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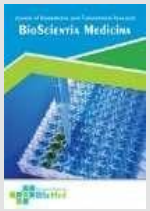

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Is Serum Vitamin D a Determinant of Carpal Tunnel Syndrome Severity? A Cross-Sectional Observational Study

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A B S T R A C T

Background: Carpal tunnel syndrome (CTS) represents one of the most frequently encountered compressive neuropathies affecting the upper extremities. Emerging evidence suggests a potential link between vitamin D status and CTS incidence and severity, with vitamin D deficiency proposed as an independent risk factor influencing symptom severity. This study aimed to investigate the association between serum 25-hydroxyvitamin D levels and the electrophysiologically determined severity of CTS in a cohort of patients in Padang, Indonesia. **Methods:** This cross-sectional observational study was conducted over eight months, from July 2024 to February 2025, at the Neurological Polyclinic of Dr. M. Djamil General Hospital Padang. Patients diagnosed with CTS based on clinical presentation and confirmed by nerve conduction studies (NCS) were consecutively enrolled. Exclusion criteria were applied to ensure a homogenous study population. Serum 25-hydroxyvitamin D levels were quantified using the Enzyme-Linked Immunosorbent Assay (ELISA) method. CTS severity was categorized as mild, moderate, or severe based on standardized NCS parameters. The association between serum 25-hydroxyvitamin D levels and CTS severity grades was analyzed using the Kruskal-Wallis test, with a p-value < 0.05 considered statistically significant. **Results:** A total of 45 subjects meeting the inclusion criteria were included in the final analysis. The median age of the participants was 36 years (range 20-71), with a predominance of female patients (n=37, 82.2%). The mean Body Mass Index (BMI) was 24.1 ± 4.66 kg/m². Based on NCS findings, CTS severity was classified as mild in 20 patients (44.4%), moderate in 16 patients (35.6%), and severe in 9 patients (20%). The overall median serum 25-hydroxyvitamin D level across all CTS patients was 27.80 ng/mL (range 10.4 - 278.4 ng/mL). When stratified by severity, the median vitamin D levels were 23.75 ng/mL for mild CTS, 27.95 ng/mL for moderate CTS, and 37.50 ng/mL for severe CTS. Despite an apparent trend of increasing median vitamin D levels with increasing CTS severity, the Kruskal-Wallis test revealed no statistically significant association between serum 25-hydroxyvitamin D levels and the severity of CTS (p = 0.094). **Conclusion:** Serum 25-hydroxyvitamin D levels were not found to be significantly associated with the severity of carpal tunnel syndrome as determined by nerve conduction studies. Further research with larger sample sizes and diverse populations is warranted to clarify the potential role of vitamin D in the pathophysiology and clinical presentation of CTS.

1. Introduction

Carpal tunnel syndrome (CTS) is a prevalent neurological condition, widely recognized as one of the most common peripheral nerve entrapment syndromes encountered in clinical settings. This syndrome arises from the compression or mechanical irritation of the median nerve as it traverses the carpal tunnel, an anatomically confined space within the

wrist. The carpal tunnel is bordered dorsally by the carpal bones and volarly by the transverse carpal ligament. This compression leads to a constellation of characteristic symptoms, including pain, paresthesia (numbness and tingling), and, in advanced stages, weakness and atrophy of the thenar muscles innervated by the median nerve. These symptoms typically manifest in the sensory distribution of the median nerve, encompassing the palmar aspect of the thumb, index finger, middle finger, and the radial half of the ring finger. The functional limitations imposed by CTS can be substantial, often interfering with occupational tasks, activities of daily living, and overall quality of life. The etiology of CTS is multifactorial, involving a complex interplay of anatomical, systemic, occupational, and idiopathic factors. Anatomical factors contributing to reduced space within the carpal tunnel include wrist fractures, dislocations, arthritis, tenosynovitis, or space-occupying lesions like ganglion cysts or tumors. Systemic conditions frequently associated with an increased risk of CTS include diabetes mellitus, hypothyroidism, rheumatoid arthritis, obesity, pregnancy, and renal failure requiring hemodialysis. These conditions are thought to contribute to CTS pathogenesis through mechanisms such as fluid retention, inflammation, altered connective tissue properties, or direct nerve ischemia. Occupational or ergonomic factors, particularly those involving repetitive hand and wrist movements, forceful gripping, awkward wrist postures, and exposure to vibration, have also been strongly implicated in the development and exacerbation of CTS. Furthermore, demographic factors such as increasing age, female gender, and higher body mass index (BMI) are well-established risk factors for developing CTS.[1-4]

In recent years, considerable research interest has focused on the potential role of micronutrients, particularly vitamin D, in the pathophysiology of peripheral neuropathies, including CTS. Vitamin D, traditionally known for its crucial role in calcium homeostasis and bone metabolism, is increasingly recognized for its pleiotropic effects extending beyond the skeletal system. The vitamin D receptor (VDR) and enzymes involved in vitamin D metabolism (e.g., 1α-hydroxylase) have been identified in various tissues, including the central and peripheral nervous systems, suggesting a direct role for vitamin D in neuronal function and health. Preclinical and clinical evidence suggests that vitamin D may exert neuroprotective effects through multiple mechanisms. These include modulation of neurotrophic factors (such as nerve growth factor), regulation of inflammatory responses, antioxidant properties, and enhancement of Schwann cell activity leading to improved nerve myelination and regeneration following injury. Vitamin D deficiency has been linked to various neurological conditions, including multiple sclerosis, Parkinson's disease, Alzheimer's disease, and peripheral neuropathies, particularly diabetic neuropathy. Specifically concerning CTS, several studies have explored the association between serum vitamin D levels and the risk or severity of the condition, yielding somewhat conflicting results. Some investigations have reported significantly lower vitamin D levels in patients with CTS compared to healthy controls, suggesting that vitamin D deficiency might be a contributing factor to its development. Furthermore, some studies have proposed that vitamin D deficiency could be an independent risk factor influencing the severity of CTS symptoms, potentially correlating with increased pain perception or more pronounced electrophysiological abnormalities. Research by Al-Khalidi and Fahad, for instance, indicated a correlation where lower vitamin D levels were associated with higher pain scores in CTS patients.[5-7]

Conversely, other studies have failed to demonstrate a significant association between vitamin D status and either the presence or the severity of CTS. These discrepancies may arise from differences in study populations, diagnostic criteria for CTS, methods for assessing vitamin D levels, sample sizes, and control for confounding factors. The primary circulating form of vitamin D, 25-hydroxyvitamin D [25(OH)D], is considered the most reliable indicator of overall vitamin D status in the body, reflecting both

dietary intake and endogenous synthesis through sunlight exposure. Therefore, measuring serum 25(OH)D levels provides a valuable tool for assessing vitamin D sufficiency or deficiency in clinical and research settings. Given the potential neuroprotective role of vitamin D and the conflicting reports regarding its association with CTS, further investigation is warranted, particularly in diverse populations. Screening for vitamin D deficiency has been suggested for patients presenting with neuropathic symptoms. Moreover, limited interventional studies have suggested that vitamin D supplementation might offer therapeutic benefits, such as pain reduction, in patients with mild to moderate CTS, although robust evidence is still lacking.[8-10] This study was conceived against this background of emerging evidence and existing controversy. The primary objective was to investigate the potential association between serum 25-hydroxyvitamin D levels and the severity of carpal tunnel syndrome, as objectively assessed by nerve conduction studies (NCS), in a cohort of patients presenting to a tertiary care hospital in Padang, Indonesia.

2. Methods

The study employed a cross-sectional observational design. Data collection was prospectively conducted over an eight-month period, spanning from July 2024 to February 2025. The study was carried out at the Neurological Polyclinic of Dr. M. Djamil General Hospital, a tertiary referral center located in Padang, West Sumatra, Indonesia. This setting provides care for a diverse patient population from the surrounding region.

The study's target population consisted of patients presenting to the Neurological Polyclinic with suspected carpal tunnel syndrome (CTS) based on clinical symptoms and physical examination findings. Suspected CTS was defined by the presence of pain, numbness, and tingling in the median nerve distribution, often worse at night, along with positive findings from physical examinations, such as Tinel's sign, Phalen's maneuver, or carpal compression test. Participants were recruited using a consecutive admission sampling strategy. All patients diagnosed with CTS, confirmed by standardized nerve conduction studies (NCS) performed during the study period, and meeting the predefined inclusion and exclusion criteria, were invited to participate.

The inclusion criteria were established to ensure the selection of appropriate participants for the study; Age 18 years or older; Clinical diagnosis of CTS based on typical symptoms and signs; Electrophysiological confirmation of CTS via NCS according to established criteria; Willingness and ability to provide informed consent. The exclusion criteria were implemented to minimize potential confounding factors and ensure a homogenous study population; Previous history of wrist surgery or significant wrist trauma; Presence of other neurological conditions that could mimic or confound CTS symptoms, such as cervical radiculopathy, diabetic polyneuropathy affecting the upper limbs, thoracic outlet syndrome, or other peripheral neuropathies; Known systemic diseases strongly associated with secondary CTS (e.g., rheumatoid arthritis, hypothyroidism, acromegaly), unless these conditions were stable and well-controlled; Pregnancy or lactation; Current use of vitamin D supplements or medications known to significantly affect vitamin D metabolism (e.g., anticonvulsants, corticosteroids) within the past three months; Inability to undergo NCS examination; Refusal to participate or provide blood samples.

The sample size was determined based on the consecutive enrollment of eligible patients during the defined study period. An initial target, based on feasibility and expected patient flow, was estimated, and the final sample size was determined after applying the inclusion and exclusion criteria. Potentially eligible patients were identified, and the study objectives and procedures were thoroughly explained by a trained research assistant or neurologist involved in the study. Written informed consent was obtained from all participants before enrollment and any study-related procedures.

For each enrolled participant, data was collected using a standardized case report form (CRF). The following data points were recorded; Demographic Information: Age (years) and gender (male/female) were recorded; Anthropometric Measurements: Height (meters) and weight (kilograms) were measured using standard equipment. Body Mass Index (BMI) was calculated as weight (kg) divided by height squared (m^2); Clinical Characteristics: Dominant hand (right/left), onset of symptoms (categorized as subacute or chronic based on duration, typically using a cutoff of 3 or 6 months), and affected hand(s) were documented; Medical History: Relevant comorbidities and medication use were recorded.

All participants underwent standardized NCS of the median nerve across the wrist. The NCS procedures were performed by an experienced neurophysiologist blinded to the participant's vitamin D status. Standard electrodiagnostic techniques were employed, utilizing surface electrodes and commercially available electromyography (EMG)/NCS equipment (Nicolet Viking Select, Medtronic Keypoint). Skin temperature was maintained above 32°C to ensure reliable results. The following parameters were assessed for the median nerve; Distal Motor Latency (DML): The time taken for the nerve impulse to travel from the wrist stimulation point to the abductor pollicis brevis (APB) muscle; Compound Muscle Action Potential (CMAP) Amplitude: A measure of the muscle response following nerve stimulation; Sensory Nerve Conduction Velocity (SNCV): The speed of impulse conduction along the sensory fibers, typically measured across the wrist-to-digit segment (e.g., digit II or III); Sensory Nerve Action Potential (SNAP) Amplitude: A measure of the sensory nerve response. Comparative tests (median vs. ulnar sensory latency comparison across the palm) were also performed according to standard protocols.

Based on the NCS findings, the severity of CTS was classified using established electrophysiological grading scales. The classification scheme was as follows; Mild CTS: Prolonged distal sensory latency or slowed sensory conduction velocity across the wrist, with normal distal motor latency; Moderate CTS: Prolonged distal sensory latency AND prolonged distal motor latency; Severe CTS: Absence of sensory response AND prolonged distal motor latency, potentially with low amplitude or absent motor response (indicating axonal loss). For participants with bilateral involvement, the severity classification was based on the more severely affected hand. In unilateral cases, the affected hand was used for classification. Participants were then categorized into mild, moderate, or severe CTS groups according to these NCS criteria.

Following informed consent and enrollment, a venous blood sample (approximately 3-5 cc) was collected from each participant by a trained phlebotomist using standard aseptic techniques. The blood was collected into serum separator tubes. After clotting, the samples were centrifuged at 3000 rpm for 10 minutes to separate the serum. The serum was carefully aliquoted and immediately transported under cooled conditions to the Biomedical Laboratory of the Faculty of Medicine, Andalas University, Padang, for analysis. Serum concentrations of 25-hydroxyvitamin D [25(OH)D] were measured using a quantitative Enzyme-Linked Immunosorbent Assay (ELISA) method. The specific ELISA kit manufacturer and assay characteristics (e.g., sensitivity, intra- and inter-assay coefficients of variation) were recorded. Results were expressed in nanograms per milliliter (ng/mL). Laboratory personnel performing the ELISA assays were blinded to the clinical and NCS data of the participants.

All collected data were coded and entered into a database. Statistical analysis was performed using IBM SPSS Statistics for Windows, Version 26.0 (IBM Corp., Armonk, NY, USA). Descriptive statistics were used to summarize the characteristics of the study population. Continuous variables with a normal distribution were presented as mean ± standard deviation (SD), while non-normally distributed continuous variables were presented as median and interquartile range (IQR) or minimum-maximum range. Categorical variables were presented as

frequencies and percentages (n, %). The normality of the distribution for continuous variables (age, BMI, serum 25(OH)D levels) was assessed using the Shapiro-Wilk or Kolmogorov-Smirnov tests. To evaluate the association between serum 25-hydroxyvitamin D levels (a non-normally distributed variable) and the ordinal categories of CTS severity (mild, moderate, severe), the non-parametric Kruskal-Wallis H test was used. This test compares the median 25(OH)D levels across the three severity groups. Relationships between baseline characteristics (age, gender, BMI, dominant hand, onset) and CTS severity were explored using appropriate statistical tests; Analysis of Variance (ANOVA) or Kruskal-Wallis test for continuous variables (age, BMI) across severity groups, depending on data distribution; Chi-square test or Fisher's exact test (for small cell counts) for categorical variables (gender, dominant hand, onset) across severity groups. A p-value of less than 0.05 (two-tailed) was considered statistically significant for all analyses.

The study protocol was reviewed and approved by the Research Ethics Committee of the Faculty of Medicine, Andalas University / Dr. M. Djamil General Hospital Padang (Ethics Certification No. DP.04.03/D.XVI.XI/486/2024). The study was conducted in accordance with the principles of the Declaration of Helsinki and relevant national ethical guidelines. All participants provided written informed consent before inclusion in the study. Confidentiality of participant data was maintained throughout the study by using anonymized codes.

3. Results

Table 1 provides a concise summary of the key demographic and baseline clinical characteristics of the 45 participants included in the study; Age: The median age of the participants was 36 years. This means that half of the participants were younger than 36 years old, and half were older. The age range was from 20 to 71 years. This indicates a fairly wide distribution of ages in the study group, suggesting that the study included both younger and older adults with CTS; Gender: The study cohort was predominantly female. There were 37 female participants, representing 82.2% of the total group. There were 8 male participants, representing 17.8% of the group. This shows a significant gender imbalance, with females being much more prevalent than males in the study population. This is consistent with the general understanding that CTS is more common in women; BMI (Body Mass Index): The mean BMI of the participants was 24.1 kg/m^2, with a standard deviation of 4.66 kg/m^2. A BMI of 24.1 falls within the "normal" to "slightly overweight" range according to standard BMI classifications. (Normal range is typically 18.5-24.9 kg/m^2, and overweight is 25-29.9 kg/m^2). The standard deviation of 4.66 suggests a moderate spread of BMI values around the mean. This means that while the average was in the normal to slightly overweight category, some participants had considerably lower or higher BMIs; Dominant Hand: The majority of participants (38 individuals, or 84.4%) were right-hand dominant. A smaller proportion (7 individuals, or 15.6%) were left-hand dominant. This reflects the typical distribution of hand dominance in the general population, where right-handedness is far more common; Onset: The onset of CTS symptoms was roughly evenly distributed between subacute and chronic presentations. 23 participants (51.1%) reported a subacute onset of symptoms. 22 participants (48.9%) reported a chronic onset of symptoms. This indicates that the study included individuals with relatively recent-onset symptoms (subacute) and those with longer-standing symptoms (chronic).

Table 1. Basic characteristics of research subjects (n=45).

Characteristic	Category	Value
Age (Years), Median (Range)		36 (20 - 71)
Gender, n (%)	Male	8 (17.8%)
	Female	37 (82.2%)
BMI (kg/m²), Mean ± SD		24.1 ± 4.66
Dominant Hand, n (%)	Right Hand	38 (84.4%)
	Left Hand	7 (15.6%)
Onset, n (%)	Subacute	23 (51.1%)
	Chronic	22 (48.9%)

Notes: BMI: Body Mass Index; SD: Standard Deviation.

Table 2 presents the relationship between several basic research characteristics of the study participants and the severity of their carpal tunnel syndrome (CTS). CTS severity was categorized as mild, moderate, or severe based on nerve conduction studies. Regarding age, there's a trend suggesting older age with increasing CTS severity. The median age progresses from 29 years in the mild CTS group to 36.5 years in the moderate group and 47 years in the severe group. However, this age difference across the severity groups was not statistically significant. For gender, the table shows a higher proportion of males in the moderate severity group compared to the other groups. Nevertheless, the overall distribution of gender across the severity categories did not reach statistical significance. When looking at BMI, the mean values were fairly similar across the mild and moderate CTS groups, with a slightly higher mean BMI observed in the severe group. Despite this difference, there was no statistically significant difference in BMI across the three severity categories. The dominant hand (right or left) showed no significant difference in distribution across the mild, moderate, and severe CTS groups. Finally, the onset of symptoms (subacute or chronic) did not show a significant association with the electrophysiological severity of CTS. The proportion of subacute and chronic cases was relatively consistent across the severity groups.

Table 2. Relationship between basic research characteristics and CTS severity.

Characteristic	CTS severity category	Mild (n=20)	Moderate (n=16)	Severe (n=9)	p-value
Age (Year)	Median (Range)	29 (20 – 59)	36.5 (20 – 65)	47 (24 – 71)	0.132#
Gender	n (%)				0.274^
	Male	1 (12.5%)	5 (62.5%)	2 (25%)	
	Female	19 (51.4%)	11 (29.7%)	7 (18.9%)	
BMI (kg/m²)	Mean ± SD	23.94 ± 4.40	23.86 ± 4.67	25.05 ± 5.62	0.812*
Dominant hand	n (%)				0.582^
	Right Hand	15 (39.5%)	15 (39.5%)	8 (21.1%)	
	Left Hand	5 (71.4%)	1 (14.3%)	1 (14.3%)	
Onset	n (%)				0.977^
	Subacute	9 (39.1%)	11 (47.8%)	3 (13.0%)	
	Chronic	11 (50.0%)	5 (22.7%)	6 (27.3%)	

Notes: # Kruskal-Wallis Test; ^ Chi-Square Test/Fisher's Exact Test; *ANOVA Test. BMI: Body Mass Index; SD: Standard Deviation.

Table 3 presents the serum 25-hydroxyvitamin D levels in relation to the severity of carpal tunnel syndrome (CTS). The CTS severity is categorized as mild, moderate, and severe. In the mild CTS group, the median serum 25-hydroxyvitamin D level was 23.75 ng/mL, with values ranging from 10.40 to 278.4 ng/mL. In the moderate CTS group, the median serum 25-hydroxyvitamin D level was 27.95 ng/mL, with

values ranging from 16.50 to 47.80 ng/mL. In the severe CTS group, the median serum 25-hydroxyvitamin D level was 37.50 ng/mL, with values ranging from 17.10 to 82.40 ng/mL. There's an observed trend of increasing median serum 25-hydroxyvitamin D levels as the severity of CTS increases (Mild < Moderate < Severe). This suggests that patients with more severe CTS tend to have higher median vitamin D levels. However, despite this apparent trend, the Kruskal-Wallis test revealed that the difference in median serum 25-hydroxyvitamin D levels across the three severity groups was not statistically significant (p = 0.094).

Table 3. Serum 25-hydroxyvitamin D levels by CTS severity.

Variable	CTS severity category	Mild (n=20)	Moderate (n=16)	Severe (n=9)	p-value
Serum 25-Hydroxyvitamin D (ng/mL)	Median (Min-Max)	23.75 (10.40–278.4)	27.95 (16.50–47.80)	37.50 (17.10-82.40)	0.094*

Notes: * Kruskal-Wallis Test.

4. Discussion

The demographic and baseline clinical characteristics of the participants in this study offer valuable context for interpreting the primary findings. These characteristics provide insights into the nature of the patient cohort and allow for comparisons with other CTS studies conducted in different populations. A notable feature of our study population was the predominance of female patients, constituting 82.2% of the total participants. This observation is consistent with a substantial body of existing literature that has consistently reported a higher incidence and prevalence of CTS in women compared to men. The reasons underlying this gender disparity are complex and multifactorial, and while the precise mechanisms remain fully elucidated, several contributing factors have been proposed. One prominent hypothesis centers on anatomical differences, specifically the generally smaller wrist dimensions observed in women. A smaller carpal tunnel inherently provides less space for the median nerve, potentially predisposing women to increased nerve compression and the development of CTS. Hormonal influences are also thought to play a significant role. Fluctuations in hormone levels, particularly during specific physiological states such as pregnancy and menopause, can lead to fluid retention and tissue swelling, further compromising the space within the carpal tunnel. These hormonal shifts may contribute to the increased susceptibility of women to CTS. Occupational exposures may also contribute to the observed gender difference. While this study did not specifically investigate occupational factors, it's conceivable that there are variations in the types of tasks and work environments that women are more likely to engage in, potentially involving more repetitive hand and wrist movements. However, it is crucial to acknowledge that this is a complex area, and further research is needed to fully understand the interplay between gender, occupation, and CTS risk. It is important to emphasize that while our study reflects the established pattern of higher CTS prevalence in women, it also highlights the need for continued research to disentangle the various contributing factors and develop targeted prevention and treatment strategies. The median age of the participants in our study was 36 years. This finding is generally consistent with the typical age range at which CTS presents, although it's important to note that CTS incidence tends to increase with advancing age, often peaking between the fourth and sixth decades of life. While our median age aligns with observations from some studies conducted in Asian populations, it's worth noting that other studies, particularly those in Western cohorts, have reported somewhat older average ages at CTS presentation.

Several factors could account for these variations in age distribution across different studies. Differences in population structures, including variations in the proportion of older adults, could contribute to these discrepancies. Lifestyle factors, such as dietary habits, physical activity levels, and occupational exposures, can also vary significantly between populations and influence the age at which individuals develop CTS. Furthermore, referral patterns and healthcare-seeking behaviors may differ across regions, potentially affecting the age distribution of patients presenting to clinics and hospitals with CTS symptoms. It is important to acknowledge that the age range in our study was relatively broad, spanning from 20 to 71 years. This indicates that CTS can affect individuals across a wide spectrum of adulthood. The observation of a median age in the mid-30s, however, suggests that CTS is a condition that can impact individuals in their prime working years, potentially leading to significant socioeconomic consequences due to work-related disability. Further research is warranted to explore the age-related factors that contribute to CTS development and progression, which could inform the development of age-specific prevention and management strategies. The mean Body Mass Index (BMI) of the participants in our study was 24.1 kg/m^2, with a standard deviation of 4.66 kg/m^2. This average BMI falls within the normal to slightly overweight range, according to standard BMI classifications. The association between BMI and CTS has been investigated in numerous studies, and a positive correlation has often been reported, suggesting that higher BMI is a risk factor for developing CTS. Several potential mechanisms have been proposed to explain this relationship. Increased adipose tissue (fat) can lead to increased fluid retention and tissue swelling, which can reduce the space within the carpal tunnel and increase pressure on the median nerve. Systemic inflammation, often associated with obesity, may also contribute to the pathogenesis of CTS by causing swelling and irritation of the tissues within the carpal tunnel. Furthermore, metabolic changes associated with higher BMI, such as insulin resistance, may affect nerve function and increase susceptibility to nerve compression. While our study's mean BMI is consistent with the general trend observed in the literature linking higher BMI to increased CTS risk, it's important to note that BMI was not significantly associated with CTS severity in our specific cohort. This finding highlights the complex interplay of factors that contribute to CTS and suggests that while BMI may be a risk factor for developing the condition, it may not be a primary determinant of its severity once it has developed. Further research is needed to better understand the role of BMI in the pathogenesis and progression of CTS, and to identify potential interventions targeting weight management as a strategy for CTS prevention and management. The vast majority of participants in our study (84.4%) reported being right-hand dominant. This observation aligns with the typical distribution of hand dominance in the general population, where right-handedness is substantially more common than left-handedness. The relationship between hand dominance and CTS has been a subject of investigation in previous research, with some studies suggesting that the dominant hand may be more frequently affected by CTS. The rationale behind this hypothesis is that the dominant hand is typically used more frequently and subjected to greater biomechanical stress, potentially increasing the risk of median nerve compression. However, other studies have not found a consistent association between hand dominance and CTS, suggesting that factors other than hand dominance may play a more significant role in the development of the condition. In our study, we did not specifically analyze the relationship between hand dominance and CTS occurrence, but the high prevalence of right-hand dominance in our cohort is a descriptive characteristic that reflects the general population. In our study, the distribution of symptom onset (subacute vs. chronic) was approximately equal, with 51.1% of participants reporting a subacute onset and 48.9% reporting a chronic onset. The categorization of symptom onset as subacute or chronic is often based on an arbitrary time cutoff, typically ranging from 3 to 6 months.

Subacute onset generally refers to a relatively rapid development of symptoms over a period of weeks to a few months, while chronic onset implies a more gradual and prolonged progression of symptoms over several months or years. The distinction between subacute and chronic CTS may have clinical implications, as it could potentially reflect different underlying pathophysiological processes or stages of disease progression. For example, subacute CTS may be associated with an acute inflammatory process, while chronic CTS may involve more long-term structural changes within the carpal tunnel. However, the clinical significance of this distinction is not always clear-cut, and further research is needed to determine whether it has prognostic value or implications for treatment decisions. In our study, we did not find a significant association between symptom onset and CTS severity, suggesting that the chronicity of symptoms at presentation may not be a primary determinant of the electrophysiological severity of nerve compression.[11-14]

Our analysis included an exploration of potential associations between the baseline demographic and clinical characteristics of the participants and the electrophysiological severity of their carpal tunnel syndrome. Understanding these relationships can provide insights into potential risk factors and prognostic indicators for CTS. We observed a trend towards older age in patients with more severe CTS. The median age increased from 29 years in the mild CTS group to 47 years in the severe CTS group. This observation aligns with the general understanding that nerve function can decline with age, and that cumulative exposure to risk factors over time may contribute to the development of more advanced disease stages. The aging process can lead to various structural and functional changes in the peripheral nervous system, including decreased nerve conduction velocity, reduced axonal transport, and increased susceptibility to nerve injury. These age-related changes may make older individuals more vulnerable to the effects of median nerve compression in the carpal tunnel. However, it's important to acknowledge that this trend in our study did not reach statistical significance. This lack of statistical significance could be attributed to several factors, including the relatively small sample size within each severity subgroup, which may have limited the statistical power to detect a true association. It is also possible that other factors, independent of age, play a more dominant role in determining CTS severity in our cohort. While some previous studies have reported a significant positive correlation between age and CTS severity, others, similar to our findings, have not found a significant association. These inconsistencies across studies highlight the complex interplay of factors influencing CTS severity, and underscore the need for further research to clarify the role of age in the pathogenesis and progression of the condition. While the proportion of male participants appeared higher in the moderate severity group compared to the other groups, the overall distribution of gender across the severity categories was not statistically significant in our study. This suggests that gender, in our cohort, was not a primary determinant of the electrophysiological severity of CTS. However, it is crucial to interpret this finding in the context of the significant gender imbalance in our study population, with a much higher proportion of female participants. The limited number of male participants, particularly in the mild and severe CTS groups, may have reduced the statistical power to detect a true association between gender and CTS severity. It is possible that with a larger and more balanced sample, a significant gender-related difference in CTS severity might have been observed. Furthermore, it is important to consider that the relationship between gender and CTS severity may be influenced by various interacting factors, such as occupational exposures, hormonal status, and anatomical variations, which were not specifically investigated in our study. Future research should aim to explore these complex interactions and clarify the potential role of gender in the clinical presentation and progression of CTS. In our study, the mean BMI was similar across the mild and moderate CTS groups, with a slightly higher mean BMI observed

in the severe group. However, this difference in BMI among the three severity groups was not statistically significant. This finding suggests that while higher BMI may be a risk factor for developing CTS, as discussed earlier, it was not significantly associated with the electrophysiological severity of the condition in our cohort. This result contrasts with some studies that have reported a link between obesity and more severe CTS. Several potential mechanisms have been proposed to explain how obesity might contribute to increased CTS severity, including increased fluid retention and tissue swelling, systemic inflammation, and metabolic changes that affect nerve function. However, other studies have also reported findings similar to ours, showing no significant association between BMI and CTS severity. These inconsistencies across studies highlight the complex and multifactorial nature of CTS severity. Individual anatomical variations, specific occupational demands, underlying systemic conditions, and genetic predispositions likely interact with demographic factors like BMI to influence the clinical presentation and progression of the condition. It is possible that in our specific patient group, other factors played a more dominant role in determining CTS severity than BMI. Further research is needed to better understand the complex interplay between BMI and other factors in CTS pathogenesis and to identify potential interventions targeting weight management as a strategy for modifying CTS severity. The distribution of right-hand versus left-hand dominance did not differ significantly across the mild, moderate, and severe CTS categories in our study. This finding suggests that hand dominance, in our cohort, was not a significant factor influencing the electrophysiological severity of CTS. While it is often hypothesized that the dominant hand, due to greater use and biomechanical stress, might be more prone to severe CTS, our results do not support this notion. It is possible that once CTS develops, the progression of nerve compression and associated electrophysiological changes may be influenced more by intrinsic nerve vulnerability, individual anatomical variations, or ongoing compression dynamics within the carpal tunnel, rather than by the initial factor of hand dominance. Furthermore, it is important to consider that our study did not specifically investigate the nature and extent of hand use in the participants, which could be a more relevant factor than simply hand dominance. Future research could explore the relationship between specific hand use patterns, occupational exposures, and CTS severity in more detail. We found no significant association between the onset of symptoms (subacute vs. chronic) and the electrophysiological severity of CTS in our study. This suggests that the chronicity of symptoms at presentation, as defined by our study's criteria, was not a primary determinant of the degree of nerve compression and associated electrophysiological abnormalities. The distinction between subacute and chronic CTS, while potentially clinically relevant, may not directly correlate with the underlying severity of nerve damage as measured by NCS. It is possible that the electrophysiological progression of CTS is influenced by factors other than the duration of symptoms, such as the intensity and frequency of nerve compression, individual variations in nerve resilience, and the presence of coexisting conditions. Furthermore, it is important to acknowledge that the categorization of symptom onset as subacute or chronic is often based on an arbitrary time cutoff, and this cutoff may not perfectly reflect the underlying pathophysiological processes. Further research is needed to explore the relationship between symptom duration, the underlying pathophysiology of CTS, and the electrophysiological severity of nerve compression.[15-17]

The primary focus of our study was to investigate the association between serum 25-hydroxyvitamin D levels and the severity of carpal tunnel syndrome. Vitamin D, traditionally known for its role in calcium homeostasis and bone metabolism, has garnered increasing attention for its potential pleiotropic effects, including its possible involvement in neurological function and peripheral neuropathies. The median serum 25(OH)D level for the entire cohort in our study

was 27.80 ng/mL, with a wide range observed from 10.40 ng/mL to 278.4 ng/mL. This median value falls within the range often considered indicative of vitamin D insufficiency, suggesting that suboptimal vitamin D status may be relatively common in this population. However, the wide range highlights the significant individual variability in vitamin D levels among the participants. The extremely high upper value (278.4 ng/mL) warrants careful consideration. While it could represent a true outlier, it also raises the possibility of measurement variability or laboratory error. Outliers can significantly influence statistical analyses, particularly when dealing with smaller sample sizes. Therefore, it is important to interpret the range with caution, recognizing that the median provides a more robust measure of central tendency in the presence of potential outliers. The observation of widespread vitamin D insufficiency in our cohort underscores the importance of addressing this public health issue, given the potential implications of vitamin D deficiency for various aspects of health, including neurological function. When we stratified the serum 25(OH)D levels by the electrophysiological severity of CTS, we observed an intriguing trend. The median 25(OH)D levels appeared to increase with increasing CTS severity. Specifically, the median vitamin D level was 23.75 ng/mL in the mild CTS group, 27.95 ng/mL in the moderate CTS group, and 37.50 ng/mL in the severe CTS group. This trend suggests a potential counterintuitive relationship, where patients with more severe CTS tend to have higher median vitamin D levels. This observation contradicts the hypothesis derived from some studies suggesting that vitamin D deficiency exacerbates CTS or is associated with more severe symptoms. If vitamin D were protective against CTS severity, one would typically expect to find lower vitamin D levels in patients with more severe disease. However, our finding aligns with some previous research that has also failed to demonstrate a significant link between vitamin D levels and CTS severity. Despite the observed trend of increasing median 25(OH)D levels with increasing CTS severity, the Kruskal-Wallis test, a non-parametric statistical test used to compare medians across multiple groups, revealed that this difference was not statistically significant. The p-value obtained from the Kruskal-Wallis test was 0.094, which is greater than the conventional threshold of 0.05 for statistical significance. This result indicates that the observed differences in median vitamin D levels across the severity groups are likely due to chance rather than a true association between vitamin D status and CTS severity. The absence of a statistically significant association between serum 25(OH)D levels and CTS severity in our study suggests that vitamin D status, within the range observed in our cohort, may not be a primary determinant of the electrophysiological severity of median nerve compression at the wrist. It is possible that other factors, such as the degree of mechanical compression, inflammation, ischemia, and individual variations in nerve vulnerability, play a more dominant role in the pathogenesis and progression of CTS.[18-20]

5. Conclusion

In conclusion, this cross-sectional study investigated the relationship between serum 25-hydroxyvitamin D levels and the severity of carpal tunnel syndrome in a cohort of patients in Padang, Indonesia. While an intriguing trend of increasing median vitamin D levels was observed with increasing CTS severity, this association did not reach statistical significance. The findings suggest that vitamin D status, within the range observed in this study, may not be a primary determinant of the electrophysiological severity of CTS. This highlights the multifactorial nature of CTS, where other factors such as mechanical compression, inflammation, ischemia, and individual nerve vulnerability likely play significant roles in the condition's pathogenesis and progression. It is important to acknowledge the limitations of this study, including the relatively modest sample size and the cross-sectional design, which precludes the establishment of causal relationships. Further research, employing larger sample sizes, longitudinal designs, and investigations

into other potential contributing factors, is warranted to provide a more comprehensive understanding of the complex interplay between vitamin D and carpal tunnel syndrome.

6. References

1. Bicer M, Cabalar M, Ecerkale O. The effects of vitamin B and tendon-nerve stretching exercises on clinical and electrophysiological parameters in the treatment of carpal tunnel syndrome. Istanb Med J. 2014; 15(1): 16–20.
2. Gürsoy AE, Bilgen HR, Dürüyen H, Altıntaş Ö, Kolukisa M, Asil T. The evaluation of vitamin D levels in patients with carpal tunnel syndrome. Neurol Sci. 2016; 37(7): 1055–61.
3. Tanik N, Balbaloğlu Ö, Ucar M, Sarp U, Atalay T, Çelikbilek A, et al. Does vitamin D deficiency trigger carpal tunnel syndrome? J Back Musculoskelet Rehabil. 2016; 29(4): 835–9.
4. Lee SH, Gong HS, Kim DH, Shin HS, Kim KM, Kim J, et al. Evaluation of vitamin D levels in women with carpal tunnel syndrome. J Hand Surg Eur Vol. 2016; 41(6): 643–7.
5. Lee SH, Gong HS, Kim J, Baek GH. Evaluation of vitamin D levels in women with carpal tunnel syndrome. Hand (N Y). 2016; 11(Suppl_1): 89S-89S.
6. Demiryurek BE, Gundogdu AA. The effect of vitamin D levels on pain in carpal tunnel syndrome. Orthop Traumatol Surg Res. 2017; 103(6): 919–22.
7. Okasha S, Abdel-latif M, Orabi M. Evaluation of vitamin D levels in women with carpal tunnel syndrome. Suez Canal Univ Med J. 2017; 20(2): 136–41.
8. Kim K, Gong HS, Kim J, Baek GH. Expression of vitamin D receptor in the subsynovial connective tissue in women with carpal tunnel syndrome. J Hand Surg Eur Vol. 2018; 43(3): 290–5.
9. Nageeb RS, Shehta N, Nageeb GS, Omran AA. Body mass index and vitamin D level in carpal tunnel syndrome patients. Egypt J Neurol Psychiatr Neurosurg. 2018; 54(1): 14.
10. Saçmaci H, Tanik N, Balbaloğlu Ö, Aktürk T, Inan LE. Electrophysiological evaluation of carpal tunnel syndrome female patients after vitamin D replacement. Arq Neuropsiquiatr. 2020; 78(4): 224–9.
11. Uysal A, Guntel M. Relationship of vitamin D level, fasting blood sugar, and body mass index, to carpal tunnel syndrome severity. Ann Med Res. 2021; (0):1.
12. Korkut AG, Dogan SK, Filiz MB, Toraman NF. The evaluation of the effect of vitamin D replacement on the symptoms of carpal tunnel syndrome in patients with low vitamin D levels. Exp Biomed Res. 2021; 4(3): 244–54.
13. Anusitviwat C, Suwanno P, Suwannaphisit S. The effects of vitamin D supplementation in carpal tunnel syndrome treatment outcomes: a systematic review. J Exp Orthop. 2021; 8(1): 73.
14. Abdulmunem SM, Al-Omary HL. Correlation of vitamin D level with electrophysiological findings and clinical grading in Carpal tunnel syndrome. Neuroquantology. 2021; 19(7): 149–55.
15. Noorizadeh K, Mohammadi SM, Seifi M, Moradi MS, Sadoni H. The effect of different doses of vitamin D on the prognosis of patients undergoing carpal tunnel syndrome surgery. J Family Med Prim Care. 2022; 11(11): 6837–42.
16. Samant PD, Sane RM. Evaluation of functional and symptomatic outcomes after vitamin D3 administration in carpal tunnel syndrome with hypovitaminosis D. Hand (N Y). 2022; 17(6): 1065–9.
17. Savadjani SA, Sherwin CM, Heidari-Soureshjani S, Darvishi M, Amiri MM. The role of Vitamin D in carpal tunnel syndrome risk and supplementation outcomes: a systematic review. Curr Rheumatol Rev. 2023; 19(4): 439–48.

18. Yıldız B, Algül FE, Yeşilada E. Associations between vitamin D receptor gene polymorphisms and Carpal tunnel syndrome. Research Square. 2024.
19. Deveci Ş, Matur Z. Does the severity of carpal tunnel syndrome symptoms vary due to vitamin and mineral deficiencies and anemia? Neurol Sci Neurophysiol. 2023; 40(4): 215–20.
20. Andrade AVD, Martins DGS, Rocha GS, Damasceno GS, Gomes FTS, Albuquerque YPF, et al. The role of vitamin D in the treatment of carpal tunnel syndrome: Clinical and electroneuromyographic responses. Nutrients. 2024; 16(12): 1947.