

SERUM LIPID PROFILE IN MIDDLE AGED FEMALE PATIENTS WITH CARPAL TUNNEL SYNDROME

By

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ABSTRACT

Background: Carpal tunnel syndrome (CTS) is the most common entrapment neuropathy. It is a combination of symptoms and signs caused by the compression of the median nerve as it passes in the carpal tunnel at the wrist. It is an important cause of functional disability, and is the commonest cause of referral to the Electro diagnostic laboratory. CTS is studied extensively. However, its pathophysiology still unclear and most of the cases still idiopathic especially in middle aged women.

Objective: To correlate between severity of CTS and abnormality of lipid profile, and to establish the relationship between severity of CTS and age, Body mass index (BMI), in Egyptian middle aged women.

Patients and Methods: This study included 155 female cases and controls recruited from the Neurology outpatient clinics of Al-Hussein University Hospital and Al Sahel Teaching Hospital during the period from November 2018 to September 2019, 103 cases with the clinical and neurophysiological diagnosis of idiopathic carpal tunnel syndrome. The study demonstrated the relation between age, lipid profile, BMI and severity of carpal tunnel syndrome in this group of females in comparison to the 52 females as a controls.

Results: Age, high BMI, higher cholesterol and LDL levels, were correlated with severity of CTS, while Cholesterol and LDL were much higher among the cases compared to controls. HDL was less in the patients.

Conclusion: Abnormal lipid profile, higher BMI, obesity and poor living circumstances could influence the incidence and severity of CTS among middle aged Egyptian women.

Keywords: Idiopathic carpal tunnel syndrome - CTS - Lipid profile - middle aged females – BMI – Cholesterol.

INTRODUCTION

Carpal tunnel syndrome (CTS) is a frequently seen medical issue. It is a compressive neuropathy of the median nerve at the wrist, which considered the most common entrapment neuropathy. It also one of the most common causes of referrals to the electro diagnostic

laboratory to confirm the clinical diagnosis (Alanzy, 2017). Furthermore, it represents an important cause of functional hand impairment and disability. CTS is often associated with loss of work, inability to perform family and social roles, living and working with pain, and physical disability. It is clinically characterized by the presence of sensory

symptoms in the form of numbness, tingling, pain, and feeling of heaviness of one or both hands in the median nerve distribution thumb, index, middle finger, and the radial side of the ring finger and a reduced strength of the grip besides functional impairment can occur in more severe cases if it wasn't treated within reasonable time. Diagnosis of CTS is based on characteristic symptoms and specific provocative stress tests such as Phalen's and Tinel's tests, or hand elevation test. It is confirmed by electrodiagnostic studies, ultrasound and MRI (*Ibrahim et al., 2012*). The vast majority of CTS cases are idiopathic, but there are many correlated risk factors with the development of this entrapment neuropathy as it is reported to occur after many situations including repetitive trauma, metabolic and hormonal changes, smoking and ganglion cysts, but most cases remain idiopathic (*De Krom et al., 2009*). Lipids are major components of a nerve cell so that the deficiencies of fat due to starvation or excess due to obesity could interfere with the neuronal function (*Naik et al., 2014*). Furthermore, metabolic syndrome and its components, like abnormal lipid profile changes and obesity, were reported as a distinct risk factor for CTS (*Yurdakul et al., 2015*).

In this study, we were trying to find a causal relationship between incidence and severity of idiopathic CTS and abnormality in lipid profile components among middle aged females, and to establish the relationship between age and BMI as an indicator for obesity and severity of CTS.

PATIENTS AND METHODS

The study design was a case-control observational study. Patients were selected randomly from attendee of the out-patient Neurology clinics of Al-Hussien University Hospital and Al-Sahel teaching Hospital Cairo Governorate, Egypt during the period from November 2018 to September 2019.

Two main groups were included in this study:

1. Carpal tunnel syndrome (CTS) group consisted of 103 adult females presented with clinical and electrophysiological characteristics of idiopathic carpal tunnel syndrome.
2. Control group consisted of 52 volunteers, free of clinical and electrophysiological evidence of CTS, they were matching the same age and BMI and socioeconomic status with the patients.

Informed consents were taken from all of the subjects after explaining the details, benefits, and risks to them.

The study was approved by the Ethics committee of Faculty of Medicine, Al-Azhar University Egypt, 2018.

Inclusion criteria:

1. Female gender in the age between 18-48 years
2. Clinical and electrophysiological evidence of CTS according to Wang (2013), beside clinical manifestations of CTS, electrophysiological results of CTS include either or both the following:

Median nerve peak sensory latency more than 3.5 ms (stimulated at wrist at 13 cm from active electrode)

Median nerve distal motor latency more than 4.4 ms (stimulated at wrist at 7 cm from active electrode).

3. Female patients with Body mass index (BMI) of 35 and below.

Exclusion criteria:

1. History, clinical signs, or electro diagnostic findings suggesting coexisting neurological conditions, e.g., polyneuropathy, hereditary neuropathy, cerebrovascular stroke and Sub-clinical sensory polyneuropathy.
2. Increased BMI > 35 and morbid obesity, age older than 48 and younger than 18.
3. Females working in jobs with known repetitive stress to hands as hairdressers
4. History or clinical signs suggesting coexisting rheumatologic disease
5. Manifestations or radiological findings of cervical radiculopathy in association with CTS.
6. Symptoms or signs of systemic clinical illness like Diabetes Mellitus, hyperthyroidism, hyperparathyroidism, hypothyroidism, inflammatory thyroiditis, malignancy, inflammatory arthritis, vasculitis, renal or hepatic failure.
7. History of previous trauma or surgery involving the upper limb and/or neck.
8. Subjects currently receiving statin or cholesterol lowering agents.

Female patients included in the study were subjected to:

1. Full history taking and full general examination
2. Neurological examination, for diagnosis of CTS and exclusion of polyneuropathy or other neurologic condition which may be associated with peripheral nerve entrapment (*Uchiyama et al., 2010*).
3. Body mass index (BMI) was calculated by dividing body weight in kilograms by height in meters square (*Nageeb et al., 2018*).
4. Serum lipid profile of both cases and controls at the same day of the electrophysiological study.
5. Routine laboratory tests to exclude other systemic affection like Diabetes Mellitus, hepatic or renal disease Electrodiagnostic studies (*Wang 2013*).

We used a Neuropack S1 EMG/EP Measuring System MEB-9400K by NIHON KHODEN Corporation, Tokyo, Japan. These electrophysiological studies included NCS, and EMG was done when needed.

Electrophysiological studies:

1. Motor nerve conduction studies Motor nerve conduction study of the median nerve was done recording from abductor pollicis brevis (APB) muscle. Stimulation site of the median nerve at wrist and elbow sites. 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 ≥ 49 m/s).

2. Sensory nerve conduction studies Antidromic median sensory recording over digit 2 while stimulating the median nerve 13 cm proximal to the active electrode. Measured Peak sensory latency and sensory nerve action potential (SNAP) (normal values: peak latency \leq 3.5 ms, SNAP amplitude \geq 20 mV).

3. Median and Ulnar nerve motor comparative study with F-wave assessment to exclude polyneuropathy.

CTS severity was detected through electrophysiological assessment and was classified into mild, moderate and severe (*Watson, 2012*).

Statistical analysis:

The collected data were coded, tabulated and subjected to statistical analysis using descriptive statistics: Means, standard deviations, ANOVA was computed.

Mean: To measure a central value for a group of data.

Standard deviation SD \pm : to measure the degree of difference between two samples means.

ANOVA (Analysis of variance) test was used to analyze the differences among patients

All statistical analysis was performed using SPSS 19 for windows.

In all statistical tests a P value $<$ 0.05 was considered significant.

RESULTS

Cholesterol range among the cases was 139 – 339, while it was 136 – 328 among controls, Mean cholesterol levels for the cases was 226.029 ± 51.792 SD, while it was 194.144 ± 46.272 SD for the controls. Also, there was a statistically significant difference in cholesterol between cases and controls P value was $<$ 0.001.

Triglycerides range among cases was 74 - 314, while it was 65 – 307 among the controls. Mean triglycerides in the cases was 159.019 ± 53.706 SD, while it was 146.788 ± 66.455 in the controls, and no

significant relationship (P-value 0.219). **HDL** range in the cases was 38 – 73, while it was 39 – 75 in the controls, mean HDL in cases was 54.340 ± 8.621 SD, and 57.663 ± 9.254 among controls, there was significant inverse relation (P value 0.029). **LDL** range in the cases was 53 – 258 and in the controls was 57 – 231, while mean in the cases was 140.450 ± 47.735 , and mean in the controls was 109.981 ± 38.636 , there was a statistically significant difference between both groups (p value $<$ 0.001 **Table 1**).

Table (1): comparison between cases and controls (Cholesterol, Triglycerides, HDL, and LDL)

Parameters \ Groups		Cases			Controls			P value
Cholesterol (mg/dl)	Range	139	-	339	136	-	328	<0.001
	Mean ±SD	226.029	±	51.792	194.144	±	46.272	
Triglycerides (mg/dl)	Range	74	-	314	65	-	307	0.219
	Mean ±SD	159.019	±	53.706	146.788	±	66.455	
HDL (mg/dl)	Range	38	-	73	39	-	75	0.029
	Mean ±SD	54.340	±	8.621	57.663	±	9.254	
LDL (mg/dl)	Range	53	-	258	57	-	231	<0.001
	Mean ±SD	140.450	±	47.735	109.981	±	38.636	

Age range among mild cases was 21-47 while it was 24 - 48 in moderate cases and 37- 48 among severe cases, mean age for mild cases was 31.871 ± 7.429 while it was 38.200 ± 5.704 for moderate cases and 42.000 ± 3.450 for severe cases, **P value** was **<0.001** which is significant that means with the advance of age the incidence and severity of CTS increases. **Body mass index BMI** mild cases showed range from 24.5 – 34.2 while it was 23.25 – 35.38 for moderate cases and 24.84 – 35.34 for severe cases, mean was 28.738 ± 2.256 for mild cases, 30.925 ± 2.801 for moderate cases and 31.966 ± 2.967 for severe, it is noticeable that BMI increases with the severity of CTS which is confirmed statistically where (**P-value <0.001**) which is significant. **Cholesterol** range in mild and moderate cases with CTS was 139 – 336 while it was 167 – 301 among severe cases, Mean in mild and moderate cases was almost the same 218.419 ± 52.642 and 218.400 ± 50.224 respectively, it was 254.091 ± 46.208 for severe cases, there was a significant relationship between CTS severity and cholesterol levels which is more obvious in the severe CTS group (**P-Value 0.015**). **Triglycerides** range was 86 – 258 for

mild, 74 – 314 for moderate and 87 – 301 for severe cases. Mean was 153.871 ± 46.181 , 154.700 ± 58.254 , 176.091 ± 51.536 for mild, moderate and severe cases respectively, highest levels were in severe cases but there wasn't a statistically significant relationship between levels of triglycerides and severity of CTS where (**P-value 0.245**). **HDL** range was 38 - 73, 40 – 73, 39 – 67 for mild, moderate and severe cases respectively. Means were 54.032 ± 8.573 , 55.920 ± 8.678 and 51.182 ± 7.986 for mild, moderate and severe cases respectively, there was no statistically significance between severity of CTS and HDL (**P-value 0.960**). **LDL** range among mild cases was 72 – 237, while it was 53 – 258 in moderate and 94 – 247 in severe cases. Mean in mild and moderate cases was almost identical as in total cholesterol where mild was 136.129 ± 45.477 and it was 131.086 ± 46.632 in moderate cases, but it was much higher in severe cases 167.818 ± 44.927 , there was a positive correlation between higher levels of LDL and severity of CTS, also there was a statistically significant relationship between LDL levels and severity of CTS where **P-Value was 0.008 (Table 2)**.

Table (2): correlation between age, BMI, Cholesterol, Triglycerides, HDL, LDL and severity of CTS

Parameters \ CTS severity		Mild			Moderate			Severe			P-value	MI&MO	MI&S	MO&S
		Range												
Age (18-48 years)	Range	21	-	47	24	-	48	37	-	48	<0.001	<0.001	<0.001	0.036
	Mean ±SD	31.871	±	7.429	38.200	±	5.704	42.000	±	3.450				
BMI (18.5-29.9) kg/m ²	Range	24.5	-	34.2	23.25	-	35.38	24.84	-	35.34	<0.001	0.002	<0.001	0.288
	Mean ±SD	28.738	±	2.256	30.925	±	2.801	31.966	±	2.967				
Cholesterol (<200 mg/dl)	Range	139	-	336	139	-	339	167	-	333	0.015	1.000	0.033	0.018
	Mean ±SD	218.419	±	52.642	218.400	±	50.224	254.091	±	46.208				
Triglycerides (<150 mg/dl)	Range	86	-	258	74	-	314	87	-	301	0.245			
	Mean ±SD	153.871	±	46.181	154.700	±	58.254	176.091	±	51.536				
HDL (>40 mg/dl)	Range	38	-	73	40	-	73	39	-	67	0.096			
	Mean ±SD	54.032	±	8.573	55.920	±	8.678	51.182	±	7.986				
LDL (<130 mg/dl)	Range	72	-	237	53	-	258	94	-	247	0.008	0.881	0.040	0.007
	Mean ±SD	136.129	±	45.477	131.086	±	46.632	167.818	±	44.927				

DISCUSSION

In this study we choosed female subjects with idiopathic CTS only as the incidence rates of CTS among females is much higher than men, about 6.8% in women and 0.6% in men of all adult population (*Ibrahim et al., 2012*). Also, in a study by *Malibary et al. (2013)* the female to male ratio was 8.5:1. We choosed to study idiopathic CTS only as it is the most common form of CTS (*Ushiyama et al., 2010*).

When we assessed severity of CTS we relied on the electrophysiological diagnostic criteria of CTS by *Watson (2012)* who made a severity classification of mild, moderate and severe. We found that most of the cases were of moderate severity, and then mild cases and the rest were severe. Many previous studies agreed with this distribution of severity as in the studies by *Komurcu et al. (2014)* and *Nageeb et al. (2018)* who had the same distribution of severity and agreed to our results as they had the same

distribution of severity, also in the study by *Mansoor et al. (2018)* obesity in relation to CTS had the same results. In contrast to our results, *Nawar et al. (2018)* had mild cases more than moderate when they assessed CTS severity in type 2 diabetic patients. Our results could be explained according to *Duncan and Kakinoki (2017)*, by the pain severity, which was found to be much higher in patients with moderate CTS compared to mild and severe.

Our results showed that there was a statistically significant relationship between age and both incidence and severity of CTS, which were compatible with the results of *Komurcu et al. (2014)* who found that CTS development risk of the age between 36-64 increased by 1.86 factor when compared to the age of 35 and younger. Also, CTS development risk of the age 65 and older people increased by a 4.167 factor in comparison to the 35 and younger group. This increased risk has been identified as independent cause for

CTS development. Also *Ushiyama et al. (2010)* agreed to our results as the age increase the incidence and severity of CTS increase. Data were deficient to disagree to our results.

We also found that BMI is positively correlated with the severity and incidence of CTS, which was compatible with the results by *Komurcu et al. (2014)* who observed that as with the increase of the BMI, the severity of CTS increased in a significant manner, we found a significant difference between mild, moderate, and severe CTS patients in respect to BMI, the highest BMI was in patients with severe CTS which was consistent with the recent studies in Egypt by *Nageeb et al. (2016)*, and another in Iraq by *Shakir and Nazar (2017)*. Also, in the study by *Shiri et al. (2015)*, they concluded that BMI is a risk factor for CTS and each 1-unit increase in BMI increases the risk of CTS by 7.4%. In contrast to our results, *Zyluk et al. (2011)* found that CTS patients had mean of 9% greater body mass index but correlation to severity wasn't applicable. The relation between CTS and increase BMI could be explained as the increased fatty tissue or the increased hydrostatic pressure throughout the carpal canal in obese individuals could increase CTS (*Shiri et al., 2015*).

Our study demonstrated that there was a statistically significant difference between cases and controls among lipid profile components, we found that total cholesterol and LDL were higher in the cases compared to controls which were consistent with the results by *Iftikhar et al. (2016)*, and also we found a significant inverse relationship in HDL between both groups. *Yi-Chuan et al. (2019)* stated that

patients with previous diagnosis of CTS were more liable to develop coronary heart disease because higher LDL levels and subsequent less HDL levels are main factors for the inflammation of the vascular walls, which supports our results. We also found that high cholesterol and LDL levels were significantly correlated to the severity of CTS especially in patients with severe CTS. In contrast to our results, *Yeo and Joo (2009)* in Korea concluded that there was a reverse correlation between LDL and severity of CTS while cholesterol was insignificant and triglycerides were significantly correlated with severity of CTS. We could explain the difference between results that in the latter study they studied few numbers of patients with CTS and both genders were involved. Besides in Asian population, there was an ethnic variation of all serum parameters, BMI and lifestyle which may influence the difference. Our results could be explained as that hypercholesterolemia and increase in LDL were found to be associated with fibrogenesis in various organs and in peripheral nerves. Besides, hypercholesterolemia often develops in middle age, mostly in menopausal women. These features match the age distribution and gender predominance in CTS (*Yurdakul et al., 2015*).

CONCLUSION

Abnormal lipid profile values (cholesterol and LDL) could influence the incidence and severity of CTS in middle aged women, Also, older age and higher BMI positively affects incidence and severity of CTS in the same subjects. Both high BMI and dyslipidemia are parts of the metabolic syndrome which was

reported to present among CTS patients and our study confirmed it.

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نمط الدهون في مصل الدم لدى مرضى متلازمة النفق الرسغي من الإناث في منتصف العمر

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خلفية البحث: تعتبر متلازمة النفق الرسغي هي الأكثر شيوعا بين أمراض الأعصاب الناتجة عن الإنضغاط في مسار العصب التشنجي و تسبب للمريض آلام باليدين و تتميل في مسار العصب خصوصا بالكفين ، و قد تسبب عجز عن العمل و قصور في مهام الحياة اليومية، وهي من أشهر الحالات التي يتم تشخيصها بواسطة رسم الأعصاب الكهربائي ، و بالرغم من الدراسات المكثفة على متلازمة النفق الرسغي ؛ فلا يزال التوصيف المرضي غير واضح و خاصة في النساء اللاتي في متوسط العمر.

الهدف من البحث: دراسة العلاقة بين نسبة الدهون في مصل الدم و السمنة و شدة و حدوث متلازمة النفق الرسغي في الإناث بمنتصف العمر.

المرضي وطرق البحث: تمت الدراسة على المريضات من العيادات الخارجية لطب المخ والأعصاب في مستشفى الحسين الجامعي التابعة لجامعة الأزهر ومستشفى الساحل التعليمي وعددهن 103 مريضة بمتلازمة النفق الرسغي بناء على التشخيص الاكلينيكي ودراسة الأعصاب الكهربائية كما تم استقطاب مجموعة ضابطة من الاناث في نفس العمر و هيئة الجسم و عددهن 52 في الفترة من شهر نوفمبر 2018 إلى شهر سبتمبر 2019.

النتائج : وجد ارتفاع في نسبة الكوليسترول و كذلك الكوليسترول خفيف كثافة الدهون في مصل الدم لدى مريضات النفق الرسغي مقارنة بالأخريات من المجموعة الضابطة كما وجدت علاقة احصائية بين شدة متلازمة النفق الرسغي و ارتفاع نسب كل من الكوليسترول و الكوليسترول قليل كثافة الدهون في مصل الدم بالاضافة إلى إثبات أن السمنة و التقدم في العمر عوامل مؤثرة في شدة المتلازمة احصائيا.

الإستنتاج: إرتفاع الدهون في مصل الدم و السمنة و التقدم في العمر من العوامل المؤثرة في حدوث و شدة متلازمة النفق الرسغي في الإناث في منتصف العمر.