Journal of Experimental and Clinical Medicine
https://dergipark.org.tr/omujecm

Research Article

J Exp Clin Med
2024; 41(3): 765-772
doi: 10.52142/omujecm.41.4.14

Systemic inflammatory markers and vitamin D in Carpal Tunnel Syndrome: Indicators of disease severity?

Zeynep Selcan ŞANLI[1,*], Emine ÇETİN[2]

[1]Department of Neurology, Adana City Training and Research Hospital, University of Health Sciences, Adana, Türkiye
[2]Department of Physical Medicine and Rehabilitation, Adana City Training and Research Hospital, University of Health Sciences, Adana, Türkiye

Received: 18.11.2024 • **Accepted/Published Online:** 09.12.2024 • **Final Version:** 31.12.2024

Abstract

The most common entrapment neuropathy affecting the upper limbs, carpal tunnel syndrome (CTS), is debilitating to quality of life. This research seeks to investigate the possible involvement of inflammation in the development of CTS by analyzing the Neutrophil/Lymphocyte Ratio (NLR), Platelet/Lymphocyte Ratio (PLR), and 25-hydroxyvitamin D [25(OH)D] levels. This investigation was carried out as a prospective observational study, a cross-sectional study. The participants comprised individuals aged 18 and above who visited the Neurology and Physical Medicine and Rehabilitation Clinics at the University of Health Sciences, Adana City Training and Research Hospital. The participants were categorized into two groups: one consisting of individuals with CTS and another serving as the control group. Electrodiagnostic examinations and biochemical studies were conducted. The research had a total of 99 participants who had been diagnosed with carpal tunnel syndrome (44 with mild cases, 31 with intermediate cases, and 24 with severe cases), as well as 43 healthy persons serving as controls. The groups differed significantly in terms of age, weight, body mass index (BMI), neutrophil count (NE#), C-reactive protein (CRP), 25(OH)D, NLR, and PLR. There was a moderate positive link between the severity of CTS and the levels of CRP, NLR, PLR, and BMI. Conversely, a moderate negative correlation was seen with 25(OH)D levels. The findings of this research suggest that NLR, PLR, and 25(OH)D levels might be useful biomarkers for the diagnosis and evaluation of CTS severity. It is advisable to do bigger, long-term studies to provide more evidence and get a more definitive understanding of the correlation between these inflammatory markers and CTS.

Keywords: Carpal tunnel syndrome, systemic inflammation, neutrophil/lymphocyte

1. Introduction

The impingement of the median nerve in the wrist area is the cause of the entrapment neuropathy that is classified as CTS. It often affects occupational groups who do repeated wrist tasks, resulting in symptoms such as discomfort, tingling sensations, and finger numbness (1,2). Although the prevalence of CTS varies depending on the social and professional context, it usually lowers the quality of life.

It is believed that a number of variables, including mechanical pressure, microvascular deficits, and hereditary predisposition, have a role in the progress of CTS, despite the fact that the entire pathophysiology of CTS is not totally known (3,4). The significance of systemic inflammation in the advancement of CTS has been progressively recognized. Recent assessments have shown that the NLR & PLR are useful and efficient measures for evaluating systemic inflammation. These ratios are essential in the body's immune and inflammatory responses (5,6).

Furthermore, there is a proposal suggesting that CTS progression may be influenced by insufficient vitamin D (7,8). To regulate immune systems and manage inflammatory reactions, vitamin D is essential. Numerous studies have shown a connection between a lack of vitamin D and a variety of neurological and inflammatory conditions (9,10).

This research investigates the influence of inflammation in the development of CTS by evaluating the levels of NLR, PLR, and 25(OH)D, aiming to identify potential biomarkers for predicting CTS severity.

2. Materials and Methods

2.1. Study Design and Participants

This investigation enrolled individuals aged 18 and above who sought treatment at the Neurology and Physical Medicine and Rehabilitation Clinics of the Health Sciences University, Adana City Training and Research Hospital, from July 20, 2023, to January 20, 2024. Participants were chosen through systematic random sampling. This study was carried out as a prospective, observational, and cross-sectional investigation. It complied with the ethical standards outlined in the Declaration of Helsinki and obtained approval from the Adana City Research and Training Hospital Ethics Committee (approval number: 131/2701)

The study group underwent electrophysiological and clinical examinations of CTS, and the control group was

*Correspondence: zeynepsanlimd@gmail.com

comprised of healthy volunteers, including hospital personnel, patients' families, and visitors to the outpatient clinic, who were assessed to establish baseline data. Before the study commenced, all participants were given detailed information on the extent and methods of the research, and they voluntarily provided written consent after being fully informed.

The study distinctly included individuals displaying various stages of bilateral CTS, specifically focusing on the more severely affected hand. Comprehensive physical and neurological evaluations were routinely administered to both the patient group and healthy volunteers. The BMI of all participants was also measured and documented.

Exclusion criteria were rigorous, prohibiting participation from individuals with conditions including diabetes mellitus, hypothyroidism, hepatic or kidney disorders, pregnancy, alcohol dependence, polyneuropathy, prior upper limb trauma, arthritis, cancer, vascular inflammation and diseases of the hematopoietic system. Furthermore, individuals who were using Vitamin D supplements or had a history of surgery for CTS were removed from the study.

2.2. Electrodiagnostic tests

Neurophysiological evaluations utilized the Cadwell Sierra Summit electromyography (EMG) system, produced by Cadwell Laboratories in Kennewick, Washington, USA. Nerve conduction assessments were conducted solely when the patient's extremity temperature surpassed 32°C; if not, the extremities were warmed accordingly. Nerve conduction studies were conducted in accordance with standard methods and established reference values (11,12).

Superficial electrodes were utilized for both stimulation and recording purposes. Stimulation was consistently administered at a supramaximal level.

Motor and sensory nerve conduction filters were set to 20Hz-10kHz and 20Hz-2kHz. Latencies were measured from the stimulus onset to the initial negative response, and amplitudes were measured from baseline to negative peak We used antidromic sensory nerve conduction testing. For motor nerve conduction experiments, the median/ulnar nerve at the wrist was 5 cm from the recording electrode. The lowest reference limit for sensory nerve action potential (SNAP) amplitude and NCV in the 2nd finger-wrist segment was 15 μV and 40.9 m/s, respectively. The lower median nerve compound motor action potential (CMAP) amplitude is 4.3 mV, while the upper median nerve CMAP distal latency is 3.7 ms.

The severity of CTS is classified based on neurophysiological data as follows: (13,14)

-Mild CTS—prolonged (relative or absolute) sensory or mixed NAP distal latency (orthodromic, antidromic, or palmar) ± SNAP amplitude below the lower limit of normal.

- Moderate CTS—abnormal median sensory latencies as above, and (relative or absolute)

prolongation of median motor distal latency.

-Severe CTS—prolonged median motor and sensory distal latencies, with either an absent SNAP or mixed NAP or low amplitude or absent thenar CMAP.

2.3. Biochemical Assessments

All subjects underwent an extensive battery of testing, which included full blood counts, thyroid, liver, and kidney function tests, as well as levels of vitamins B-12 and D, CRP, rheumatoid factor, glucose, electrolytes, and lipids. We collected peripheral venous blood samples from all participants and centrifuged them to enable comprehensive blood count evaluations. We counted blood cells using a Beckman Coulter UniCel DxH 800 hematology analyzer in our US location. We split the neutrophil-to-lymphocyte and platelet-to-lymphocyte ratios to produce the NLR and PLR.

2.4. Statistical Evaluation

We used SPSS version 25.0 for the purpose of data analysis. Categorical data were reported as frequencies and proportions, while continuous data were summarized using measures of central tendency (means) and measures of dispersion (standard deviations), as well as measures of central tendency (medians) and measures of dispersion (interquartile ranges) when appropriate. The Shapiro-Wilk test assessed the normality of the distribution of research parameters. The Mann-Whitney U test is employed for comparing pairs of non-normally distributed data, whereas the Kruskal-Wallis test is utilized for analyzing data from multiple groups exceeding two. The Post Hoc Bonferroni test was used to investigate significant differences across several groups. To determine the relationships between continuous variables, Spearman's rho correlation coefficient was computed. A multivariate logistic regression analysis was employed to identify the characteristics influencing the incidence of CTS. A significance limit of 0.05 was established for all statistical analyses.

3. Results

The study encompassed 99 patients diagnosed with CTS, categorized into 44 mild, 31 moderate, and 24 severe cases. Additionally, 43 healthy individuals were included as the control group (referenced in Table 1). The statistical analysis showed substantial disparities in age, weight, BMI, neutrophil count (NE#), CRP, 25(OH)D, NLR, and PLR between the patient and control groups ($*P < 0.05$). More precisely, the Post Hoc Bonferroni test revealed that the observed differences were mostly attributed to the control group having a lower average age and weight compared to all the CTS groups.

The gender distribution showed no statistically significant distinction between the two groups ($P > 0.906$). The mean age of patients with CTS was significantly higher than that of the control group ($***P < 0.001$). However, there was no correlation between NLR and PLR levels and age in the patient and control groups. Consequently, as NLR and PLR remain constant with age, the age disparity between patients in the

CTS group and those in the control group did not influence the outcomes of this investigation. Consequently, the age disparity between individuals in both randomly selected research groups was disregarded. The analysis of BMI differences indicated that the control group had lower BMI values than the mild and moderate CTS groups, while the severe CTS group displayed higher BMI values than both the mild CTS and control groups (*$P < 0.05$).

In the severe CTS group, NE# levels increased significantly compared to the moderate CTS and control groups (*$P < 0.05$). Increased CRP and NLR values were similarly observed in the severe CTS group when compared to the mild and moderate CTS groups and additionally to the control population (*$P < 0.05$). The concentrations of 25(OH)D were increased in the mild CTS group relative to the severe CTS group, while the control group exhibited higher levels than both the moderate and severe CTS groups (*$P < 0.05$).

Table 1. Distribution of related parameters in groups

	CTS			**Control (d) (n=43)**
	Mild CTS (a) (n=44)	**Moderate CTS (b) (n=31)**	**Severe CTS (c) (n=24)**	
	n(%)	**n(%)**	**n(%)**	**n(%)**
Gender				
Male	11 (25)	9 (29)	5 (20.8)	10 (23.3)
Female	33 (75)	22 (71)	19 (79.2)	33 (76.7)
	Med (25-75th)	**Med (25-75th)**	**Med (25-75th)**	**Med (25-75th)**
Age	49.5 (41.8-57)	50 (40-63)	57 (43-64.3)	38 (31-44)
Height	165 (158.5-169)	163 (158-170)	161.5 (155.3-168)	162 (156-168)
Weight	79 (72.8-89.5)	78 (74.5-87)	85.5 (80-95.5)	70 (62-80)
BMI	28.0 (26.2-32.5)	29.7 (27.6-33.6)	34.3 (31.5-36.2)	26.3 (24.1-29.5)
PLT	234.5 (200-293.8)	286 (223-318)	261 (215.5-300.3)	257 (215-301)
NE#	4.1 (3.1-5.83)	3.9 (3.5-5.2)	5 (4.3-6.1)	4 (3-5)
LY#	2.1 (1.8-2.58)	2.2 (1.6-2.5)	1.85 (1.45-2.18)	2 (1.6-2.5)
CRP	2.25 (1.32-4.25)	3 (2-3.8)	5.2 (2.5-7.8)	2 (1.56-2.8)
25(OH)D	13.15 (11.2-20.65)	13.8 (8.1-19.6)	9.7 (6.0-13.7)	19.7 (16.4-21.4)
NLR	1.84 (1.46-2.29)	1.95 (1.25-2.58)	2.62 (1.88-3.79)	1.80 (1.56-2.31)
PLR	108.5 (83.4-135.8)	122.4 (104.4-163.9)	145 (109.2-185.1)	128.9 (102.4-158.4)

Abbreviations: CTS= carpal tunnel syndrome. BMI = body mass index. PLT = platelet. NE# = neutrophil. LY# = lymphocyte. CRP = C-reactive protein. 25(OH)D = 25-hydroxyvitamin D. NLR = neutrophil/lymphocyte ratio. PLR = platelet/lymphocyte ratio

Table 2. Differences of related parameters between groups

	CTS			**Control (d) (n=43)**	***P†***	
	Mild CTS (a) (n=44)	**Moderate CTS (b) (n=31)**	**Severe CTS (c) (n=24)**			
	n(%)	**n(%)**	**n(%)**	**n(%)**		
Gender						
Male	11 (25)	9 (29)	5 (20.8)	10 (23.3)	0.906	
Female	33 (75)	22 (71)	19 (79.2)	33 (76.7)		
	Med (25-75th)	**Med (25-75th)**	**Med (25-75th)**	**Med (25-75th)**	***P‡***	**Post Hoc Bonferroni p**
Age	49.5 (41.8-57)	50 (40-63)	57 (43-64.3)	38 (31-44)	**<0.001***	a-b; *P*=0.004 a-c; *P*=0.001 a-d; *P*=0.001
Height	165 (158.5-169)	163 (158-170)	161.5 (155.3-168)	162 (156-168)	0.412	
Weight	79 (72.8-89.5)	78 (74.5-87)	85.5 (80-95.5)	70 (62-80)	**<0.001***	a-b; *P*=0.017 a-c; *P*=0.003

						a-d; *P*<0.001
BMI	28.0 (26.2-32.5)	29.7 (27.6-33.6)	34.3 (31.5-36.2)	26.3 (24.1-29.5)	**<0.001*** **	a-d; *P*=0.033 b-d; *P*=0.002 c-a; *P*=0.009 c-d; *P*<0.001
PLT	234.5 (200-293.8)	286 (223-318)	261 (215.5-300.3)	257 (215-301)	0.197	
NE#	4.1 (3.1-5.83)	3.9 (3.5-5.2)	5 (4.3-6.1)	4 (3-5)	**0.011***	c-b; *P*=0.024 c-d; *P*=0.028
LY#	2.1 (1.8-2.58)	2.2 (1.6-2.5)	1.85 (1.45-2.18)	2 (1.6-2.5)	0.275	
CRP	2.25 (1.32-4.25)	3 (2-3.8)	5.2 (2.5-7.8)	2 (1.56-2.8)	**<0.001*** **	c-a; *P*<0.001 c-b; *P*=0.006 c-d; *P*<0.001
25(OH)D	13.15 (11.2-20.65)	13.8 (8.1-19.6)	9.7 (6.0-13.7)	19.7 (16.4-21.4)	**<0.001*** **	a-c; *P*=0.004 d-b; *P*=0.030 d-c; *P*<0.001
NLR	1.84 (1.46-2.29)	1.95 (1.25-2.58)	2.62 (1.88-3.79)	1.80 (1.56-2.31)	**0.003****	c-a; *P*=0.005 c-b; *P*=0.002 c-d; *P*=0.002
PLR	108.5 (83.4-135.8)	122.4 (104.4-163.9)	145 (109.2-185.1)	128.9 (102.4-158.4)	**0.021***	c-a; *P*=0.038

**p<0.05. **p<0.01. ***P <0.001. †: chi-square. ‡: Kruskal Wallis. Post Hoc Bonferroni*

Table 3. Differences of the relevant parameters between CTS and control groups

	CTS (n=99)	**Control (n=43)**	***P†***
	n(%)	**n(%)**	
Gender			
Male	25 (25.3)	10 (23.3)	0.906
Female	74 (74.7)	33 (76.7)	
	Med (25-75th)	**Med (25-75th)**	***Pμ***
Age	50 (42-61)	38 (31-44)	**<0.001****
Height	163 (158-169)	162 (156-168)	0.661
Weight	80 (75-90)	70 (62-80)	**<0.001****
BMI	29.9 (27.6-34.4)	26.3 (24.1-29.5)	**<0.001****
PLT	258 (214-306)	257 (215-301)	0.896
NE#	4.3 (3.5-5.5)	4 (3-5)	0.173
LY#	2.1 (1.7-2.5)	2 (1.6-2.5)	0.829
CRP	2.9 (1.7-5)	2 (1.56-2.8)	**0.005****
25(OH)D	12.7 (9.1-18.3)	19.7 (16.4-21.4)	**<0.001****
NLR	1.96 (1.55-2.79)	1.80 (1.56-2.31)	0.400
PLR	128.3 (97.5-158)	128.9 (102.4-158.4)	0.547

PLR values exhibited significant differences, with higher levels observed in the severe CTS group relative to the mild group (**P* = 0.038). No noticeable distinctions were detected in gender, height, platelet count (PLT), and lymphocyte count (LY#) among the groups (*P* > 0.05).

The CTS group exhibited significantly higher mean values for age, weight, BMI, and CRP (****P* < 0.001; ***P*= 0.005; ****P* < 0.001, respectively), while mean 25(OH)D levels were lower in comparison to the healthy control group (****P* < 0.001). No noticeable distinctions were detected between the CTS and control groups for the other parameters listed in Table 3 (*P* > 0.05).

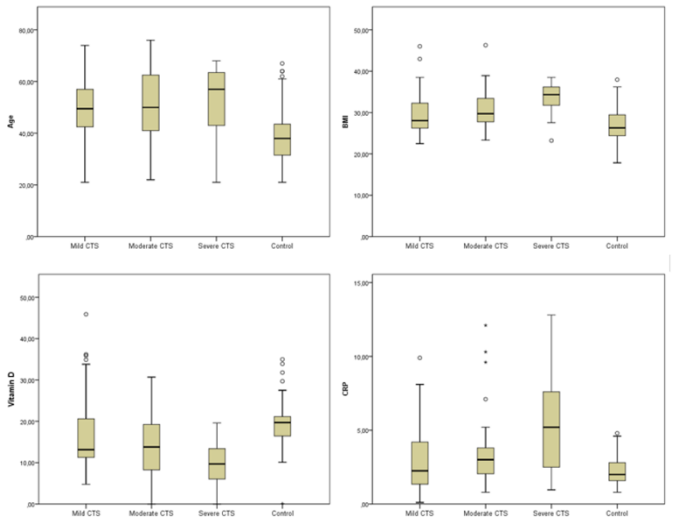

Fig. 1. Relationships between severity of carpal tunnel syndrome (CTS) and age, body mass index (BMI), Vitamin D, C-reactive protein (CRP)

Key parameters identified in the univariate analysis presented in Table 3 were subsequently examined using a multivariate logistic regression model, as shown in Table 4. The model indicated that the association among the independent and dependent variables explained 27.7% of the variance as per Cox and Snell pseudo-R2 statistics and 39.3% according to Nagelkerke pseudo-R2 statistics. The odds ratio (OR: 1.104) suggests that a one-unit increase in BMI correlates with a higher probability of CTS occurrence.

Table 4. Determination of factors affecting carpal tunnel syndrome by logistic regression analysis

	P	OR	95% CI Lower	95% CI Upper
Age	**0.001***	1.065	1.028	1.105
BMI	**0.049***	1.104	1.000	1.220
CRP	0.056	1.292	0.993	1.680
25(OH)D	**0.010***	0.928	0.876	0.982
Constant	**0.004****	0.012		

Cox & Snell pseudo-R2 = 0.277. Nagelkerke pseudo-R2 = 0.393

The analysis indicated a moderate negative correlation between the severity of CTS and 25(OH)D levels (r = -0.304), alongside moderate positive correlations with CRP, NLR, PLR, and BMI values (r = 0.341; r = 0.290; r = 0.304; r = 0.356, respectively). Figure 1 provides a detailed comparison of age, BMI, 25(OH)D, and CRP among CTS subgroups.

Table 5. Relationship between CTS severity and related parameters

	CTS severity	
	r	*P*
Age	0.131	0.196
CRP	0.341**	**0.001****
NLR	0.302**	**0.004****
PLR	0.304**	**0.002****
BMI	0.356**	**<0.001*****
PLT	0.151	0.136
NE#	0.214	0.034
LY#	-0.178	0.079
25(OH)D	-0.304**	**0.002****

4. Discussion

Our research found a modest positive correlation between CTS severity and biomarkers, including CRP, NLR, PLR, and BMI. CTS intensity is somewhat negatively correlated with 25(OH)D levels. Age is recognized as a separate factor that might predict the likelihood of developing CTS. It mostly affects individuals aged 40 to 60 years (15). Research indicates that the increased risk associated with age may be due to extended exposure to repeated movements that strain the wrist, as well as age-related degradation of the nerves and blood vessels, which might explain the relationship between age and CTS (16,17). The mean age of the individuals in our research was 50, consistent with prevailing statistics. There is a hypothesis that suggests the reason for the greater occurrence of CTS in women, which is up to 10 times more frequent than in males, may be attributed to women having a somewhat smaller cross-sectional area of the carpal tunnel compared to men (18,19). Our findings echo this distribution, showing that the number of female patients was threefold that of male patients. Research consistently demonstrates a correlation between elevated BMI and the onset of CTS (20–22), suggesting that obesity may enhance CTS risk due to increased adipose tissue or high carpal tunnel hydrostatic pressure (23). A recent investigation involving 300 CTS sufferers revealed that each unit increase in BMI escalates the risk of CTS by approximately 1.566 times (****P*<0.001) (24), supporting our observations that elevated BMI significantly impacts CTS presence.

While neuroinflammation is proposed as a contributing factor to CTS pathogenesis, supporting data remains scant (25,26). Observations suggest that in CTS patients, the diameter of the median nerve is reduced in the compressed region, with edema forming proximally to the entrapment site (27). These changes might be linked to accumulations of axoplasm, edema, or fibrosis due to ongoing inflammatory responses. However, Baričić et al. did not observe any substantial disparity in the levels of inflammatory cytokines between CTS patients and healthy controls(28), while another study affirmed that variations in serum levels of inflammatory mediators were inconsequential among CTS patients (29). However, Moalem-Taylor et al. detected significant elevations in serum cytokine and chemokine levels in CTS patients compared to controls (30).

Furthermore, Altun et al. compared CRP levels between control subjects and CTS patients and found no notable differences that could substantiate inflammation as a causative factor (31). The authors of this study suggested that increasing

the sample size could change the study results. In our study, we found a significant relationship between CRP level and CTS severity (***P<0.001). In contrast, our research found a strong connection between higher CRP levels and greater severity of CTS (***P<0.001). Discrepancies in NLR and PLR results have been noted across studies, with some failing to demonstrate significant differences (32),(33). Our research found that severe instances of CTS had substantially increased NLR and PLR than milder cases and controls (**P=0.003, *P=0.021, respectfully). This shows that latent systemic inflammation promotes cytokine-driven fibrosis and worsens CTS (34).

Current research has focused on investigating the impact of vitamin D on periphery nerve function. Studies have shown that vitamin D may have neuroprotective and neurotrophic properties, potentially enhancing neuron regeneration and minimizing damage (35). Increased levels of vascular endothelial growth factor (VEGF), linked to increased vascular proliferation and inflammatory synovial fibrosis, are proposed to initiate CTS, with vitamin D possibly acting as a suppressive agent(36). A study conducted on 48 individuals diagnosed with CTS found that elevated levels of vitamin D in the blood are associated with a substantial decrease in the chance of developing CTS (37). Research has shown that there is an inverse correlation between 25(OH)D levels and the severity of CTS and a direct correlation between 25(OH)D levels and BMI. This suggests that taking vitamin D supplements and managing weight might potentially reduce the severity of CTS symptoms (8,38). Furthermore, Saçmacı et al. discovered that vitamin D supplements in the initial stages of CTS may enhance pain relief and electrophysiological outcomes (39).

While insightful, our study is constrained by its single-center design and reliance on data from initial screenings without long-term follow-ups. Further extensive research comparing longitudinal data would enhance understanding of the relationships between these biomarkers and CTS progression.

In conclusion, this study is pioneering in examining the combined effects of NLR, PLR, and 25(OH)D on CTS, establishing them as potential diagnostic and severity markers. However, to solidify these findings, more extensive and prolonged investigations are necessary. Future research must concentrate on long-term patient follow-ups to clarify the complex relationships among inflammatory markers, disease duration, and the prognosis of CTS.

Ethical Statement

The protocol of the study has been approved by the ethics committee of Adana City Research and Training Hospital (20.07.2023 date and registration number 2023-131/2701), and written informed consent was obtained from all of the study participants before their participation in this study.

Conflict of interest

The authors declared no conflict of interest.

Funding

No funding was used for the study.

Acknowledgments

We thank all the study participants for their participation and contribution.

Authors' contributions

Concept: Z.S.Ş., EÇ. Design: : Z.S.Ş., E.Ç. Data Collection or Processing: : Z.S.Ş., E.Ç. Analysis or Interpretation: Z.S.Ş., E.Ç, Literature Search: Z.S.Ş.,E.Ç. Writing: Z.S.Ş.

References

1. Lee IH, Kim YK, Kang DM, Kim SY, Kim IA, Kim EM. Distribution of age, gender, and occupation among individuals with carpal tunnel syndrome based on the National Health Insurance data and National Employment Insurance data. Ann Occup Environ Med [Internet]. 2019 Nov 7 [cited 2024 Jul 14];31:e31. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6850790/
2. Park DJ, Kang JH, Lee JW, Lee KE, Wen L, Kim TJ, et al. Cross-cultural adaptation of the Korean version of the Boston carpal tunnel questionnaire: its clinical evaluation in patients with carpal tunnel syndrome following local corticosteroid injection. J Korean Med Sci. 2013 Jul;28(7):1095–9.
3. Aboonq MS. Pathophysiology of carpal tunnel syndrome. Neurosciences [Internet]. 2015 Jan [cited 2024 Jul 14];20(1):4–9. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4727604/
4. Wahab KW, Sanya EO, Adebayo PB, Babalola MO, Ibraheem HG. Carpal Tunnel Syndrome and Other Entrapment Neuropathies. Oman Med J [Internet]. 2017 Nov [cited 2024 Jul 14];32(6):449–54. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5702987/
5. Duan Z, Jia A, Cui W, Feng J. Correlation between neutrophil-to-lymphocyte ratio and severity of myasthenia gravis in adults: A retrospective study. J Clin Neurosci [Internet]. 2022 Dec 1 [cited 2024 Jun 4];106:117–21. Available from: https://www.sciencedirect.com/science/article/pii/S0967586822004271
6. Ekici H, Imamoglu M, Okmen F, Gencosman G, Ak G, Ergenoglu M. Evaluation of neutrophil-to-lymphocyte ratio and platelet-to-lymphocyte ratio in pregnant women with systemic lupus erythematosus. J Obstet Gynaecol J Inst Obstet Gynaecol. 2022 Jul;42(5):872–6.
7. 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 [İnternet]. [cited 2024 Jul 15];19(4):439–48. Available from: https://www.eurekaselect.com/article/131516
8. 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 [Internet]. 2016 Jan 1 [cited 2024 Jul 15];29(4):835–9. Available from: https://content.iospress.com/articles/journal-of-back-and-musculoskeletal-rehabilitation/bmr696
9. Breuer J, Loser K, Mykicki N, Wiendl H, Schwab N. Does the environment influence multiple sclerosis pathogenesis via UVB light and/or induction of vitamin D? J Neuroimmunol. 2019 Apr 15;329:1–8.
10. Mellor-Pita S, Tutor-Ureta P, Rosado S, Alkadi K, Granado F,

Jimenez-Ortiz C, et al. Calcium and vitamin D supplement intake may increase arterial stiffness in systemic lupus erythematosus patients. Clin Rheumatol. 2019 Apr;38(4):1177–86.

11. Fidanci H, Öztürk I, Köylüoğlu AC, Yildiz M, Buturak Ş, Arlier Z. The needle electromyography findings in the neurophysiological classification of ulnar neuropathy at the elbow. Turk J Med Sci. 2020 Jun 23;50(4):804–10.

12. Buturak Ş, Fidancı H, Yıldız M, Arlıer Z. Relationship between Gravidity, Parity, and Neurophysiological Features in Carpal Tunnel Syndrome (CTS) Patients with a History of Pregnancy. Niger J Clin Pract. 2024 Mar 1;27(3):345–51.

13. Werner RA, Andary M. Electrodiagnostic evaluation of carpal tunnel syndrome. Muscle Nerve. 2011 Oct;44(4):597–607.

14. Padua L, Lo Monaco M, Padua R, Gregori B, Tonali P. Neurophysiological classification of carpal tunnel syndrome: assessment of 600 symptomatic hands. Ital J Neurol Sci. 1997 Jun;18(3):145–50.

15. Alamir MA, Alfouzan RK, Alhumaidan A, Abozaid HS, Alhudhaif HM, Alsuhaim R, et al. Awareness of Carpal Tunnel Syndrome Among the Middle-Aged Population in Riyadh, Saudi Arabia. Cureus [Internet]. [cited 2024 Jul 27];15(11):e49544. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC10753518/

16. Guan W, Lao J, Gu Y, Zhao X, Rui J, Gao K. Case-control study on individual risk factors of carpal tunnel syndrome. Exp Ther Med [Internet]. 2018 Mar [cited 2024 Jul 27];15(3):2761–6. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5867472/

17. Pourmemari MH, Heliövaara M, Viikari-Juntura E, Shiri R. Carpal tunnel release: Lifetime prevalence, annual incidence, and risk factors. Muscle Nerve. 2018 Oct;58(4):497–502.

18. Joshi A, Patel K, Mohamed A, Oak S, Zhang MH, Hsiung H, et al. Carpal Tunnel Syndrome: Pathophysiology and Comprehensive Guidelines for Clinical Evaluation and Treatment. Cureus [Internet]. [cited 2024 Jul 27];14(7):e27053. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9389835/

19. Cazares-Manríquez MA, Wilson CC, Vardasca R, García-Alcaraz JL, Olguín-Tiznado JE, López-Barreras JA, et al. A Review of Carpal Tunnel Syndrome and Its Association with Age, Body Mass Index, Cardiovascular Risk Factors, Hand Dominance, and Sex. Appl Sci [Internet]. 2020 Jan [cited 2024 Jul 27];10(10):3488. Available from: https://www.mdpi.com/2076-3417/10/10/3488

20. Razavi AS, Karimi N, Bashiri F. The relationship of serum lipid profiles and obesity with the severity of carpal tunnel syndrome. Pan Afr Med J. 2021;39:90.

21. Madani AM, Gari BS, Zahrani EMA, Al-Jamea LH, Woodman A. A literature review of carpal tunnel syndrome and its association with body mass index, wrist ratio, wrist to palm ratio, and shape index. J Hand Ther Off J Am Soc Hand Ther. 2023;36(3):568–79.

22. Mokhtarinia HR, Parsons D, Bain CR, Gabel CP. Independent risk factors of carpal tunnel syndrome: Assessment of body mass index, hand, wrist and finger anthropometric measurements. Work Read Mass. 2022;73(1):157–64.

23. Komurcu HF, Kılıc S, Anlar O. Relationship of Age, Body Mass Index, Wrist and Waist Circumferences to Carpal Tunnel Syndrome Severity. Neurol Med Chir (Tokyo) [Internet]. 2014 May [cited 2024 Jul 27];54(5):395–400. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4533441/

24. Gölen MK, Okuyan DY. Are body mass index and the systemic immune-inflammation index risk factors for carpal tunnel syndrome? Eur Res J [Internet]. 2023 May 4 [cited 2024 Jul 27];9(3):468–76. Available from: https://dergipark.org.tr/en/pub/eurj/issue/76123/1120577

25. Sandy-Hindmarch O, Bennett DL, Wiberg A, Furniss D, Baskozos G, Schmid AB. Systemic inflammatory markers in neuropathic pain, nerve injury and recovery. Pain [Internet]. 2022 Mar 1 [cited 2024 Jul 27];163(3):526–37. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7612369/

26. Joshi P, Lele V. Lighting the tunnel: FDG PET/CT findings leading to incidental diagnosis of carpal tunnel syndrome. Clin Nucl Med. 2014 Jan;39(1):e78-79.

27. Freeland AE, Tucci MA, Barbieri RA, Angel MF, Nick TG. Biochemical evaluation of serum and flexor tenosynovium in carpal tunnel syndrome. Microsurgery. 2002;22(8):378–85.

28. Baričić M, Cvijanović Peloza O, Jerbić Radetić AT, Šantić V, Omrčen H, Zoričić Cvek S. Serum Levels of Inflammatory and Fibrotic Cytokines in Patients with Carpal Tunnel Syndrome and Hip Osteoarthritis. Biomedicines [Internet]. 2022 Dec 21 [cited 2024 Jul 27];11(1):11. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9855820/

29. Karimi N, AbedianKenari S, Darvari F. Serum levels of inflammatory cytokines in patients with idiopathic carpal tunnel syndrome. Int J Neurosci. 2021 Mar;131(3):228–32.

30. Moalem-Taylor G, Baharuddin B, Bennett B, Krishnan AV, Huynh W, Kiernan MC, et al. Immune dysregulation in patients with carpal tunnel syndrome. Sci Rep [Internet]. 2017 Aug 15 [cited 2024 Jul 27];7:8218. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5557984/

31. Altun Y, Tak AZA. Can serum C-Reactive Protein and Procalcitonin levels associate with carpal tunnel syndrome? Med Sci Discov [Internet]. 2019 Feb 28 [cited 2024 Jul 27];6(2):18–23. Available from: https://medscidiscovery.com/index.php/msd/article/view/201

32. Sariçam G. Neutrophil/Lymphocyte, Platelet/Lymphocyte and Neutrophil/Monocyte Rates in Carpal Tunnel Syndrome. Turk Klin Cardiovasc Sci [Internet]. 2018 [cited 2024 Jul 27];30(3):107–12. Available from: https://www.turkiyeklinikleri.com/article/en-neutrophillymphocyte-plateletlymphocyte-and-neutrophilmonocyte-rates-in-carpal-tunnel-syndrome-83540.html

33. Altun Y. Are C-reactive protein, neutrophil to lymphocyte, and platelet to lymphocyte ratios related to the severity of idiopathic carpal tunnel syndrome? Ann Med Res [Internet]. 2022 [cited 2024 Jul 27];29(9):915–9. Available from: http://search/yayin/detay/1130665

34. Güneş M, Büyükgöl H. Correlation of neutrophil/lymphocyte and platelet/lymphocyte ratios with the severity of idiopathic carpal tunnel syndrome. Muscle Nerve. 2020 Mar;61(3):369–74.

35. 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 [Internet]. 2024 Jun 19 [cited 2024 Jul 14];16(12):1947. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC11207057/

36. Bellone F, Catalano A, Sottile AR, Gaudio A, Loddo S, Corica F, et al. Early Changes of VEGF Levels After Zoledronic Acid in Women With Postmenopausal Osteoporosis: A Potential Role of Vitamin D. Front Med. 2021;8:748438.

37. Abdul-Razzak KK, Kofahi RM. Carpel tunnel syndrome: A link with vitamin D and calcium. Biomed Rep [Internet]. 2020 Sep [cited 2024 Jul 14];13(3):15. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7391289/

38. Nageeb RS, Shehta N, Nageeb GS, Omran AA. Body mass index

and vitamin D level in carpal tunnel syndrome patients. Egypt J Neurol Psychiatry Neurosurg. 2018;54(1):14.

39. Saçmaci H, Tanik N, Balbaloğlu Ö, Aktürk T, İnan LE. Electrophysiological evaluation of carpal tunnel syndrome female patients after vitamin D replacement. Arq Neuropsiquiatr [Internet]. 2020 Apr 9 [cited 2024 Jul 14];78:224–9. Available from: https://www.scielo.br/j/anp/a/BPBsCNQB6HtHhqqQRvKPQBq/?lang=en