and the response to paraffin therapy. Hand osteoarthritis and CTS have distinct underlying mechanisms. In hand osteoarthritis, symptoms are mainly related to joint degeneration, periarticular stiffness, pain, reduced grip strength, and functional limitation. In this setting, paraffin therapy may provide symptomatic benefit through superficial heating, reduction of stiffness, increased soft-tissue extensibility, and facilitation of hand use and exercise, as supported by previous studies in symptomatic hand osteoarthritis and by recent systematic reviews of paraffin therapy in hand disorders (1,2,12,15,17). By contrast, CTS is primarily a compression neuropathy of the median nerve, and paraffin therapy should not be expected to directly reverse the mechanical or electrophysiological basis of nerve compression. Its potential benefit in CTS is more likely related to short-term symptom modulation, local comfort, reduced soft-tissue tension, and improved tolerance to hand activity or splint-based rehabilitation (16). Therefore, vitamin D status may not interact with paraffin therapy through a single disease-specific pathway. Rather, adequate vitamin D levels may reflect a more favorable neuromuscular and musculoskeletal background, potentially influencing pain perception, muscle performance, functional recovery, and rehabilitation responsiveness in both degenerative and neuropathic-like hand conditions (3,18). In addition, previous evidence suggests that vitamin D deficiency may be associated with CTS symptom severity and that supplementation may improve pain and functional outcomes in some CTS studies, although the level of evidence remains limited (19). This interpretation remains hypothesis-generating because the present study was not designed to test diagnosis-specific mechanisms or vitamin D-by-diagnosis interactions.

The association between vitamin D status and clinical response may be clinically meaningful in rehabilitation, where pain, muscle performance, neuromuscular control, and functional hand use are closely linked. Although the relationship between vitamin D and musculoskeletal pain is inconsistent, vitamin D status may be relevant to pain perception, muscle function, and physical performance in selected patient groups (3,18). In the present study, the ≥30 ng/mL threshold was more strongly associated with clinical response than the conventional deficiency threshold of <20 ng/mL. This may suggest that in patients undergoing rehabilitation for hand symptoms, avoiding severe deficiency alone may not be sufficient to define an optimal metabolic status for functional recovery. However, this association should not be interpreted as evidence that vitamin D supplementation improves response to paraffin therapy.

From a biological perspective, vitamin D may influence the response to paraffin therapy through several complementary mechanisms. Vitamin D has recognized roles in neuromuscular function, skeletal muscle performance, pain modulation, and peripheral nerve health (3,18). Therefore, adequate vitamin D status may create a more favorable biological background for symptomatic and functional recovery after a superficial heat intervention. In hand osteoarthritis, paraffin therapy may reduce pain and stiffness by increasing tissue extensibility, improving periarticular soft-tissue flexibility, and enhancing joint compliance (1,2,12,15). In this context, sufficient vitamin D levels may support muscle function and pain regulation, thereby facilitating better hand use after thermal treatment. In CTS, the mechanism is likely different. Paraffin therapy cannot directly reverse median nerve compression, but local heat may improve comfort, enhance microcirculation, reduce soft-tissue tension, and increase the symptom threshold (16). Because vitamin D deficiency has been linked to neuromuscular dysfunction and neuropathic-like symptoms, better vitamin D status may partly modulate sensory symptoms and functional tolerance in CTS (19). Thus, the observed association between 25(OH)D levels and clinical response may reflect an interaction between the local thermal and mechanical effects of paraffin therapy and systemic neuromuscular or pain-related factors. However, this proposed mechanism remains hypothetical and should

Table 3. Comparison of baseline characteristics according to clinical response status

Variable	Non-responder (n=65)	Responder (n=63)	p-value
Demographic characteristics			
Age (years)	55.12±11.85 55 (27-73)	56.78±11.99 60 (25-75)	0.290
BMI (kg/m^2)	28.56±4.07 27.41 (18.42-38.21)	29.85±6.26 29.14 (17.36-48.48)	0.422
Female sex, n (%)	54 (83.1)	53 (84.1)	0.873
Smoking, n (%)	12 (18.5)	11 (17.5)	0.883
Alcohol use, n (%)	3 (4.6)	3 (4.8)	0.969
Clinical characteristics			
Diabetes mellitus, n (%)	20 (30.8)	15 (23.8)	0.370
Night awakening due to symptoms, n (%)	26 (40.0)	38 (60.3)	0.022
Appearance discomfort score	4.35±3.59 4 (0-10)	5.95±3.10 7 (0-10)	0.009
Diagnostic categories			
Hand osteoarthritis, n (%)	39 (60.0)	30 (47.6)	0.478
Carpal tunnel syndrome, n (%)	14 (21.5)	16 (25.4)	
Tenosynovitis / trigger finger, n (%)	5 (7.7)	9 (14.3)	
Other diagnoses, n (%)	7 (10.8)	8 (12.7)	
Laboratory parameters			
Vitamin B12 (pg/mL)	418.46±279.50 342 (132-1624)	513.98±217.76 471 (188-1025)	0.001
25(OH)D (ng/mL)	23.94±17.67 20.0 (5.52-91.0)	30.25±15.10 27.7 (7.5-75.0)	0.001
Baseline symptom severity			
VAS pain score (0-10)	5.08±2.12 6 (0-9)	5.37±2.42 6 (0-9)	0.317
VAS numbness score (0-10)	2.98±3.88 0 (0-10)	5.19±3.58 6 (0-10)	0.002
PRWHE total score (0-100)	58.52±19.91 61 (10.5-96.5)	59.81±23.06 63 (7-99)	0.625
Vitamin categories			
Vitamin D <20 ng/mL, n (%)	34 (52.3)	15 (23.8)	0.001
Vitamin D ≥20 ng/mL, n (%)	31 (47.7)	48 (76.2)	
Vitamin D <30 ng/mL, n (%)	55 (84.6)	34 (54.0)	<0.001
Vitamin D ≥30 ng/mL, n (%)	10 (15.4)	29 (46.0)	
Vitamin B12 <300 pg/mL, n (%)	41 (63.1)	23 (36.5)	0.003
Vitamin B12 ≥300 pg/mL, n (%)	24 (36.9)	40 (63.5)	
Vitamin B12 <200 pg/mL, n (%)	4 (6.2)	1 (1.6)	0.182*
Vitamin B12 ≥200 pg/mL, n (%)	61 (93.8)	62 (98.4)	

Values are presented as mean±standard deviation and median (minimum-maximum) or n (%). Percentages are column percentages. Continuous variables were compared using the Mann-Whitney U test. Categorical variables were compared using Pearson's chi-square test or Fisher's exact test when appropriate
PRWHE: Patient-rated wrist/hand evaluation, VAS: Visual analogue scale, 25(OH)D: 25-hydroxyvitamin D, *: Fisher's exact test

be confirmed in prospective studies designed separately for hand osteoarthritis and CTS.

The relationship between vitamin D status and response may also be relevant for patients presenting with numbness or neuropathic-like hand symptoms. In the present cohort, CTS was the second most common diagnostic group, and baseline VAS numbness scores were higher among responders. Previous evidence suggests that vitamin D deficiency may be associated with the severity of symptoms in CTS, although available data are limited. In a systematic review, Anusitviwat et al. reported that vitamin

Table 4. Multivariable logistic regression analysis of factors associated with clinical response

Variable	B	SE	OR (95% CI)	p-value
Night awakening due to symptoms	-0.021	0.635	0.98 (0.28-3.40)	0.973
Baseline VAS numbness score	0.160	0.085	1.17 (0.99-1.39)	0.061
Hand appearance importance (overall)	—	—	—	0.761
├ Somewhat important vs. very important	-0.334	0.458	0.72 (0.29-1.76)	0.465
└ Not important vs. very important	-0.218	0.710	0.80 (0.20-3.23)	0.758
25(OH)D ≥30 ng/mL	1.499	0.505	4.48 (1.66-12.05)	0.003
Vitamin B12 ≥300 pg/mL	0.609	0.417	1.84 (0.81-4.16)	0.144

Binary logistic regression analysis. Variables entered the model were night awakening due to symptoms, baseline VAS numbness score, hand appearance importance, vitamin B12 status (≥300 pg/mL), and vitamin D status (≥30 ng/mL)
OR: Odds ratio, CI: Confidence interval, VAS: Visual analogue scale, 25(OH)D: 25-hydroxyvitamin D

Table 5. Correlations between vitamin levels and clinical improvement outcomes

Variables	PRWHE improvement (r_s, p)	VAS numbness improvement (r_s, p)
Vitamin B12	0.282, p=0.001	0.347, p<0.001
25(OH)D	0.355, p<0.001	0.260, p=0.003

Spearman correlation coefficients (r_s). Positive coefficients indicate greater clinical improvement with increasing vitamin levels
PRWHE: Patient-rated wrist/hand evaluation, VAS: Visual analogue scale, 25(OH)D: 25-hydroxyvitamin D

D supplementation was associated with improvements in pain, functional status, and sensory conduction velocity in some studies of patients with CTS; however, the authors also emphasized the low level of evidence and the lack of a standardized supplementation dose or duration (19). These findings are compatible with the present results and suggest a possible link between vitamin D status and improvement in hand symptoms, particularly numbness. However, because our study did not evaluate vitamin D supplementation and included a heterogeneous group of hand disorders, this association should be considered hypothesis-generating, rather than confirmatory.

Vitamin B12 showed a different pattern. Patients with vitamin B12 levels ≥300 pg/mL had a higher clinical response rate, and higher serum vitamin B12 levels correlated with greater improvements in PRWHE and VAS numbness scores. This is biologically plausible because vitamin B12 is required for normal peripheral nerve function, and low or borderline-low levels may contribute to paresthesia and neuropathic-like symptoms. However, vitamin B12 status did not remain an independent predictor after adjustment, suggesting that its association with improvement may partly reflect baseline numbness severity or its correlation with vitamin D status. Limited previous evidence has examined B vitamins in hand disorders, but available studies are small and not directly comparable with the present rehabilitation cohort (20). Therefore, the B12 findings in our study should be interpreted as supportive but not definitive. Clinically, these findings may help explain variable responses to commonly used rehabilitation modalities. Patients receiving the same paraffin protocol may exhibit varying degrees of improvement, which are unlikely to be explained solely by diagnosis or baseline symptom severity. Vitamin D status and, to a lesser extent, vitamin B12 status, may therefore be considered part of a comprehensive rehabilitation assessment, particularly in patients with hand pain accompanied by numbness, paresthesia, or non-specific musculoskeletal complaints.

Study Limitations

This study has several limitations. First, its retrospective, single-center design limits the ability to control for all potential confounding factors. Second, the absence of a control group precludes causal conclusions regarding the efficacy of paraffin therapy, and the observed improvements cannot be clearly distinguished from the natural course of symptoms, placebo effects, regression to the mean, or other routine care factors. Third, the study population was diagnostically heterogeneous, including patients with hand osteoarthritis, CTS, tenosynovitis (trigger finger), and other causes of hand pain or paresthesia. Although this reflects routine rehabilitation practice, it limits diagnosis-specific interpretation. In addition, the sample size was not sufficient to perform robust subgroup analyses or interaction models separately for hand osteoarthritis and CTS. Therefore, the observed association between vitamin D status and clinical response should be interpreted as a general patient-related rehabilitation factor rather than a diagnosis-specific effect. Fourth, although CTS was diagnosed by electrophysiological assessment, the study was not designed to perform diagnosis-specific analyses of severity or to evaluate whether electrophysiological

severity modified the treatment response. Fifth, serum vitamin B12 and 25(OH)D levels were obtained from routine clinical records, and the study did not evaluate the effect of vitamin supplementation. Therefore, the findings should be interpreted as associations between baseline vitamin status and clinical response rather than evidence of a therapeutic effect of vitamin replacement. Finally, only short-term outcomes after a 10-session treatment program were assessed, and longer follow-up is needed to determine whether these associations persist over time.

CONCLUSION

Baseline vitamin D status was independently associated with short-term clinical response to paraffin therapy in patients with hand pain and/or numbness. Serum 25(OH) D ≥30 ng/mL was associated with a higher likelihood of clinically meaningful improvement. Vitamin D status may, therefore, be considered part of the broader rehabilitation assessment in patients with hand-related symptoms. Prospective controlled studies are needed to determine whether correction of vitamin D deficiency can improve rehabilitation outcomes.

ETHICS

Ethics Committee Approval: Ethical approval was obtained from the University of Health Sciences Türkiye, Bakırköy Dr. Sadi Konuk Training and Research Hospital Clinical Research Ethics Committee (approval no: 2026-10-02, date: 22.04.2026).

Informed Consent: Because of the retrospective design, the requirement for individual informed consent was waived.

FOOTNOTES

Authorship Contributions

Concept: D.F., Y.A., S.Ç., Design: D.F., B.G.A., T.S., T.Ş., Data Collection or Processing: D.F., B.G.A., M.Ç., T.S., Y.A., Analysis or Interpretation: D.F., M.Ç., T.Ş., Literature Search: D.F., B.G.A., M.Ç., Y.A., S.Ç., Writing: D.F., T.S., T.Ş., S.Ç.

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