Relationship between the severity of carpal tunnel syndrome and lipid profile in patients with type 2 diabetes mellitus

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Abstract

Background/Aim: Diabetes mellitus (DM) accelerates the development of neuropathy, and carpal tunnel syndrome (CTS) is the most common form of entrapment neuropathy. The pathogenesis of diabetic neuropathy is multifactorial with its vascular and metabolic factors. In this study, we aimed to evaluate the relationship among the electrophysiological severity of CTS, lipid profile and serum atherogenic index in patients with Type 2 DM.

Methods: In this hospital-based retrospective cross-sectional study, we retrospectively evaluated 202 type 2 DM patients, who presented to the electrophysiology laboratory of Zonguldak Bulent Ecevit University Faculty of Medicine between 2016-2019 and investigated the relationship among the electrophysiological severity of CTS, lipid profile and serum atherogenic index of 131 patients diagnosed with CTS.

Results: The patients with CTS had significantly higher values of fasting blood glucose and HbA1c compared to those without CTS (P=0.010). In terms of the severity of CTS, the patients were divided into three groups as mild, moderate, severe. In terms of the lipid panel, the mean values of cholesterol, triglyceride, and HDL-C were similar among the groups (P=0.098, P=0.321, P=0.706), while LDL-C levels were higher in the severe CTS group. (P=0.024). There was a significant positive correlation between age (R=0.126 P=0.004), HbA1c (R=0.245, P=0.002) and CTS severity.

Conclusion: We identified a relationship between CTS severity and LDL-C. CTS should be considered in patients with DM and hyperlipidemia. Further larger-scale studies with control groups are recommended.

Keywords: Carpal tunnel syndrome, Low-density lipoprotein, Cholesterol, Serum atherogenic index

Introduction

Carpal tunnel syndrome (CTS) is the most common entrapment neuropathy, which occurs when the median nerve is compressed as it passes under the carpal ligament at the wrist [1]. It is more common in females [2]. Most CTS cases are idiopathic; however, there are many associated risk factors such as recurrent trauma, metabolic and hormonal changes, smoking, female gender, and obesity [1,3-6]. Diabetes mellitus (DM) accelerates CTS, and multiple etiopathogenetic factors, both vascular and metabolic, are responsible for the development of neuropathy [7]. Endothelial dysfunction and atherosclerosis have a significant impact on microvascular and macrovascular complications in patients with diabetes. Diabetic and entrapment neuropathies are the most common among the microvascular complications in diabetic patients [8]. Microangiopathic changes in vasonevromus due to atherosclerosis lead to the development of neuropathy by negatively affecting the nutrition of peripheral nerves. It also affects the neuronal membrane lipid content and causes the development of both entrapment neuropathy and polyneuropathy. Hypercholesterolemia, especially high low-density lipoprotein cholesterol (LDL-C) has also been associated with fibrinogenesis in many organs and peripheral nerves [8,9].

In this study, we aimed to evaluate the relationship between the electrophysiological severity of carpal tunnel syndrome, lipid profile and serum atherogenic index in patients with diabetes mellitus.

Materials and methods

In our study, we retrospectively evaluated 202 type 2 DM patients who visited the electrophysiology laboratory of Zonguldak Bulent Ecevit University Faculty of Medicine between 2016-2019 and underwent Electromyography (EMG). We aimed to evaluate the relationship between the electrophysiological severity of CTS, lipid profile and serum atherogenic index of 131 patients diagnosed with CTS. EMG results, recent (including 3 months before and after the EMG date) blood test results (glycated hemoglobin a1c (HbA1c), fasting blood glucose, white blood cell, TSH, Free T4, LDL-C, high-density lipoprotein cholesterol (HDL-C), cholesterol, triglyceride), demographic data (age, gender), Body Mass Index (BMI) and duration of diabetes of each patient included in the study were obtained from the patient files.

The exclusion criteria for the study included patients with chronic infection, malignancy, hypertension, peripheral artery disease, cerebrovascular diseases, entrapment neuropathies, and other diseases that cause neuropathy (B12 deficiency, rheumatological diseases, chronic kidney disease, vasculitis, drug-related), and patients on antilipidemic drugs, with a BMI greater than 25 kg/m² and with an EMG result indicating polyneuropathy.

Patients underwent standard electrophysiological study. All physiological studies were performed with 2 channelled Medelec EMG device. In all recordings, superficial electrodes were used. In motor conduction studies, the median, ulnar, peroneal and tibial nerves were stimulated, and compound muscle action potentials (CMAPs), distal latency (DL) and nerve conduction velocities (NCVs) were recorded. Sensory responses were obtained with orthodromic methods. In sensory conduction studies, the median, ulnar and sural nerves were stimulated, and sensory conduction velocities (SCVs), sensory response peak latencies and sensory action potentials (SAPs) were recorded.

Nerve conduction velocities below 50 m/s in the upper limb and 40 m/s in the lower limb, median nerve SAP amplitude below 12 µV, CMAP amplitude below 5 mV and motor DL values above 4.0 ms, ulnar nerve SAP amplitude values below 8 µV, CMAP amplitude below 5 mV and motor distal latency above 4.0 ms, posterior tibial nerve CMAP amplitude values below 4 mV, peroneal nerve CMAP amplitude below 2 mV, and sural nerve SAP amplitude below 10 µV were considered abnormal values.

Electrophysiological classification of all subjects in terms of CTS severity is as follows [10].

- **Mild Carpal Tunnel Syndrome**: Prolonged median sensory latency ± reduced amplitude of median sensory nerve action potential below the normal values
- **Moderate Carpal Tunnel Syndrome**: Prolonged median sensory latency and prolonged median motor distal latency
- **Severe Carpal Tunnel Syndrome**: Prolonged median motor and sensory distal latency with low or absent median compound muscle action potential

Statistical analysis

The data obtained in the research were analyzed using SPSS (Statistical Package for Social Sciences) for Windows 22.0 software package. Number, percentage, mean, and standard deviation were used as descriptive statistical methods in the evaluation of the data. Mann Whitney U test was used to compare two non-normally distributed groups of variables and Chi-square tests were used for categorical variables. One-way ANOVA and Kruskal Wallis tests were used in groups showing normal and non-normal distributions, respectively, to determine the significant differences among the means of three or more independent groups. Ordinal Logistic Regression Analysis was used to examine the adjusted relationships. For all statistical analyses, P-value<0.05 indicated significance.

Results

CTS was observed in 131 of 202 patients. The patients with CTS had significantly higher values of fasting blood glucose and HbA1c compared to those without (P=0.010) (Table 1).

Forty-five patients had mild, 50 patients had moderate, and 36 patients had severe CTS. There were sixty females, and 71 males. Patients with mild, moderate, and severe CTS had mean ages of 61.44 (10.77) years, 62.4 (11.20) years, and 65.58 (10.03) years, respectively (P=0.229). CTS was more severe among females (P=0.045) (Table 2). The mean duration of diabetes, HbA1c, and fasting blood glucose levels of the groups were similar (P=0.481, P=0.379, P=0.364), just as mean 25(OH) Vitamin D levels. There was no statistical difference among the groups in terms of kidney function tests and electrolytes (Table 3). The mean values of cholesterol, triglyceride, and HDL-C did not significantly differ between the groups (P=0.098, P=0.321, P=0.706), while the LDL-C levels did (P=0.024). The mean values of Triglyceride/HDL-C,
Cholesterol/HDL-C, and LDL-C/HDL-C, which are approved as the atherogenic index, were similar among all groups (P=0.237, P=0.202, P=0.660) (Table 3).

The ordinal logistic regression analysis, which was carried out to determine the cause-effect relationship between LDL-C, HDL-C, TG, age, and HbA1c and the severity of CTS, was significant. There was a significant positive correlation between age (R=0.126 P=0.004), HbA1c (R=0.245, P=0.002) and CTS severity (Table 4).

Table 1: Laboratory characteristics of patients with and without CTS

<table>
<thead>
<tr>
<th></th>
<th>Without CTS</th>
<th>With CTS</th>
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<tbody>
<tr>
<td></td>
<td>Median</td>
<td>Median</td>
</tr>
<tr>
<td></td>
<td>(Min-Max)</td>
<td>(Min-Max)</td>
</tr>
<tr>
<td>Glycated HbA1c (%)</td>
<td>6.9 (4.6-13.1)</td>
<td>7.9 (5.3-14.2)</td>
</tr>
<tr>
<td>Fasting blood glucose level (mg/dl)</td>
<td>125 (85-374)</td>
<td>163 (85-532)</td>
</tr>
<tr>
<td>Cholesterol(mg/dl)</td>
<td>193 (36-372)</td>
<td>187 (71-356)</td>
</tr>
<tr>
<td>LDL-C (mg/dl)</td>
<td>111 (43-281)</td>
<td>113 (51-213)</td>
</tr>
<tr>
<td>Triglyceride(mg/dl)</td>
<td>153 (90-538)</td>
<td>157 (55-1287)</td>
</tr>
<tr>
<td>HDL-C (mg/dl)</td>
<td>47 (28-140)</td>
<td>44 (42.5-85)</td>
</tr>
<tr>
<td>Triglyceride/HDL-C (AIP)</td>
<td>3.3 (0.06-14.38)</td>
<td>3.35 (14.45-96)</td>
</tr>
<tr>
<td>Cholesterol / HDL-C</td>
<td>4.28 (0.26-7.55)</td>
<td>4.37 (0.2- 12.71)</td>
</tr>
<tr>
<td>LDL-C/CHDL-C</td>
<td>2.37 (0.5-79.5)</td>
<td>2.52 (0.2-79.1)</td>
</tr>
<tr>
<td>25(OH) Vitamin D</td>
<td>21.65 (5.73.7)</td>
<td>18.41 (1-53.2)</td>
</tr>
<tr>
<td>Calcium</td>
<td>33 (15.222)</td>
<td>39.5 (15-189)</td>
</tr>
<tr>
<td>Creatinine</td>
<td>0.8 (1.7-3)</td>
<td>0.9 (0.5-9.9)</td>
</tr>
<tr>
<td>GFR</td>
<td>87 (100-125)</td>
<td>78.5 (10-149)</td>
</tr>
<tr>
<td>HDX</td>
<td>9.6 (7.1-10.8)</td>
<td>9.8 (7.7-11.4)</td>
</tr>
<tr>
<td>Magnesium</td>
<td>1.9 (1-4.2)</td>
<td>1.96 (1-4.2)</td>
</tr>
<tr>
<td>Sodium</td>
<td>140 (134-145)</td>
<td>139 (134-141)</td>
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</table>

Table 2: Gender among CTS groups of increasing electrophysiological severity

<table>
<thead>
<tr>
<th></th>
<th>Female (n=60)</th>
<th>Male (n=71)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mild CTS</td>
<td>45</td>
<td>15</td>
<td>0.045</td>
</tr>
<tr>
<td>Moderate CTS</td>
<td>50</td>
<td>23</td>
<td></td>
</tr>
<tr>
<td>Severe CTS</td>
<td>36</td>
<td>22</td>
<td></td>
</tr>
</tbody>
</table>

Table 3: Laboratory characteristics of CTS groups of electrophysiological severity

Table 4: Correlation between Glycated HbA1c, age and CTS severity

Discussion

DM is a chronic systemic disorder with a variety of complications, including the musculoskeletal system [11]. It is one of the important risk factors for CTS, and it is thought that the lifetime risk of symptomatic CTS in Type 1 diabetes mellitus is high [12]. In many studies, higher rates of CTS were observed in patients with type 2 DM [11-15]. In our study, CTS was observed in 65.5% of patients with type 2 DM, which is consistent with other studies.

Carpal tunnel syndrome is more common in female patients and frequently affects those aged between 40-60 years [6]. Similar to these findings, in the present study, the patients with CTS were aged 62.83±10.85 years. In contrast to many studies, 54.5% of the patients in the present study were male [13,16]. Fasting blood glucose and HbA1c values were significantly higher in patients with CTS. Perkins et al., and Islam et al. found that patients with CTS had higher HbA1c in comparison to patients without CTS in their study, similar to our findings [17,18]. Pasnoor et al. showed that in diabetic patients, vascular disorders, such as hypoxia or ischemia due to chronic hyperglycaemia, cause carpal tunnel syndrome, and thus, multifocal neuropathies, while symmetrical polyneuropathies mostly result from metabolic causes [15,19].

In this study, most cases were mild and moderate in terms of CTS severity. Similar results were also found in many previous studies regarding severity [20-22]. We also observed that CTS was more severe among females.

In this study, age and HbA1c were independent risk factors for CTS severity. The results of the studies investigating the relationship between age and CTS severity were similar [20,23].

A low axonal density may lead to median nerve neuropathy. Advanced glycation end-products have been found to increase the production of circulating inflammatory cytokines and vascular endothelial growth factor may cause impaired microvascular circulation, resulting in demyelination and axonal degeneration in the median nerve [24]. HbA1c values were significantly higher in patients with CTS but a few studies have determined the relationship between electrophysiological severity of CTS and HbA1c [25].

Hypercholesterolemia and especially the increase in high LDL-C levels were associated with CTS [26]. A study by Nakamichi and Tachibana [9] showed that high LDL-C levels increased its prevalence. In another study, a correlation was found between the LDL-C level and the severity of CTS [26]. Hypercholesterolemia and particularly high LDL-C have been associated with fibrogenesis. In idiopathic CTS, the proliferation of the intraneural connective tissue causes enlargement of the median nerve within the carpal tunnel. Physiologically, the amount of connective tissue in the median nerve in the carpal tunnel is increased compared to the areas without entrapment, and in CTS, connective tissue production, and the nerve expands. Oxidative LDL-C, which increases collagen production through transforming growth factor-beta, a highly fibrogenic cytokine, thus increasing fibrogenesis, causes CTS [6,9]. In this study, we found that high LDL-C levels were significantly correlated to the electrophysiological severity of CTS, especially in patients with severe CTS. There are few studies on the relationship between fat levels and the electrophysiological severity of carpal tunnel syndrome [23]. Atherogenic index of plasma (AIP) is calculated as the ratio between the triglyceride value and high density lipoprotein value (mg/dL). (TG/ HDL-C) AIP is a major risk factor for metabolic syndrome and cardiovascular diseases [27]. The high TG / HDL ratio causes endothelial dysfunction, impaired endoneurial blood flow, nerve hypoxia and ischemia.
and consequently, neuropathy. Miric et al. [28] showed that AIP was higher in patients with type 2 DM who developed neuropathy. In our study, patients with moderate and severe CTS had insignificantly higher AIP values than those with mild CTS. Future case-control studies with larger samples are recommended.

Limitations
This was a hospital-based retrospective cross-sectional study. Our sample size was limited to only 131 individuals. Further large-scale prospective studies are recommended.

Conclusion
Our study identified a relationship between CTS severity and HDL-C. Being a independent risk factors for CTS severity, Diabetes is a well-known risk factor for CTS, a disease which should be considered in patients with DM and hyperlipidemia.

References


This paper has been checked for language accuracy by JOSAM editors. The National Library of Medicine (NLM) citation style guide has been used in this paper.