Original Article

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Risk factors for carpal tunnel syndrome in patients attending the primary care center of a tertiary hospital in Riyadh, Saudi Arabia: A case–control study

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Abstract:

BACKGROUND: Carpal tunnel syndrome (CTS), the most common entrapment neuropathy in the upper extremity, is known to be a multi-factorial disease that raises medical and nonmedical risk factors. The aim of the current study was to determine the risk factors of CTS in patients attending the primary care center at a tertiary hospital.

MATERIALS AND METHODS: A case–control study was conducted by reviewing all medical records of patients above the age of 18 years old diagnosed with CTS from 2015 to 2021. The selected cases were evaluated by physical examination and confirmed by a nerve conduction study. Cases and controls were matched by age, gender, and nationality, with a case-to-control ratio of 1:2. Odds ratios were calculated for association between carpel tunnel syndrome and various factors and Chi-sqauare test determined statistical significance. Multiple logistic regression was performed to adjust for confounding.

RESULTS: The study recruited 144 cases with a mean age of 53.38 ± 12.20 years and 288 controls with a mean age of 53.80 ± 12.27 years. The majority of subjects were female (84.7%) and of Saudi nationality (68.3%). There was a significant difference in body mass index, employment status, number of years of employment, occupation, mean systolic blood pressure, mean low-density lipoprotein cholesterol level, and mean blood urea level between cases and controls ($P < 0.05$). Laboratory tests that were found to be significantly associated with CTS in univariate analysis were thyroid-stimulating hormone (crude odds ratio [COR] = 0.828) and urea level (COR = 0.802). In fully adjusted analyses, obesity (adjusted odds ratio [AOR] =3.080), chronic kidney disease (AOR = 3.629), and the use of corticosteroid (AOR = 0.470) were also significantly associated with CTS.

CONCLUSION: Similar to the findings of other studies, this study identified several potential risk factors for CTS. More large-scale longitudinal studies are required to establish a precise causal association.

Keywords:

Carpal tunnel syndrome, case control, primary healthcare, risk factors

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Introduction

Carpal tunnel syndrome (CTS) is one of the most prevalent entrapment neuropathies affecting the upper extremities. The median nerve and nine flexor tendons of the forearm travel through the carpal tunnel, which is enclosed by the transverse carpal ligament and carpal bones. Any abnormality of the tunnel's structure or dynamics can result in compression and damage to the nerve. In fact, 90% of all neuropathies are caused by such

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a compression, which leads to the disruption of the distribution of the nerve. Although the exact etiology of CTS is not entirely understood, several studies have shown that the nerve's myelin sheath and axon acquire lesions and the surrounding connective tissues become inflamed and lose their protective and supporting functions.[1]

Symptoms of CTS can vary, from occasionally limited effects on the wrist and the entire hand, radiating to the forearm, or, in rare cases, traveling to the shoulder.[2] Typically, the thumb, second, and third fingers, as well as the radial part of the fourth finger, are impacted.[1] The most frequent symptoms of CTS are pain, numbness, paresthesia, weakness, clumsiness, and temperature changes in the affected limb. Many patients have reported that the severity of the symptoms increases at night or is triggered by certain activities[1,3] It has also been reported that 73% of CTS cases have bilateral symptoms, with the dominant hand usually the first affected even if manifestation is not concurrent.[4] In the United States, 1–3/1000 persons are diagnosed with CTS every year, a rate similar to that in most developed countries.[1]

A number of studies have shown that individual characteristics and other co-morbidities can precipitate or cause the symptoms of CTS. Demographic risk factors that are known to be associated with an increased risk of CTS are age above 40 years, female gender, higher body mass index (BMI), smoking, and certain occupations, such as office and administrative support.[1,2,5-10] Equally important, co-morbidities including type 2 diabetes mellitus, chronic kidney disease, rheumatoid arthritis, osteoarthritis, hypothyroidism, vitamin B6 deficiency, and history of wrist fracture have also been suggested as risk factors for CTS.[5-7,10-14] Even though there is a strong suspicion that hormonal changes can have an effect, there is no evidence to support this.[4,15]

Few studies have been conducted in Saudi Arabia to measure the prevalence of CTS and its associated risk factors. The reported prevalence rate ranged from 14% to 30.5%, while the range increased to 10%–56.1% in diabetic patients.[16-19] Nevertheless, it is suspected that all the previous assessments were an overestimation, since all the studies used structured questionnaires to measure the symptoms of CTS and but not electro-diagnostic studies (EDSs) nor physical examination to confirm the CTS diagnosis. Only one retrospective chart review in Saudi Arabia was completed to measure the association between CTS and hypothyroidism, and only patients who underwent carpal tunnel release surgery were included in the study.[14] At present no known study has measured the risk factors for CTS in Saudi Arabia.

Therefore, the aim of this study was to determine the risk factors of CTS in patients attending the primary care center in a tertiary hospital in Riyadh, Saudi Arabia. The objectives of the study were to measure in a hospital-based setting, the association of the sociodemographic risk factors, and the association of the medical risk factors of CTS.

Materials and Methods

A case–control study was conducted at a tertiary hospital in Riyadh, Saudi Arabia. For the selection of the cases, a retrospective chart review was performed from the database records of all patients aged 18 years and older, who had visited the primary care center in a tertiary hospital from January 1, 2015 until December 31, 2021. Ethical approval was obtained from the Research Ethics Committee at King Faisal Specialist Hospital and Research Center vide letter No. FMPC/691/43 dated 14/02/2022 with a waiver of informed written consent since the study had no direct involvement with human subjects.

Only CTS cases that were both evaluated by physical examination and confirmed by a nerve conduction study (NCS) were included in the study. Although patients who had had carpal tunnel release surgery were good candidates, patients who had undergone surgery prior to the time of the review were excluded. Patients diagnosed with other peripheral neuropathy resulting from secondary causes were also excluded. For the control group, patients from the same population who had not been diagnosed with CTS but had visited the clinics during the same month of the case diagnosis were selected with a case-to-control ratio of 1:2 to increase the precision and power of the study.[20] The individual matching approach was used according to age (within the range of ± 1 year), gender, and nationality. The purpose of this technique was to guarantee comparability between the case and control groups with respect to the distribution of matched variables.

All statistical analyses of the data were carried out using the Statistical Package for Social Sciences software package version 26 (IBM Corporation, SPSS Package Version 26.0. Armonk, NY; 2019).[21] Descriptive statistics for the continuous variables were reported as mean and standard deviation. The categorical variables were summarized as frequencies and percentages. Inferential statistics were performed on continuous variables using the independent *t*-test to measure their associations with CTS. Categorical variables were compared using the Chi-square test and Fisher's exact test. The crude odds ratio (COR) of CTS and 95% confidence intervals (CIs) were calculated, given all previous exposures using univariate logistic regression. Additionally, multivariate logistic regression, with stepwise backward elimination methods, was done to calculate the adjusted odds ratio (AOR) of CTS after adjusting for all significant risk factors. For model fit, the post estimation analysis of the multivariate logistic regression, using the Hosmer and Lemeshow (HL) goodness of fit test and receiver operating characteristic (ROC) curve, was performed. The hypothesis was tested at a 0.05 significance level and 95% CI.

Results

Of the 432 subjects recruited for the study, 144 cases and 288 controls were matched successfully. The mean ages of cases and controls were 53.38 ± 12.20 years and 53.80 ± 12.27 years, respectively. The predominant groups of the study population were female (84.7%) and of Saudi nationality (68.3%). A comparison of the sociodemographic characteristics of the case and control groups is reported in Table 1. The bivariate analysis showed a significant difference in the distribution between cases and controls in BMI, employment status, and number of years of employment ($P < 0.05$). However, as summarized in Table 2, there were no significant differences in the distribution of the medical conditions in the two groups although the percentages of hypertension and chronic kidney disease in the cases compared to the controls were higher. The results of the laboratory tests did not reveal significant differences in any of the variables, as indicated in Table 3. Only the mean systolic blood pressure, low-density lipoprotein cholesterol level, and blood urea level were significantly different when the two groups were compared ($P < 0.05$). The mean years of employment was higher in the cases with a significant difference. In addition, there was no significant difference in the frequency distribution between the cases and the control groups regarding the family history of CTS.

Univariate analysis performed on the matched factors confirmed that there was no evidence of statistical significance in the relationship of the sociodemographic factors, except for BMI, with the COR for the obese group being 2.95 (CI = 1.389–6.246, $P < 0.05$). Furthermore, risk factors related to medical conditions were not significantly associated with CTS in the initial univariate regression. Laboratory tests found to have a statistically significant association with CTS were thyroid stimulating hormone (TSH) and urea level (TSH: COR = 0.828, CI = 0.687–0.998, $P < 0.05$; urea level: COR = 0.802, CI = 0.678-0.949, $P < 0.05$). In the fully adjusted analyses, BMI, chronic kidney disease, and the use of corticosteroid were included in the final model, as shown in Table 4. The results of the HL test demonstrated a good model

Table 1: Sociodemographic characteristics of patients with carpal tunnel syndrome and controls

Characteristics	Cases (*n*=144) N (%)	Controls (*n*=288) *N* (%)	Total (*n*=432) *N* (%)	*P*-value
Age, mean±SD	53.38±12.20	53.80±12.27	53.66±12.23	0.737
Gender				
Male	22 (15.3)	44 (15.3)	66 (15.3)	0.851
Female	122 (84.7)	244 (84.7)	366 (84.7)	
Nationality				
Saudi	99 (68.8)	196 (68.1)	295 (68.3)	0.884
Non-Saudi	45 (31.2)	92 (31.9)	137 (31.7)	
Employment status				
Employed	36 (38.3)	50 (37.1)	86 (37.6)	0.001
No-retired	14 (14.9)	30 (22.2)	44 (19.2)	
No-housewife	44 (46.8)	40 (29.6)	84 (36.7)	
No-never worked	0	15 (11.1)	15 (6.6)	
Years of employment, mean±SD	18.66±9.21	14.77±9.52	16.25±9.56	0.023
Working hours (h/week), mean±SD	42.34±8.40	41.78±5.93	41.99±6.95	0.655
Smoking				
Nonsmoker	116 (81.6)	239 (86.6)	355 (84.9)	0.393
Previous smoker	13 (9.2)	20 (7.2)	33 (7.9)	
Smoker	13 (9.2)	17 (6.2)	30 (7.2)	
Family history of CTS				
Yes	30 (31.9)	41 (29.7)	71 (30.6)	0.721
No	64 (68.1)	97 (70.3)	161 (69.4)	
BMI				
Normal	10 (6.9)	44 (15.2)	54 (12.5)	0.009
Overweight	44 (30.6)	103 (35.8)	147 (34.0)	
Obese	90 (62.5)	141 (49.0)	231 (53.5)	

CTS=Carpal tunnel syndrome, BMI=Body mass index, SD=Standard deviation

Table 2: Prevalence of the medical conditions in patients with carpal tunnel syndrome and controls

Comorbidity	Cases (*n*=144) *N* (%)	Controls (*n*=288) *N* (%)	Total (*n*=432) *N* (%)	*P*-value
Diabetes				
Yes	49 (34.0)	120 (41.7)	169 (39.1)	0.125
No	95 (66.0)	168 (58.3)	263 (60.9)	
Hypertension				
Yes	61 (42.4)	106 (36.8)	167 (38.7)	0.264
No	83 (57.6)	182 (63.2)	265 (61.3)	
Chronic kidney disease				
Yes	7 (4.9)	6 (2.1)	13 (3.0)	0.137
No	137 (95.1)	282 (97.9)	419 (97.0)	
Oral contraceptives use				
Yes	11 (7.6)	28 (9.7)	39 (9.0)	0.476
No	133 (92.4)	260 (90.3)	393 (91.0)	
Corticosteroid use				
Yes	13 (9.0)	45 (15.6)	58 (13.4)	0.058
No	131 (91.0)	243 (84.4)	374 (86.6)	
Pregnancy				
Yes	13 (9.0)	32 (11.1)	45 (10.4)	0.504
No	131 (91.0)	256 (88.9)	387 (89.6)	
Hypothyroidism				
Yes	23 (16.0)	54 (18.8)	77 (17.8)	0.477
No	121 (84.0)	234 (81.2)	355 (82.2)	
Rheumatoid arthritis				
Yes	8 (5.6)	23 (8.0)	31 (7.2)	0.356
No	136 (94.4)	265 (92.0)	401 (92.8)	
Osteoarthritis				
Yes	30 (20.8)	71 (24.7)	101 (23.4)	0.377
No	114 (79.2)	217 (75.3)	331 (76.6)	

Table 3: Comparison of laboratory results between patients with carpal tunnel syndrome and controls

Laboratory test	Mean±SD			*P*-value
	Cases (*n*=144)	Controls (*n*=288)	Total (*n*=432)	
Systolic blood pressure	124.33±13.43	127.40±12.35	126.38±12.78	0.019
Diastolic blood pressure	76.84±7.55	78.99±16.59	78.28±14.28	0.143
HgA1c	6.23±1.34	6.12±1.09	6.15±1.17	0.403
FBG	6.14±2.22	6.02±1.81	6.06±1.94	0.609
Total cholesterol	4.81±0.81	4.73±0.80	4.75±0.80	0.361
HDL cholesterol	1.35±0.33	1.55±2.69	1.48±2.24	0.412
LDL cholesterol	3.26±1.57	3.00±0.70	3.08±1.06	0.024
Triglycerides	1.48±0.71	1.38±0.65	1.41±0.67	0.165
TSH	2.02±0.95	3.14±13.81	2.77±11.34	0.338
Vitamin B12	376.98±222.64	360.75±177.39	365.29±190.97	0.498
Urea	4.12±1.28	4.66±2.62	4.48±2.28	0.019
Albumin	43.46±3.37	43.66±3.87	43.59±3.71	0.586
eGFR, *N* (%)				
≤60	136 (94.4)	271 (94.1)	407 (94.2)	0.884
>60	8 (5.6)	17 (5.9)	25 (5.8)	

LDL: Low-density lipoprotein, HDL=High-density lipoprotein, TSH=Thyroid-stimulating hormone, FBG=Fasting blood glucose, HgA1c=Hemoglobin A1c, SD=Standard deviation, eGFR=Estimated glomerular filtration rate

fit (χ^2 = 2.094, P = 0.978). The plotting of the ROC curve was based on the logistic regression model's predicted probabilities of CTS. The area under the ROC curve = 0.610 (P = 0.001, 95% CI = 0.555–0.666), which indicates acceptable accuracy of the overall discrimination ability of the model.

Discussion

Although several studies have investigated the risk factors of CTS, there is no consensus on the findings on these factors. In this study, cases and controls were matched according to age, gender, and nationality to

Table 4: Association between carpal tunnel syndrome and comorbidities

Variable	COR* (95% CI)	*P*-value	AOR* (95% CI)	*P*-value
BMI				
Normal	Reference			
Overweight	1.919 (0.883-4.175)	0.100	2.001 (0.908-4.411)	0.085
Obese	2.946 (1.389-6.246)	0.005	3.080 (1.436-6.605)	0.004
Chronic kidney disease				
No	Reference			
Yes	2.442 (0.795-7.506)	0.119	3.629 (1.050-12.550)	0.042
Corticosteroid use				
No	Reference			
Yes	0.537 (0.279-1.032)	0.062	0.470 (0.236-0.936)	0.032

*Adjusted for age, gender, and nationality. BMI=Body mass index, COR=Crude odds ratio, AOR=Adjusted odds ratio, CI=Confidence interval

control for potential confounders, avoid the loss of validity, and increase the precision of the analysis. Many studies have used a similar approach with different matching factors. Age and gender were the most constant matching variables found throughout the literature, as they are known to strongly contribute to the development of CTS.[1,7,12,22,23] All studies including those conducted in the same region have reported varied means and/or ranges of age.

Smoking status was the same in both the case and control groups and did not have a significant contribution to the development of CTS. The data from the univariate analysis for smoking were not presented, as they were invalid and not included in the final model. In fact, smoking was not considered a potential risk factor in any local studies, and only a cross-sectional study measured the frequency of smoking and its significance. The local study showed that the smoking percentage was not significantly different among the participants who had CTS symptoms and those who did not, which supports our finding.[16] Although other global studies have reported results similar to our findings, some findings are rather interesting. A case–control study conducted in the United States reported a higher proportion of smokers in the control group (33%), with a significant difference when compared to the case group. It also stated that the OR of smoking in patients with CTS was less by 0.17 times compared to the controls.[22] In contrast, a prospective cohort study also conducted in the United States observed that smoking increased the OR of CTS by 1.32 times.[5] The association between smoking and CTS might have been influenced by the targeted population, as both studies focused on diabetic patients. This explanation can be confirmed by the matched case–control in the study by Geoghegan *et al*., which did not limit participants to diabetic patients but covered all CTS diagnosed patients.[7]

The results for BMI demonstrated that the distribution of the obese subgroup was higher in CTS cases, with a statistically significant difference. This finding does not accord with a local study that measured the BMI of its participants and found that the percentage of obesity was significantly higher in those who did not show CTS symptoms.[16] However, several global studies have reported a significant increase in the frequency of obesity in CTS patients and the risk of CTS development.[5,7,10,22] In addition, the adjusted OR of obesity in the CTS patients in our study showed an increase of 3.080 times (95% CI: 1.436–6.605) over the control group, which agrees with several reports.[5,7,10,22] Similarly, a matched case–control study reported that the OR of CTS was 2.06 times higher in obese patients,[7] while a national-based cohort study conducted in Taiwan estimated AOR as = 3.33.[10] Other studies have also reported an increased OR of CTS in obese patients, but with a different magnitude.[5,6,22]

The study was unable to assess the role of occupational status in relation to the development of CTS. Although the relationship between occupational status and CTS is considered complex, an increased incidence rate of CTS in several occupations was found. According to the California Department of Public Health, the top three occupations with the highest incidence rates were production, moving of materials, and jobs in the office and administrative support.[9] Moreover, the descriptive analysis found that currently all cases were either employed, retired, or housewives, but none that had never worked. The majority of the cases in this study were housewives, with a significantly higher percentage compared to the control group, which is consistent with the literature. For instance, in a Malaysian study, a similar increase in the percentage of CTS in housewives was reported, accounting for 34% of all CTS patients who underwent release surgery.[24] An Italian study that investigated the risk factors for CTS release surgery in nonretired subjects reported that housewives had an OR of 4.4 compared to other females with white-collar occupations.[25]

Several concomitant CTS medical conditions were assessed in this study according to the literature. However, our data analysis did not reveal any evidence of a statistical difference in the distributions of these conditions between the two groups. None of the previous local studies have investigated the risk of CTS in patients with these conditions. Only prevalence was measured. For example, Abumunaser's cross-sectional study estimated the prevalence of diabetes, hypertension, and hypothyroidism in CTS patients and reported respective prevalence of 27.5%, 26.0%, and 15%, but did not measure their association to CTS.[26]

Some studies in relevant literature indicate that several medical conditions, including diabetes, hypertension, hypothyroidism, and others, have widely varying prevalence in CTS patients, with a significant association compared to non-CTS patients, while other studies could not detect any statistical association between the previously mentioned conditions and CTS.[5,7,10-12] These variations were well explained in a systematic review that aimed to evaluate the increased prevalence of specific medical conditions in CTS patients. The study reports that the literature has indicated that 28 conditions had been investigated and statistically proven to be associated with CTS. However, it also identified potential sources of bias that explain the discrepancies in the results. The observed sources were the inclusion of patients who had undergone CTS release surgery, the lack of adjustment for differences in gender and age, and reliance on the chart review for the data collection.[11]

On the association of such conditions with the development of CTS, the univariate analysis of our study did not manifest any significant relationship, whereas the multivariate analysis revealed statistical evidence of a significant association between CTS and obesity, chronic kidney disease, and corticosteroid use. These results are not in line with all of the previous findings of the other studies. The etiology of the interaction of each of these conditions with CTS must be understood to explain the differences.

It is well documented that diabetes impacts the peripheral nerves in the upper extremities, resulting in certain musculoskeletal conditions in the hands, especially for longstanding diabetic patients with suboptimal glycemic control. Yet, the exact pathogenic contribution of DM to CTS is not obvious. Many studies have assessed the relationship between DM and CTS in diverse settings, with some suggesting an increasing incidence and risk of CTS in diabetic patients, and others not finding any significant association in multivariate analysis.[5,6,13,22,27,28] Such variance can imply that the association between DM and CTS remains vague. In agreement with many studies in a similar setting, our study did not detect any statistical association between diabetes and CTS. It is possible that this lack of relationship can occur only in specific subgroups, such as controlled diabetic patients. As reported in Table 3, both the hemoglobin A1c and fasting blood glucose levels were conveniently controlled, which may justify the assumption.

Even though diabetes is one of the leading causes of peripheral neuropathy, chronic kidney disease can also contribute to the development of CTS.[29] This can be a result of abnormalities in the increase of fluid distribution, changes in synovial volume, edema up-growth, and increased levels of uremic neurotoxins.[30] The particular association between chronic kidney disease and CTS has not been much investigated in the literature. The study of Low *et al*., showed that there was no significant association (AOR = 0.19; 95% CI: 0.027–1.40).[5] Although the univariate analysis of our study did not reveal any association, the multivariate analysis demonstrated a significant increase in OR of 3.629 times in CTS patients. It is suggested that the change in statistical significance is related to the adjustment of the other confounders. Furthermore, a corticosteroid, which is an anti-inflammatory medication used for a wide range of diseases, has also been proven to play a therapeutic role in the treatment of CTS.[31] This confirms the finding that it decreases the OR of CTS.

To the best of our knowledge, this study is the first to investigate multiple CTS risk factors in Saudi Arabia. It is also the first to investigate CTS risk factors after matching for multiple confounders by using a multivariate logistic regression model after adjusting for several relevant variables and nominating the best model fit. In addition, most of the previous local research mainly relied on identifying CTS based only on symptoms or cases that underwent CTS release surgery, which might have led to selection bias. However, it is suggested that by using a combination of physical examination and EDSs in the study the accuracy of diagnosing CTS was raised and the potential of overdiagnosing and/or misdiagnosing eliminated.

Owing to the retrospective nature of the study, a causation relationship between the investigated factors and CTS could not be established. However, an attempt was made to discover the existence of correlations, and measure the magnitude of these factors in predicting outcomes. Notably, the extent of missing data was not anticipated prior to the study, for two main reasons. A number of variables, such as vitamin B6, had huge missing values, as they were not routinely checked for most of the included subjects. The sociodemographic characteristics and the epidemiology of CTS-associated medical risk factors can also vary widely. Thus, the results will have limited generalizability to similar populations only.

Conclusion

This study identified some of the possible risk factors related to the development of CTS that are similar to most international findings. The main associated risk factors found in this study were obesity and chronic kidney disease. Corticosteroid use was found to decrease the risk of CTS. During the selection of the cases, it was noticed that a large proportion of previously diagnosed cases were not confirmed by NCSs. Consequently, there was concern about overdiagnosing. Moreover, the lack of sufficient local studies on CTS and its risk factors indicates inadequate awareness. Further longitudinal, large-scale studies are also needed to demonstrate the etiological relationships of the associations and establish an accurate causal relationship.

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Conflicts of interest

There are no conflicts of interest.

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