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Carpel Tunnel Syndrome: A Link with Vitamin D, Body Mass Index and Hyperlipidemia

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Abstract

Introduction: Carbai tunnel syndrome [CTS] is compression of the median nerve at the wrist , this causes tingling in the hands, pain, numbness, tingling in the fingers particularly the thumb, index and middle fingers, loss of sensation in the hands and fingers, also weakness in the hands. The aim of the present study was to study a possible association which could be found between electrophysiological data in CTS, BMI, hyperlipidemia, and vitamin D [Vit D] levels. **Methods:** We used a sample of 40 females of the same age group, who were divided into Group 1 as a control consists of 18 healthy females and Group II consisted of 22 age matched females with clinical and electrophysiological evidence of CTS. We measured atherogenic index [AI] as a marker of hyperlipidemia, body mass index [BMI], Vit D status and electrophysiological tests of CTS. **Results**: Subjects with CTS had deficient Vit D status, they had significantly high atherogenic index (AI), and significant high BMI all compared to control Group I. Median sensory conduction velocity was significantly correlated negatively with BMI and atherogenic index, and positively correlated significantly with Vit D status. But median sensory and motor action potential latency were significantly correlated positively with BMI and atherogenic index, and negatively correlated significantly with Vit D status The analysis revealed BMI, atherogenic index and Vit D status as predictors of median nerve sensory and motor action potential latency and sensory nerve conduction velocity in CTS. **Conclusion:** The results of this study suggest that obesity and hyperlipidemia are potent CTS risk factors and declared the direct association between Vit D status and CTS occurrence. Our study supports the notion of the compensatory neuroprotective role of Vit D which could have a direct impact on the nerves integrity as it has an anti-inflammatory property which acts in relieving nervous insults and stress.

Keywords

Carpal Tunnel Syndrome, Vitamin D, Body Mass Index

1. Introduction

The main cause of CTS is compression of the median nerve at the wrist, this causes tingling in the hands, pain, numbness, tingling in the fingers particularly the thumb, index and middle fingers, loss of sensation in the hands and fingers, also weakness in the hands [1].

This type of entrapment neuropathy [CTS] is the most common one of the upper extremity that results in significant functional disability [2]. It has a multifactorial etiology including systemic, anatomical, and idiopathic causes. The increased pressure in the carpal tunnel on the median nerve initiates deterioration of nerve function due to changes in intraneural microcirculation, alterations in vascular permeability, impairment of axonal action potential transport, with edema formation [3].

Vitamin D is a steroid molecule obtained through the diet or synthesized in the skin from 7-dehydrocholesterol by ultraviolet irradiation [4]. It has a broad range of actions being effective in calcium-phosphorus metabolism and in musculoskeletal system health [5]. In addition, it plays an important role in neuroprotection and neurotrophism [6]. Previous studies reported that it reduced animal brain neurological injury and/or neurotoxicity by protection of neurons against oxidative stress through its antioxidant and anti-inflammatory properties [7] [8]. Also, its administration improved recovery of myelination after nerve injuries [9]. Up to our knowledge the exact role of Vit D in CTS is not elucidated.

CTS is an important and disabling condition. Previous studies indicate that obesity and hypertriglyceridemia are significant early diabetic neuropathy risk factors, also glucose control more closely correlated with large myelinated fiber function and nerve conduction velocity, while hypertriglyceridemia and obesity significantly correlated with small fiber integrity (IENFD) [10].

Up to our knowledge, there is a little information about the role of hyperlipidemia as a risk factor for CTS.

Body mass index [BMI] has been attributed as a risk factor for the development of CTS. It has been found that obese individuals had higher probability of CTS as compared to a slender individual, a recent gain in weight and increased fluid accumulation in the tissue spaces in the carpal tunnel is a risk factor for CTS [11].

Hyperlipidemia describes as elevated plasma concentration of lipid Triglyceride [TG] and Total Cholesterol [TC] and their blood transporting lipoproteins [HDL-Cholesterol, LDL-Cholesterol, VLDL-Cholesterol]. It is often calculated to estimate cardiovascular risk as indicated by strong scientific evidence. On the other hand, high level of TG has been related with an increased LDL-C particles

and increased cardiovascular risk [12]. Atherogenic dyslipidemia, defined as high LDL-C/HDL-C ratio calculated in mmol/L and hyper TG, it has recently been proposed as a marker of plasma Hyperlipidemia. It is associated with high cardiovascular risk [12]. Atherogenic Index [AI] is inversely related and significantly correlated with insulin resistance [HOMA-IR]. But its relation to CTS needs more investigations to be clarified and highlighted.

As CTS is considered as the most common entrapment neuropathy. A fuller understanding of factors predicting CTS risk is essential to better define disease pathogenesis and develop effective prevention or treatment strategies. Several efforts have been made in seeking emergent or new risk factors to improve CTS prediction.

To the best of our knowledge, the correlation of vitamin D deficiency as a risk factor in patients with CTS is rarely investigated in Saudi patients, so it remains unclear and needs to be elucidated. The goal of the present study is to evaluate a possible association between vitamin D deficiency and CTS. Also the current study aimed to determine the correlation of as Body Mass Index [BMI] and, Atherogenic Index [AI] as possible risk factors for CTS, and to correlate vitamin D levels and these risk factors with the electrophysiological measures of nerve impairment and sensory loss which are the gold standard for determining motor and sensory nerve function in CTS.

The aim of the present study was to assess and study a possible association could be found between electrophysiological data and functional status in CTS on the one hand and BMI, hyperlipidemia AI, as well as vitamin D levels on the other hand. Moreover, our findings could suggest disparate pathogenesis for CTS injury and offer additional support to a competing narrative to the traditional understanding of CTS as driven by prolonged sustained entrapment neuropathy.

2. Methods

2.1. Subjects and Sample Size

This study was carried out from March 2022 to February 2023 at the Clinical Physiology Laboratory of King Abdul Aziz University Hospital (Riyadh, Saudi Arabia). All biochemical parameters were measured in a biochemistry laboratory at the Physiology Department (King Abdul Aziz University Hospital). The study was approved by the Ethics Committee of King Khalid University Hospital, and all of the procedures were performed in accordance with ethical approval institutional guidelines. The study protocol followed the ethical guidelines of the most recent Declaration of Helsinki. Written consent was obtained from the participants prior to the start of the study.

Variables and Data Collection In this cross-sectional study a total of 60 eligible outpatient who had initially agreed to participate were enrolled and identified, they were females attending the Clinical Physiology Laboratory of King Abdul Aziz University Hospital (Riyadh, Saudi Arabia), diagnosed with or without

CTS. Patients were in the same age group of 35 - 50 years, they were subjected to history taking, thorough clinical examination, and laboratory investigations to establish diagnosis of CTS, they were diagnosed according to American Association standards. Fifteen did not agree to participate in this study and the remained 45 patients signed the informed consent. Of those who signed, five patients were excluded from the study as they have diabetes and diabetes complications as mentioned in the exclusion section. Three had prolipherative retinopathy and two had nephropathy as diagnosed by the laboratory investigations and fundus ophthalmoscopy. The final analysis was performed based on data obtained from the remaining forty participants. Prior to the start of the study, they received information about the study and its aims and gave their informed consent to participate. CTS was defined based on certain criteria: symptoms, signs abnormal NCS [defined as abnormal medianmotor or sensory amplitude or motor and sensory conduction velocity using age adjusted normative data]. Subjects who fulfilled 0 criteria were classified as having no CTS. We found 18 patients has no signs and symptoms of CTS according to electrophysiological findings, they were included as a control group.

So we used a sample of 40 females their mean age (range 35 - 45 years). They were divided into two main groups: Group 1 as a control group consists of 18 healthy females not having CTS clinically or electrophysiologically and Group II consisted of 22 aged matched females presented with clinical and electrophysiological evidence of CTS.

2.2. Inclusion Criteria

Eligible patients for inclusion in this study were if they had clinical symptoms and electrophysiological evidence of CTS. According to [Wang 2013] [13] evidence of CTS characterized by either or both the following:

- Median nerve peak sensory latency > 3.5 ms (stimulated at wrist at distance from active electrode = 14 cm).
- Median nerve distal motor latency > 4.4 ms (stimulated at wrist at distance from active electrode = 8 cm).

2.2. Exclusion Criteria

Subjects were excluded if any of the following was detected:

- Systemic clinical illness like diabetes mellitus, hyperthyrodism, hyperparathyroidism, inflammatory thyroiditis, malignancy, inflammatory arthritis, renal and hepatic failure.
- Electrodiagnostic findings suggesting e.g., polyneuropathy, hereditary neuropathy), cervical radiculopathy, sub-clinical sensory polyneuropathy, rheumatologically disease. Previous surgery or trauma involving the upper limb and/or neck, also subjects receiving calcium/vitamin D supplementation.

All patients included in the present study were subjected to:

1) Full history taking.

2) Thorough general and neurological examination, for diagnosis of CTS and exclusion of polyneuropathy.

3) Body mass index (BMI) was calculated by dividing body weight in kilograms by height in meters squared. BMI was divided into the following categories: normal weight < 25 kg/m^2, overweight 25 - < 30 kg/m^2, and obesity was defined as a BMI of > 30 kg/m^2 [14].

2.3. Biochemical Investigations

Sample Collection: All diabetic individuals fasted for 8 hours and 10 ml of their venous blood was collected in EDTA tubes, centrifuged at 3500 rpm for 10 min for plasma collection and stored at −70˚C. Plasma analysis was done to measure the standard range of biochemical parameters that would be tested for in patients with CTS, using standard methods. Routine laboratory tests for the exclusion of diabetes mellitus and renal or hepatic failure. All participants underwent a 24 h urinary albumin excretion test by measuring urinary albumin [N antiserum to human albumin kit; BN prospec, Siemens, Germany] and urinary creatinine [Creatinine Plus version 2 kit; Cobas c701, Roche, Germany] according to the manufacturer's instructions to exclude diabetic nephropathy.

The fasting serum low-density lipoprotein cholesterol [LDL-C] and fasting serum high-density lipoprotein cholesterol fasting serum [HDL-C] were measured by an enzymatic assay [Wako Diagnostics, Tokyo, Japan]. Then the plasma atherogenic index was calculated as LDL-C/HDL-C.

Estimation of serum vitamin D levels

Fasting blood samples were collected from patients and controls for serum vitamin D assays. Serum was collected using standard sampling tubes or tubes containing separating gel. 25(OH) Vitamin D is stable for 8 h at 18°C - 25°C, 4 days at 2°C - 8˚C, and 24 weeks at −20˚C. Vitamin D was determined by the radioimmunoassay method using 25-OH Vitamin D EIA Kit [Immundiagnostik, Bensheim and Biomedica, Wien]. Patients with vitamin D < 20 ng/ml were considered to have vitamin D deficiency and those between 20.0 and 30.0 ng/ml as "insufficient," while optimal levels were defined as vitamin D concentrations greater than 30.0 ng/ml [15].

Quantitative Sensory and Motor Electrodiagnostic studies [13]

The nerve conduction tests were performed as described by previous reports [13] in the Department of Clinical Physiology with standard surface recording techniques using an electromyography type Spirit Nicolet Viking [Nicolet-Biomedical Inc, Madison, WI, USA]. Upper extremity temperature was maintained at or above 30˚C at time of the electrodiagnostic studies.

Quantitative Sensory and Motor Tests for: All groups were compared for presence of CTS in median nerves [motor & sensory]. Concerning the procedures for determining the diagnosis of CTS, it was assessed by consultants of clinical physiology.

Unilateral sensory NCS were performed antidromically on median, motor nerve conduction studies [NCS] were performed on the median. For motor nerves, the

electromyographic settings of the machine were: frequency (8 Hertz [Hz]-8 kilo Hertz [kHz], sweep speed [5 msec/division], gain [1000 uV], stimulation intensity [400 V, and duration [0.1 msec].

While the settings for sensory nerves were frequency [8 Hz - 1.6 kHz], sweep speed [5 msec/division], gain [10 uV], stimulation intensity [208 V], and duration [0.05 msec]. Measurements of distance, response latencies, and amplitude were carried out in a standard fashion using onset latencies, and base line to peak amplitude. Measurements of peak-peak amplitudes were used for sensory responses [13].

2.4. Motor Nerve Conduction Studies

Median nerve motor conduction study was done by recording from abductor pollicisbrevis [APB] muscle while stimulating the median nerve at wrist and elbow sites. The compound muscle action potentials [MNAP] of the median were obtained using supramaximal stimulation of the nerves at the wrist and elbow, with the distal distance for motor NCV 80 mm above the recording electrode and for ulnar nerve was done at wrist and elbow [13]. Distal latency, compound muscle action potential [CMAP], and forearm motor conduction velocities were recorded [normative values: distal latency ≤ 4.4 ms, CMAP amplitude ≥ 4.0 mV, conduction velocities ≥ 50 m/s].

Sensory nerve conduction studies

While stimulating the median nerve 14 cm proximal to the active electrode Antidromic median sensory recording over digit was done, sensory peak latency and sensory nerve action potential (SNAP) amplitude were measured [normative values: peak latency ≤ 3.5 ms, SNAP amplitude ≥ 20 mV and conduction velocities ≥ 40 m/s] [13].

Statistical analysis: All data are reported as mean ± standard deviation. Two-way analysis of variance was performed to compare the study groups, with differences considered significant for $p < 0.05$, with 95% Confidence Intervals. The Spearman rho correlation coefficient was applied to find the strength of correlation between continuous quantitative variables. To study predictors of CTS Linear regression analysis was performed for Vit D and atherogenic index (as independent variables), and median nerve sensory latency and conduction velocity (as a dependent variable). All statistical analysis performed with SAS 9.2 statistical software [version SAS 9.2 Institute, Inc, Cary, North Carolina, USA].

3. Results

Subjects with CTS had deficient Vit D status compared to normal Vit D status in group I [$p = 0.002^*$], they had significantly high atherogenic index [AI] [$p < 0.003^*$] compared to group I, and there was significant change between group II compared to group I in relation to BMI [$p < 0.012^*$].

The comparison of CTS group II with Group I in relation to nerve conduction studies [NCSs] showed that there is significant prolongation of motor nerve ac-

tion potential latency of median in Group II compared to group I [p < 0.012*], Also there was significantly reduced motor conduction velocity of median nerve in Group II compared to group I [p < 0.025*]. Concerning the sensory nerve conduction studies there was significant prolongation of sensory nerve action potential latency of median nerve in Group II compared to group I [p < 0.019*].

Also, there was significantly reduced sensory conduction velocity of Median nerve in Group II compared to group I [p < 0.012*].

Correlations and Linear Regression

The relationship between risk factors and individual CTS characteristics was examined for those with CTS. Table 1 represents CTS measures by electrophysiological examination as dependent variables in Group II correlated with potential risk factors as Vit D status, BMI and atherogenic index [as independent variables]. Median nerve sensory action potential latency as well as sensory conduction velocity which directly reflects sensory nerve fiber integrity [as dependent variables] showed that the latency significantly correlated positively with BMI and atherogenic index [r = 0.521 and r = 0.0771 respectively], [p < 0.001*] and [p < 0.001*] respectively, but there was a significant negative strong correlation with Vit D levels[r = −0.921] [p < 0.001*].

Whereas the median sensory conduction velocity is significantly correlated negatively with BMI and atherogenic index [r = −0.521 and r = −0.556] [p < 0.001* and p < 0.000*] respectively, and positively correlated significantly with Vit D status[r = 0.733*] and [p < 0.001*] respectively.

Linear regression analysis was done for BMI, atherogenic index and Vit D status as independent variables and Median nerve sensory action potential latency and median sensory conduction velocity as dependant variables. The analysis revealed BMI, atherogenic index and Vit D status as predictors of median nerve action potential latency and sensory conduction velocity in CTS beta coeffient = 0.566 [p = 0.026*], beta coeffient = 0.644 (p = 0.0122*), beta coeffient = 0.545 (p = 0.034*) respectively all for median nerve action potential latency but for median sensory conduction velocity in CTS the values were beta coeffient = 0.522 [p = 0.016*], beta coeffient = 0.621 [p = 0.0133*], beta coeffient = 0.541 [p = 0.034*] respectively (See Tables 1-3).

Table 1. The characteristics of CTS group [II] compared to Group I control group in relation to Vit D status, BMI and Atherogenic Index [AI].

Features	Group I: controls (n = 18)	Group II: Patients with CTS (n = 22)	p-values
Vit D level (25-OH-Vit D) (ng/ml)	21 ± 0.01	15 ± 0.3	0.002*
BMI kg/m^2	22.2 ± 0.9	29.0 ± 5.5	0.012*
Atherogenic Index (AI)	21 ± 1.01	15.03 ± 0.4	0.003*

Note: Results are expressed as mean ± standard deviation; *Significant changes Group II compared with Group I [p < 0.05].

Table 2. The characteristics of CTS group (II) compared to Group I in relation to median nerve motor and sensory electrophysiological parameters.

Nerve Conduction Study parameters (NCS)	Group I controls (n = 18)		Group II with CTS (n = 22)		
-Median nerve Motor conduction parameters (MNCS)	Latency (msec)	Conduction velocity (m/sec)	Latency (msec)	Conduction velocity (CV m/sec)	p-values
	3.0 ± 0.1	51 ± 1.0	4.7 ± 0.13	42.1 ± 1.03	0.012* 0.025¥
-Median nerve Sensory conduction parameters (SNCS)	3 ± 0.11	40.1 ± 1.01	4.1 ± 0.33	31.3 ± 0.32	0.019* 0.012¥

Note: Results are expressed as mean ± standard deviation; *Significant changes of median nerve sensory and motor latency in Group II compared with Group I [$p < 0.05$].); ¥ Significant changes of median nerve sensory and motor conduction velocity in Group II compared with Group I [$p < 0.05$].

Table 3. The correlation between some electrophysiological variables in CTS Group II correlated with BMI, AI and Vit D status as different risk factors.

CTS **Variables**	Correlation coefficient	P value
Median sensory latency-BMI	0.521	$p < 0.001$*
Median sensory latency - Atherogenic Index	0.771	$p < 0.001$*
Median sensory latency - Vit D status	−0.921	$p < 0.001$*
Median sensory conduction velocity - BMI	−0.525	$p < 0.001$*
Median sensory conduction velocity - Atherogenic index	−0.556	$p < 0.000$*
Median sensory conduction velocity - Vit D status	0.533	$p < 0.001$*

Note: Correlation coefficients and p values are displayed for different relationships. *Significant correlation [$p < 0.05$].

4. Discussion

Limits of the Study

The limits of the study relate to the small size of the sample, the missing data in certain files, and the escape of some females from the study due to their fear of the nerves elecrtrical stimulation was obviously the biggest weakness

A series of studies have examined CTS risk factors among subjects who underwent sequential nerve conduction studies. The most notable finding of the present study was the presence of a high prevalence of vitamin D deficiency among Saudi female patients with CTS compared with healthy individuals. CTS patients had significantly lower vitamin D levels compared with the controls as shown in Table 1. Additionally, serum vitamin D levels total score were predictors of CTS. Regarding the association between vitamin D deficiency and CTS, the results are in agreement with previous studies [16] [17].

In contradiction to the finding of this study is study of Lee *et al.* [18] who showed that there was no difference in vitamin D levels between the patients with CTS and the controls.

Previous numerous studies showed the association between parameters as high BMI and CTS. CTS patients have higher BMI values compared with controls is consistent with findings from the present study [19], also the present study showed that BMI is a predictor of CTS. Patients with CTS were obese compared with the controls. Derangement of median nerve function in obese patients may be due to compression of the median nerve by the fat deposition in the carpel tunnel. Consequently, these results greatly strengthen the case for investment in trials investigating weight loss for treatment of CTS.

Concerning the negative correlation between median nerve sensory and motor conduction velocity as well as the positive correlation between median nerve sensory and motor action potential latency with obesity and atherogenic index observed in this study that indicate obesity and hypertriglyceridemia are significant early CTS risk factors. Moreover, hypertriglyceridemia and obesity are predictors of CTS as shown by multiple linear regressions. The correlation data suggests there may be differential impact of obesity and dyslipidemia on CTS measures.

5. Conclusion

The observation that there is a differential relationship between CTS measures versus dyslipidemia and obesity supports development of potential CTS measures. CTS measures may be particularly important in any study examining the effect of a treatment designed to lower lipids or ameliorate the deleterious effects of central adiposity. More longitudinal studies are required to evaluate the extent to which these risk factors predict future CTS and their cumulative impact on median nerve sensory and motor functions. We report here the relationship between obesity, dyslipidemia and CTS risk. The results suggest that obesity and dyslipidemia are potent CTS risk factors. For the first time the findings of the present study declared the direct association between Vit D status and CTS occurrence. Our study supports the notion of the compensatory neuroprotective role of Vit D which could have a direct impact on the nerves integrity as it has anti-inflammatory properties which act in relieving nervous insults and stress.

Consent for Publication

Written informed consent for publication was obtained from the patients.

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Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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