**RESEARCH ARTICLE** / *Araştırma Makalesi*

# Association of Diabetic Polyneuropathy and Carpal Tunnel Syndrome: Role of Glycemic Control and Microvascular Complications

## Diyabetik Polinöropati ve Karpal Tünel Sendromu İlişkisi: Glisemik Kontrol ve Mikrovasküler Komplikasyonların Rolü

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**Abstract**

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|---|---|
| Introduction | Carpal tunnel syndrome (CTS) is more common in diabetes mellitus (DM), especially in individuals with diabetic polyneuropathy (DPN). This study aimed to retrospectively investigate the effects of elevated glycosylated hemoglobin (HbA1c) levels, duration of diabetes, and other microvascular complications of DM on the frequency and severity of CTS in patients with DPN. |
| Materials and Methods | 124 DPN patients were included in the study. In these patients, fasting blood glucose (FBG) and HbA1c levels, duration of DM, antidiabetic drugs used, comorbidities, and other complications of diabetes were questioned. According to the results of the electrophysiological examination, the patients were divided into 2 groups: those with only DPN and those with DPN + CTS. |
| Results | When diabetes complications were investigated, diabetic nephropathy was found only in those with DPN + CTS (p=0.045). Electrophysiologically, in sensory fibers in all patients, In 43 patients (34.7%), involvement of motor fibers was accompanied. A positive correlation was found between the severity of CTS and duration of diabetes, FBG and HbA1c levels, and subcutaneous insulin use (p=0.018, p=0.014, p=0.003, p=0.029, respectively). |
| Conclusion | Good glycemic control can reduce the risk of developing CTS with microvascular complications of diabetes. Therefore, it is important for patients to protect their hand function and prevent the development of CTS by being informed about the complications of diabetes. |
| Keywords | Carpal tunnel syndrome, Diabetic polyneuropathy, HbA1c, Microvascular complications, Glycemic control. |

**Öz**

| | |
|---|---|
| *Amaç* | *Karpal tünel sendromu (KTS) diabetes mellitusta (DM), özellikle de diyabetik polinöropatisi (DPN) olan bireylerde daha sık görülmektedir. Bu çalışmada, DPN'li hastalarda yüksek glikozile hemoglobin (HbA1c) düzeylerinin, diyabet süresinin ve DM'nin diğer mikrovasküler komplikasyonlarının KTS sıklığı ve şiddeti üzerindeki etkilerinin retrospektif olarak araştırılması amaçlanmıştır.* |
| *Yöntem ve Gereçler* | *124 DPN hastası çalışmaya dahil edildi. Bu hastalarda; açlık kan şekeri (AKŞ) ve HbA1c düzeyleri, DM süresi, kullanılan antidiyabetik ilaçlar, eşlik eden hastalıklar ve diyabetin diğer komplikasyonları sorgulandı. Elektrofizyolojik inceleme sonuçlarına göre hastalar sadece DPN olanlar ve DPN + KTS olanlar olmak üzere 2 gruba ayrıldı.* |
| *Bulgular* | *Diyabet komplikasyonları araştırıldığında, diyabetik nefropati sadece DPN + KTS olanlarda saptandı (p=0.045). Elektrofizyolojik olarak tüm hastalarda duyusal liflerde; 43 hastada (%34,7) ise motor liflerde tutulum eşlik etti. KTS şiddeti ile diyabet süresi, AKŞ ve HbA1c düzeyleri ve subkutan insülin kullanımı arasında pozitif korelasyon bulundu (sırasıyla p=0.018, p=0.014, p=0.003, p=0.029).* |
| *Sonuç* | *İyi glisemik kontrol, diyabetin mikrovasküler komplikasyonları ile KTS gelişme riskini azaltabilir. Bu nedenle hastaların diyabetin komplikasyonları hakkında bilgi sahibi olarak el fonksiyonlarını korumaları ve KTS gelişimini önlemeleri önemlidir.* |
| *Anahtar Kelimeler* | *Karpal tünel sendromu, Diyabetik polinöropati, HbA1c, Mikrovasküler komplikasyonlar, Glisemik kontrol.* |

## INTRODUCTION

Diabetes mellitus (DM) is a metabolic disease with high morbidity. According to the World Health Organization (WHO), the number of patients with diabetes is expected to reach 300 million in the first quarter of the 21st century.[1] According to the results of the Turkish Diabetes Epidemiology Study-II (TURDEP-II) conducted in 2010, the prevalence of diabetes in Turkey was 16.5% (6.5 million people).[2]

Complications caused by diabetes, a systemic disease, are categorized into microvascular and macrovascular. Microvascular complications include diabetic polyneuropathy (DPN), diabetic nephropathy, and diabetic retinopathy, while macrovascular complications include diabetic heart disease and stroke. DPN is the most common chronic complication of DM and occurs in approximately 50% of patients with diabetes for more than 20 years.[3] Findings suggestive of polyneuropathy in patients include marked numbness, tingling, burning sensation, pain, itching, and hyperalgesia in the distal extremities.[4] Diabetes causes increased inflammation in the nerve tissue and microvascular damage in the vasa nervorums, leading to nerve ischemia and subsequent neuropathy.[5]

Diabetes causes many different forms of involvement of peripheral nerves, most commonly distal symmetrical sensory neuropathy. Carpal tunnel syndrome (CTS) is the most common entrapment neuropathy causing numbness, pain, and weakness in the hands,[6] prevalence is higher in patients with DPN than in the general population.[7] In one study, CTS was 2% in the reference population, 14% in diabetic individuals without DPN, and 30% in those with DPN.[8]

Elevated glycosylated hemoglobin (HbA1c), high body mass index (BMI), and long duration of diabetes are risk factors for the development of CTS and ulnar entrapment neuropathies and play an essential role in the development of entrapment neuropathy in the presence of diabetic retinopathy.[9]

Considering the co-occurrence of DPN and CTS, the relationship between them, and their effects on quality of life, further investigation of how these two diseases affect each other's severity may be helpful in the treatment of patients. The primary aim of this study was to investigate the effect of elevated HbA1c levels on the development and severity of CTS in patients with DPN. The secondary aim was to examine the effect of diabetes duration, BMI, and other microvascular complications of DM on the frequency and severity of CTS.

## MATERIAL and METHODS

In this study, we retrospectively reviewed the clinical and laboratory findings of 2921 patients who were referred for electromyography (EMG) examination to the Clinical Electroneurophysiology Laboratory, Neurology Clinic, Başakşehir Çam and Sakura City Hospital with a prediagnosis of polyneuropathy between May 2022 and April 2023 from the hospital data system. According to the results of the EMG examination, a total of 143 diabetic patients with polyneuropathy only and CTS with polyneuropathy were identified. Fasting blood glucose (FBG) and HbA1c levels in the last 60 days, duration of DM, antidiabetic drugs used, comorbidities, and other complications of diabetes were questioned. We excluded nine patients whose hospital data were unavailable, three with chemotherapeutic drug use, and seven whose HbA1c levels had not been checked in the last 60 days. The study's local ethics committee approval was obtained (2023- 175).

A 4-channel EMG device (Natus UltraPro S100 EMG/NCS/EP Neurodiagnostic System, Galway, Ireland) was used for all subjects' electrophysiologic EP examinations. Care was taken to ensure limb temperatures were around 32-34 °C. In each patient, median, ulnar, radial, superficial peroneal, sural sensory, median, ulnar, tibial, and peroneal motor nerve conduction studies were performed on the side with more symptoms. Sensory and motor nerve con-

duction studies were also performed in the opposite extremity in patients with entrapment neuropathy. In sensory nerve conduction studies (NCSs), sensory conduction velocity (SCV), sensory nerve action potentials (SNAPs), peak latency, and peak-to-peak amplitude were measured. In motor NCSs, compound muscle action potentials (CMAPs), distal motor latency (DML), basal-negative peak amplitude, and motor conduction velocity (MCV) were calculated. For the diagnosis of CTS, median nerve SCV ≤ 50 m/s and median nerve DML duration ≥ 4.2 ms were considered abnormal. When standard tests yielded the expected results, a median-ulnar comparison was performed for the fourth finger, and the difference between the median and ulnar SNAP peak latency of the fourth finger was calculated. A difference greater than 0.4 ms was considered abnormal. The electrophysiologic severity of CTS was determined according to Padua et al.'s neurophysiologic grading system: extreme severe CTS, loss of motor and sensory response; severe CTS, loss of median SNAP and prolonged DML; moderate CTS, slowing of median SCV and prolonged DML; mild CTS, slowing of median SCV and normal DML; very mild CTS, normal with standardized tests but impaired in comparative or segmental stimulation tests; negative, all tests including comparative or segmental stimulation tests were regular.[10] According to the results of the electrophysiologic examination, the patients were divided into two groups: DPN only and DPN + CTS.

### Statistical Analysis

For statistical analysis, the distribution of parametric data in the groups was analyzed by the Shapiro-Wilks test. For comparison between groups, parametric (T-test) tests were used for numerical data with normal distribution, and nonparametric (Mann-Whitney U) tests were used for numerical data without normal distribution. Groups were compared with a chi-square test for non-numerical data. IBM SPSS-25 program was used for statistical analysis. The statistical significance level was accepted as $p<0.05$.

## RESULTS

A total of 124 patients were included in the study. There were 21 (8 females) patients with DPN only with a mean age of 60.0 ± 7.7 years, and 103 (52 females) patients with DPN + CTS with a mean age of 63.03 ± 11.4 years. There was no difference in gender distribution between the groups. Although the mean age of patients with DPN + CTS was slightly higher than those with DPN alone, there was no significant difference between the groups (p=0.150). The two groups' mean height, weight, and BMI were similar. There was no difference between the groups regarding the frequency of concomitant hyperlipidemia, hypertension, and thyroid dysfunction (Table 1).

**Table 1.** Demographic data and comorbidities of the groups

| | DPN | DPN +CTS | Total | p |
|---|---|---|---|---|
| | n=21 | n=103 | n=124 | |
| Female: Male | 8:13 | 52:51 | 60:64 | 0.308 |
| Age (years) | 60.0 ± 7.7 (44-75) | 63.03 ± 11.4 (36-87) | 62.5 ± 10.9 (36-87) | 0.150 |
| Height (cm) | 169.4 ±10.6 (150-186) | 166.3 ± 10.4 (140-193) | 166.8 ± 10.5 (140-193) | 0.227 |
| Weight (kg) | 84.2 ± 12.8 (65-113) | 82.2 ± 16.7 (44-134) | 82.6 ± 16.1 (44-134) | 0.602 |
| BMI (kg/m²) | 29.5 ± 4.8 (20-38) | 29.8 ± 5.9 (17-54) | 29.7 ± 5.7 (17-54) | 0.839 |
| Thyroid dysfunction | 5 (%23.8) | 18 (%17.5) | 23 | 0.496 |
| Hypertension | 17 (%81) | 77 (%74.8) | 94 | 0.546 |
| Hyperlipidemia | 9 (% 42.9) | 55 (%53.4) | 64 | 0.378 |

Parametric values are mean ± standard deviation (minimum-maximum), and categorical variables are given as numbers (percentage). DPN: diabetic polyneuropathy, CTS: carpal tunnel syndrome, BMI: body mass index.

Although FBG and HbA1c values were higher in patients with DPN + CTS, there was no statistically significant difference between the two groups (p=0.166, p=0.262, respectively). Duration of diabetes was longer in patients with DPN + CTS, but there was no significant difference between the two groups (p=0.199). Eighty-four patients were using oral antidiabetics, and 75 patients were using

subcutaneous insulin, and there was no difference between the groups in terms of treatment. When diabetic complications were investigated, diabetic nephropathy was found only in patients with DPN + CTS (17 patients, 16.5%). There was no significant difference between the groups in the incidence of diabetic retinopathy and diabetic foot (Table 2).

**Table 2.** Diabetes characteristics of the groups

| | DPN | DPN +CTS | Total | p |
|---|---|---|---|---|
| | n=21 | n=103 | n=124 | |
| Fasting blood glucose (mg/dL) | 178 ± 64.7 (104-312) | 209.3 ± 96.8 (80-625) | 204.1 ± 92.6 (80-625) | 0.166 |
| HbA1c (%) | 8 ± 1.6 (5.5-11.9) | 8.6 ± 2.3 (5.1-15.8) | 8.5 ± 2.2 (5.1-15.8) | 0.262 |
| Duration of Diabetes (years) | 12.8 ± 8.8 (2-30) | 15.5 ± 8.8 (0.5-50) | 15.1 ± 8.8 (0.5-50) | 0.199 |
| Diabetic retinopathy | 4 (%19) | 30 (%29,1) | 34 | 0.345 |
| Diabetic nephropathy | 0 | 17 (%16.5) | 17 | 0.045* |
| Diabetic foot | 3 (%14.3) | 19 (18.4) | 22 | 0.649 |

Parametric values are mean, standard deviation (minimum-maximum), and categorical variables as numbers (percentage). DPN: diabetic polyneuropathy, CTS: carpal tunnel syndrome, HbA1c: glycosylated hemoglobin.
*P < 0.05.

Electrophysiologically, sensory fibers were involved in all patients, and motor fibers were involved in 34.7% (43 patients). There was no significant difference in motor fiber involvement between the two groups. When the degree of CTS was classified as EP, moderate severity of CTS was found for both the right and left sides: 40 patients (38.8%) in the right hand and 48 patients (46.6%) in the left hand (Figure 1). There was a positive correlation between the severity of CTS and duration of diabetes, FBG and HbA1c levels, and subcutaneous insulin use (Table 3).

**Table 3.** Significant correlates associated with carpal tunnel syndrome

| | Correlation | Spearman rho / p |
|---|---|---|
| CTS severity | Fasting blood glucose | 0.150 / 0.018* |
| | HbA1c | 0.155 / 0.014* |
| | Duration of diabetes | 0.187 / 0.003** |
| | Subcutaneous insulin use | 0.139 / 0.029* |

CTS: carpal tunnel syndrome, HbA1c: glycosylated hemoglobin.
*P < 0.05, **P < 0.01.

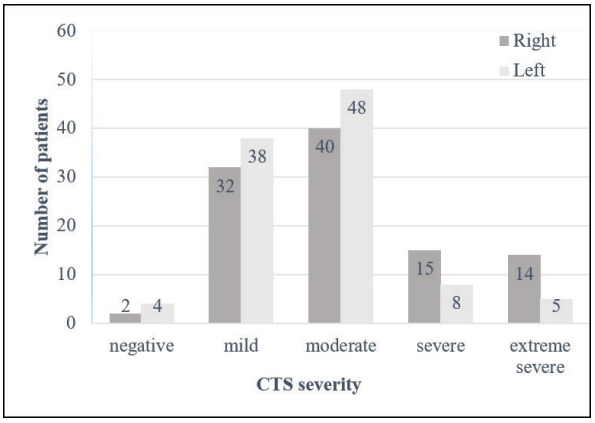


*Figure 1. Distribution of electrophysiologic severity of CTS in diabetic polyneuropathy group with carpal tunnel syndrome (CTS).*

## DISCUSSION

It is known that the prevalence of CTS in patients with diabetic polyneuropathy is higher than in the general population. In 2020, a nationwide population-based study showed that DM patients with DPN were more prone to CTS than those without DPN.[11] In another study of 353 Type 2 DM patients, DPN was detected in 235 patients and CTS in 139 of them, with a prevalence of 39.3%.[12] This study found CTS of varying severity in 83% of patients with DPN as EP. The pathogenesis of CTS in diabetic patients has not been fully explained. Metabolic and vascular factors may be influential. Studies have shown that glycemic control and aldose reductase inhibitor treatment improve nerve conduction velocities in patients with CTS.[13,14] In other words, the mechanism of CTS in diabetic patients is thought to

originate from metabolic factors related to hyperglycemia. The reason why the frequency of CTS was found to be higher in our group compared to previous studies may be related to the fact that FBG and HbA1c values were higher and, therefore, glycemic control was worse.

Duration of diabetes is an essential factor in developing peripheral neuropathy and CTS.[15] The duration of diabetes in our study group ranged between 6 months and 50 years after the diagnosis of diabetes. Although the duration of diabetes diagnosis was longer in the group with CTS (15.5 years versus 12.8 years), no significant difference was found between the two groups. Again, although age and BMI were slightly higher in the group with CTS, no significant difference was found. The influence of other factors, such as occupation and duration of hand use, on the development of CTS may explain this.

Glycosylated hemoglobin level is accepted as the gold standard in evaluating long-term glycemic control in diabetic patients. It is a good indicator of blood glucose control in the last 2-3 months.[16] It has been shown that elevated HbA1c level increases the risk of complications such as DPN and diabetic retinopathy, and lowering HbA1c level decreases the risk.[5] Microvascular complications of diabetes mellitus occurred quite frequently in the patients in our study group. Uremia is a risk factor for both polyneuropathy and CTS.[17] In our study, diabetic nephropathy was observed only in DPN patients with CTS.

It is reported that type 2 DM patients are frequently diagnosed with metabolic syndrome, a potential risk factor in the pathogenesis of CTS. In these patients, median CMAP amplitudes were found to be lower and sensory thresholds were found to be increased.[18] In a study by Nazish et al., it was shown that age, BMI, systolic blood pressure, low serum HDL, high triglycerides, high FBG, and HbA1c levels were parameters that may affect the electrophysiologic severity of CTS in diabetic patients.[19] Our study found a positive correlation between the severity of CTS and duration of diabetes, FBG and HbA1c levels, and subcutaneous insulin use.

The limitations of our study are that it is a retrospective, single-center study with a small sample size.

## CONCLUSION

We found a strong association between CTS and diabetic nephropathy in our study; poor glycemic control increased the severity of CTS. The occurrence of polyneuropathy and CTS in diabetes, a multisystemic disease, increases disability and impairs quality of life. Reasonable glycemic control in diabetic patients will reduce the risk of developing CTS and microvascular complications of diabetes. Patients must be informed about the complications of diabetes and the prevention of CTS development by preserving hand function.

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