Electrophysiologic severity of carpal tunnel syndrome in diabetic patients of the Saudi population

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ABSTRACT

Objectives: To study the frequency of multiple vascular risk factors and electrophysiologic severity of carpal tunnel syndrome (CTS) in Saudi diabetic patients.

Methods: This retrospective cross-sectional study was conducted in Neurology Department, King Fahd Hospital of University, Al-Khobar, Kingdom of Saudi Arabia from April 2017 to March 2018 and included 200 patients with CTS. Body parameters, such as blood pressure (BP), weight, height, and body mass index (BMI), along with laboratory and median nerve electrophysiological parameters, of diabetic and non-diabetic patients were compared, and a p-value < 0.05 was considered significant.

Results: Frequency of hypertension (HTN) and obesity was significantly higher in diabetic patients (p < 0.05). Mean median nerve sensory amplitude (MNSA) was lower in diabetic patients (p < 0.05). Non-recordable nerves, as well as bilateral and extremely severe CTS (p < 0.05), were more frequently seen in diabetic patients. Age, BMI, systolic BP, low serum high density lipoprotein (HDL), high triglycerides, high fasting blood sugar, and high glycated hemoglobin (Hba1c) levels, known to affect the electrophysiologic severity of CTS, had a statistically significant association with diabetes.

Conclusion: Diabetes mellitus (DM) and obesity are the most commonly identified risk factors of CTS. Dyslipidemia, HTN and obesity are more frequently seen in diabetic patients with CTS. These concurrent risk factors are confounding the electrophysiologic severity of CTS in these patients. Further larger-scale studies with the control of confounding factors are recommended.
Carpal tunnel syndrome (CTS) is known to have a frequent nerve entrapment syndrome and encompasses 45% of non-traumatic nerve lesions. Carpal tunnel syndrome can result in various problems, including pain and paresthesia in the median nerve distribution, swelling, and in severe cases weakness of the thumb and lateral 3 fingers. It affects the daily life activities, such as holding and gripping things by hand, brushing teeth, and driving. Carpal tunnel syndrome can be associated with any risk factor that causes pressure on the median nerve in the wrist, including coexisting comorbidities and working conditions of the individuals. Some common conditions that can lead to CTS includes obesity, DM, oral contraceptives, smoking, corticosteroid use, pregnancy, hypothyroidism, rheumatoid arthritis, osteoarthritis, and wrist fracture.

The prevalence of CTS in diabetic patients is 14% without diabetic neuropathy and 30% with diabetic neuropathy. Literature has shown a high incidence of CTS in pre-diabetic states. Some researchers have also found a relationship between duration of diabetes, HbA1c, and micro vascular complications. Although type 2 diabetes is more frequently diagnosed among CTS patients, some studies had reported that the association between diabetes and CTS represents a confusion bias, mostly likely due to the strong relationship between obesity and type 2 diabetes. It has been shown that age, BMI, and other vascular risk factors, including metabolic syndrome, could affect the electrophysiological severity of CTS. Elevated low density lipoprotein (LDL) cholesterol and hyperglycemia were reported as independent risk factors for CTS in some studies. Similarly, obesity, elevated triglycerides, elevated LDL cholesterol and hypertension were shown to be strongly associated with CTS. In the study conducted by Balci et al., 75% of the CTS patients were found to have metabolic syndrome, and the electrophysiological parameters (median nerve sensory onset latency, sensory conduction velocity, sensory amplitude, distal motor latency, motor conduction velocity, and motor amplitude) were worse in patients with metabolic syndrome. Gül et al. similarly showed that severity of CTS was even more severe in patients with metabolic syndrome than in those with diabetes.

The aim of the present study was to study the frequency of multiple vascular risk factors, such as HTN, dyslipidemia and obesity in CTS patients, and to compare the electrophysiological severity of CTS in Saudi diabetic and non diabetic patients. This population is facing a high burden of multiple vascular risk factors, which are also affecting the severity of CTS.

**Methods.** This retrospective cross-sectional study was carried out in Neurology Department, King Fahd Hospital of University in Al-Khobar, Kingdom of Saudi Arabia, from April 2017 to March 2018, after gaining the approval of the University Institutional Review Board (IRB Number: IRB-2017-01-052). The data of 315 adult patients of both genders with the clinical diagnosis of CTS were retrospectively collected from the neurophysiology laboratory and medical records. Carpal tunnel syndrome was defined as pain, paresthesia, or numbness in the median nerve distribution, and one of the followings: nocturnal exacerbation of symptoms, positive Tinel’s test, positive Phalen’s test, loss of motor function with wasting of abductor pollicis brevis, and abnormal nerve conduction time.

Patients with history of previous CTS surgery, wrist trauma, and pregnant patients were excluded from the study. Only 200 electro diagnostically confirmed CTS patients (whether diabetic or non-diabetic) who had been investigated with the fasting blood sugar, fasting lipid profile, HbA1c, and thyroid function tests were included in this study. Other parameters, such as height, weight, BMI, and BP were also noted. Hypertension was defined as systolic BP>140 mmHg or diastolic BP of 90 mmHg, or use of antihypertensive medications. Diabetes mellitus was defined according to the American diabetes association criteria as either: 1) a fasting glucose level ≥126mg/dl, 2) HbA1c level ≥6.5%. Dyslipidemia was defined as fasting serum cholesterol level of >200mg/dl, triglyceride level of >150mg/dl, LDL of >120mg/dl, and HDL <40mg/dl. Higher HDL cut-off point is more commonly used in females. The BMI was used to identify overweight and obese individuals. It is calculated by dividing the weight in kilograms, by the square of height in meters. Obesity was defined as a BMI of 30.0 or greater.

Nicolet™, EDx -Viking, Middleton, WI, USA, Version 20 software or Newer system, was used.

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for standard nerve conduction studies (NCS). The studies were performed and reported by consultant neurologists, according to the standard protocol used in our department, adopted from guidelines of American academy of electrodiagnostic association (AAEDA).

For motor studies, starting stimuli of (0.1m/s) duration, with a stimulation rate of (1Hz), were given. For sensory studies, stimulation of (1mV) intensity was given and the voltage was slowly increased. Electromyography (EMG) was performed as required. A diagnosis of CTS was carried out based on presence of one or more of the following criteria: 1) abnormal sensory nerve conduction velocity (NCV) in the finger-wrist segment, 2) abnormal sensory NCV in the palm-wrist segment, and 3) prolonged terminal latency. Carpal tunnel syndrome severity was graded based on electrophysiological findings, according to the following scale: normal (grade 0); very mild (grade 1), normal NCS, but there is a symmetry when comparing both sides; mild (grade 2), sensory nerve conduction velocity, normal terminal motor latency; moderate (grade 3), sensory potential preserved with motor slowing, distal motor latency to abductor pollicis brevis (APB) <6.5ms; severe (grade 4), sensory potentials absent but motor response preserved, distal motor latency to APB <6.5ms; very severe (grade 5), terminal latency to APB >6.5ms; and extremely severe (grade 6), sensory and motor potentials effectively non-recordable.

Glycosylated hemoglobin type A1C was measured by liquid chromatography method using Tosoh G8 Chromatographer, South San Francisco,USA. Certified by national glycol hemoglobin standardization program (NGSP). The collected data was analyzed by the SPSS (Statistical package for social sciences) version 20.0 computer software (IBM Corp., Armonk, NY, USA). The results were computed as frequency and percentage for age, gender, CTS grade, non-recordable nerves, vascular and CTS risk factors, such as diabetes, HTN, dyslipidemia, obesity, hypothyroidism, Corticosteroid use and rheumatoid arthritis. Mean and standard deviation (SD) were calculated for age, BP, fasting blood glucose, fasting triglycerides, and HDL cholesterol. Unpaired t-test was used to compare 2 means and other parameters of diabetic and non-diabetic patients, such as age, BMI, systolic BP, diastolic BP, serum cholesterol, serum LDL, serum HDL, serum triglycerides, fasting blood sugar, and HbA1c. In addition, neurophysiological parameters, such as median nerve sensory onset latency (MNSOL), median nerve sensory conduction velocity (MNSCV), median nerve sensory amplitude (MNSA), median nerve distal motor latency (MNMDL), median nerve motor conduction velocity (MNMCV), and median nerve motor amplitude (MNMA) were compared between the 2 groups. Chi-squared test was used to compare categorical variables and a p-value<0.05 was considered significant.

Results. The study sample comprised of 200 patients with CTS. The demographic and clinical characteristics of the study participants are presented in Table 1. Distribution of vascular and CTS risk factors among diabetic and non-diabetic patients is presented in Table 2. There was no significant difference in the vascular and CTS risk factors among the 2 groups, except HTN (p=0.003) and obesity (p=0.01), which were significantly higher in diabetic patients. Comparison of electrophysiological parameters and CTS severity

| Characteristics | n (%)      |
|-----------------|-----------|
| **Gender**      |           |
| Male            | 34 (17)   |
| Female          | 166 (83)  |
| **Mean Age and range (Years)** | 54.4±11.9 (27-96) |
| **CTS sites**   |           |
| Bilateral       | 131 (65.5)|
| Unilateral      | 69 (34.5) |
| Right           | 46 (23)   |
| left            | 23 (11.5) |
| **Non recordable nerves** | 29 (14.5) |
| **CTS risk factors** |       |
| Diabetic        | 112 (56)  |
| Non-Diabetic    | 88 (44)   |
| **Other risk factors** |       |
| Hypertension    | 90 (45)   |
| Dyslipidemia    | 127 (63.5)|
| Obesity         | 146 (73)  |
| Hypothyroidism  | 15 (7.5)  |
| Rheumatoid arthritis | 2 (1)  |
| Corticosteroid use | 1 (0.5) |
| **Body parameters Means±SD** |           |
| Height          | 156.5±7.7 |
| Weight          | 83±16.1   |
| BMI             | 34.1±6.5  |
| Systolic BP     | 135±16.1  |
| Diastolic BP    | 78±8.6    |
| **Lab parameters Means±SD** |           |
| Serum cholesterol (<200mg/dl) | 180.8±39.9 |
| Serum LDL (<100mg/dl)       | 110±34.4  |
| Serum HDL (35-60mg/dl)      | 51±15.1   |
| Serum triglyceride (<150mg/dl)| 115±69.1 |
| Fasting blood sugar (70-99mg/dl) | 128±54.8 |
| **Mean HbA1c and range (4.5-13.4)** | 6.9±1.76 (4.6-8) |

CTS - carpal tunnel syndrome, HbA1c - glycosylated hemoglobin type A1C, BMI - body mass index, BP - blood pressure, LDL - low-density lipoprotein, HDL - high density lipoprotein, SD - standard deviation.
among diabetic and non-diabetic patients is presented in Table 3 and Table 4. Among the electrophysiological parameters, mean MNSA was lower in diabetic patients \((p=0.02)\), and the bilateral CTS \((p=0.004)\) and non-recordable nerves \((p=0.005)\) were more frequently observed in diabetic patients. Similarly, a comparison of CTS severity among the 2 groups revealed that very mild CTS \((p=0.006)\) and extremely severe CTS \((p<0.005)\) were more frequently seen in diabetic patients and the difference was statistically significant. Age, BMI, systolic BP, low serum HDL, high triglycerides, high fasting sugar, and high Hba1c levels, all of which could affect the electrophysiological severity of CTS, were found to have a significant association with diabetes, as shown in Table 5.

**Discussion.** Many predictive factors contributing to the severity of CTS have been addressed\(^{22,23}\). The aim of the present study was to compare the electrophysiological severity of CTS in diabetic and non-diabetic patients and analyze the impact of multiple confounding factors on the severity of CTS in diabetic patients.

The demographic data of the study participants shows a marked female CTS preponderance, with male to female ratio of \((1:4.8)\), which is similar to the previous local studies.\(^{24,26}\) The mean age of participants was \(54.1\pm11.9\) years, which is higher than in the previous local studies but similar to Western studies. This difference could be due to different inclusion criteria, as we have excluded pregnant patients and those with post-traumatic CTS, which is seen in relatively young patients. In our study, bilateral CTS was observed in \(131\) (65.5\%) cases, and unilateral in \(69\) (34.5\%) patients, with right hand 46 (23\%) dominance, as proven by other Western studies.\(^{27}\)

Associated comorbidities and CTS risk factors, such as diabetes, HTN, dyslipidemia, and obesity, have been examined in many local studies.\(^{28,30}\) When compared with the results yielded by these studies, our findings show a higher prevalence of all these comorbidities in CTS patients, as 112 (56\%) of the patients had diabetes, compared to only 39\% in Awada et al’s study.\(^{29}\) In the study conducted by Abumunaser et al,\(^{28}\) approximately 27.5\% of participants were diabetic. Another study on CTS in females from the Eastern province of Kingdom of Saudi Arabia included 68\% of diabetic patients.\(^{30}\)

Hypertension is a factor associated with CTS. It has been reported after treatment with beta blockers in hypertensive patients.\(^{31}\) In our study, 90 (45\%) of patients had HTN, compared to 26\% in Abumunaser et al’s study.\(^{28}\) More than half, 127 (63.5\%), of the current study participants had dyslipidemia. Many studies have shown that elevated cholesterol levels and LDL are associated with the increased of CTS, and high HDL is recognized as a protective factor for CTS.\(^{32,33}\) Onder et al,\(^{14}\) found a correlation between serum LDL-C and severity of CTS.\(^{34}\) Overall, prevalence of obesity in Kingdom of Saudi Arabia is 35\%.\(^{35}\) More than two thirds \([146 (73\%)]\) of our patients were obese. This number is slightly higher than 69\% reported by Abumunaser et al,\(^{28}\) reflecting an increasing prevalence of obesity in our population. Obesity and DM are independent risk factors for CTS. Becker et al,\(^{34}\) stated that prevalence of CTS is around 3 times higher in obese females compared to males. Hypothyroidism is shown to be associated with high prevalence and

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**Table 2** - Description of demography and prevalence of other CTS risk factors among diabetic and non-diabetic with CTS in study population \((N=200)\).

| Variables          | Diabetic \((n=140)\) | Non-diabetic \((n=104)\) | \(P\)-value* |
|--------------------|----------------------|--------------------------|--------------|
| Gender             |                       |                          |              |
| Male               | 23 (20.5)            | 11 (12.5)                | 0.13         |
| Female             | 89 (79.5)            | 77 (87.5)                |              |
| Hypertension       | 61 (54.5)            | 29 (33.3)                | 0.003        |
| Dyslipidemia       | 74 (66.1)            | 53 (60.2)                | 0.39         |
| Obesity            | 90 (80.4)            | 56 (63.3)                | 0.01         |
| Hypothyroidism     | 7 (6.3)              | 8 (9.1)                  | 0.44         |
| Rheumatoid arthritis | 0 (0)                | 2 (2.3)                  | 0.10         |
| Steroid therapy    | 1 (0.9)              | 0 (0)                    | 0.37         |

*Chi-square test, CTS - carpal tunnel syndrome

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**Table 3** - Description of electrophysiologic parameters and comparison among diabetic and non-diabetic.

| Electrophysiologic parameter | Diabetic Mean±SD | Non-diabetic Mean±SD | \(P\)-value* |
|------------------------------|------------------|----------------------|--------------|
| MNMCV                        | 4.4±0.8          | 4.2±1.2              | 0.19*        |
| MNSA                         | 19.6±11.5        | 23.7±12.8            | 0.02*        |
| MNSCV                        | 40.8±7.8         | 43.2±12.6            | 0.08*        |
| MNDML                        | 4.7±1.1          | 4.6±1.3              | 0.42*        |
| MNMA                         | 7.8±2.6          | 8.7±6.5              | 0.19*        |
| MNMCV                        | 54.2±26.4        | 54.8±7.4             | 0.84*        |
| Non recordable nerves, \(n(\%\) | 23 (20.5)        | 6 (6.8)              | 0.005*       |
| Bilateral CTS, \(n(\%\)      | 83 (74)          | 48 (54.5)            | 0.004*       |

*Independent sample t-test, *Chi-square test, MNMCV - median nerve motor conduction velocity, MNDML - median nerve motor distal latency, MNMA - median nerve motor amplitude, MNMCV - median nerve motor conduction velocity, CTS - carpal tunnel syndrome, SD - standard deviation

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incidence of CTS.\(^36,37\) Only 15 (7.5\%) of our patients had hypothyroidism, while it was observed in 15\% of Abumunaser et al.’s sample.\(^28\) In our study only 1\% of patients were found to have rheumatoid arthritis and we find only 1 patient, who was on corticosteroid therapy. Geoghegan et al.,\(^38\) evaluated the risk factors of CTS, based on the United Kingdom general practice research database records, and found rheumatoid arthritis in 2\% of the cases, as well as history of corticosteroid therapy in 6\% of the cases. These authors showed a significant association between rheumatoid arthritis and CTS.

In our study, HTN (\(p=0.003\)) and obesity (\(p=0.01\)) were significantly higher in diabetic patients, in line with the findings reported in extant literature.\(^39\) Among the electrophysiological parameters, MNSA was lower in diabetic patients (\(p=0.02\)). Similar findings were observed in another study.\(^40\) Non-recordable nerves and bilateral CTS were more prevalent in diabetic patients. One multi ethnic study on Asian population showed that diabetic patients are at a higher risk of severe CTS, and similar findings were yielded by a French study.\(^23,41\) A comparison of CTS severity among the 2 groups revealed that very mild CTS (\(p=0.006\)) and extremely severe CTS (\(p<0.005\)) were seen more often in diabetic patients, and the difference was statistically significant. Very mild CTS could be related to either early referral of diabetic patients for electrodiagnostic evaluation of CTS, or sometimes severity of symptoms is not always correlated with the NCS findings. Our study showed that age, BMI, systolic BP, low serum HDL, high triglycerides, high fasting blood sugar, and high Hba1c levels were parameters that could affect the electrophysiological severity of CTS and had statistically significant association with diabetes. Similar observations were yielded by other international and local studies.\(^33,42,43\)

The present study has some limitations. First, as this was a hospital-based retrospective cross-sectional study, the exact duration of diabetes leading to the development of CTS could not be established. Second, the patients observed in our study had multiple risk factors, including pre-diabetic states, which can confound the real association between diabetes and CTS; having a risk factor adjustment would certainly make the study findings more robust. Third, we did not include objective clinical findings between diabetic and non-diabetic patients to further correlate it with electrophysiological severity. Fourth, we investigated CTS without considering concurrent underlying diabetic polyneuropathy, which can affect the electrodiagnostic findings of CTS, especially low sensory amplitude secondary to possible underlying sensory axonal neuropathy. Finally, our sample size was limited to only 200 individuals. Further large-scale prospective studies with the use of median nerve ultrasound correlating NCS findings of CTS in diabetic patients are thus recommended.

In conclusion, CTS is multi-factorial in the Saudi population. Diabetes mellitus and obesity are the most

### Table 4 - Comparison of CTS severity in patients with and without diabetes.

| Electrophysiologic parameter severity | CTS hands | Diabetic n (\%) | Non-diabetic n (\%) | \(P\)-value* |
|--------------------------------------|-----------|-----------------|---------------------|-------------|
| Very Mild CTS                        | 34 (17)   | 12 (10.7)       | 23 (25)             | 0.006       |
| Mild CTS                             | 155 (77.5)| 86 (77.7)       | 69 (77.3)           | 0.88        |
| Moderate CTS                         | 45 (22.5) | 28 (27.7)       | 14 (16)             | 0.14        |
| Severe CTS                           | 48 (24)   | 29 (25.9)       | 19 (21.6)           | 0.50        |
| Very severe CTS                      | 26 (9.4)  | 11 (9.9)        | 5 (9.1)             | 0.36        |
| Extremely severe CTS                 | 31 (15.5) | 27 (24.1)       | 4 (4.5)             | <0.005      |

*Chi-square test, CTS - carpal tunnel syndrome.

### Table 5 - Comparison of factors that could affect the severity electrophysiological findings among diabetic and non-diabetic patients.

| Risk factors | Diabetic Mean±SD | Non-diabetic Mean±SD | \(P\)-value* |
|--------------|------------------|----------------------|-------------|
| Age          | 57.6±11.05       | 50.3±11.7            | <0.001      |
| BMI          | 35.3±6.9         | 32.5±5.6             | 0.002       |
| Systolic BP  | 137.8±6.9        | 131.4±6.9            | 0.005       |
| Diastolic BP | 79.6±6.9         | 77.6±6.9             | 0.24        |
| Serum cholesterol | 175±41.0 | 188±37.5            | 0.02        |
| Serum LDL    | 105±33.3         | 116±34.9             | 0.02        |
| Serum HDL    | 48.1±14.8        | 55.6±14.3            | <0.001      |
| Serum triglyceride | 134.7±78.9 | 91±43.7            | <0.001      |
| Fasting sugar| 152.1±62.6       | 97.3±13.2            | <0.001      |
| Hba1c        | 7.6±1.8          | 5.6±0.35             | <0.001      |

*Independent sample t-test.

BMI - body mass index, BP - blood pressure, LDL - low-density lipoprotein, HDL - high density lipoprotein, Hba1c - glycosylated hemoglobin type A1C, SD - standard deviation.
commonly identified risk factors of CTS. Dyslipidemia, HTN and obesity, known to cause neuropathic and compressive damage of median nerve in carpal tunnel, are more frequently seen in diabetic patients with CTS. These concurrent risk factors are confounding the electrophysiological severity of CTS in these patients. Further larger-scale studies with the control of confounding factors are recommended.

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