

Original Research Article

Are Carpal Tunnel Syndrome And Migraine Related?

ABSTRACT

Background: Compression neuropathies have previously been associated with one another. Migraine have not been considered a type of compression neuropathy but, some recent studies found that some types of migraines may be treated by targeted peripheral nerve decompression. So, the association between migraines and carpal tunnel syndrome (CTS), {the most common compression neuropathy} may exists.

Objective: The aims of this study is to found whether there is a relationship between carpal tunnel syndrome and migraine, and if so to determine the factors causing this relationship.

Methods: The present study is a cross-sectional case control study of 120 patients with CTS in addition to age and sex matched 120 healthy controls. It was conducted at Mansoura University Hospitals, Egypt in the period from July, 2017 through June, 2018. All subjects underwent neurological examination, nerve conduction study of median nerve bilaterally, and evaluation according to headache by the International Headache Society, 2016 criteria. Also, the clinical severity of CTS was assessed and calculation of body mass index(BMI) were done. Evaluation of patients by Boston questionnaire form(BQF) {composed of two parts, Symptom Severity Scale (SSS) and the Functional Status Scale (FSS)}. Lastly, assessment of patients by Beck Depression Inventory(BDI).

Results: Patients had significantly higher rates of migraine headache (28.3 %) either alone (17.5 %) or combined with tension headache (10.8 %) when compared to controls. No statistically significant differences were found between the studied groups regarding the frequency of isolated tension headache. However, the total rate of cases with tension headache (n=43) including those in association with migraine is significantly higher in patients when compared to controls. Patients had significantly higher rates of various grades

of symptoms severity. All patients but 17 are functionally affected while none of the controls group is affected. Patients had significantly higher rates of borderline and moderate depression when compared to controls. Univariate logistic regression analysis for predictors of migraine headache in the studied patients shows that, older age (P value = **0.0001**), female sex (P value = 0.003), being manual worker (P value = 0.005), obesity class 11 (P value = 0.023), very severe functional severity scale (P value = 0.001), borderline and moderate depression (P value = 0.008 and 0.002 respectively) were significant predictors of migraine.

Conclusion: There is a significant association between CTS and migraine headache. This association suggests the possibility of a common risk factors for development of migraine headache include older age, female gender, obesity, low functional and high symptoms scores and depressive symptoms.

Key words: Carpal Tunnel Syndrome , Migraine , body mass index(BMI), Boston questionnaire form(BQF) and Beck Depression Inventory(BDI).

Declaration of interest: None

Introduction:

Carpal tunnel syndrome (CTS) is the most common upper extremity compressive neuropathy (1). Apart from the neuropathy itself, the most common findings are fibrosis of the subsynovial connective tissue (SSCT) and increased intra carpal tunnel pressure (2). The prevalence of it was reported to be between 3,72% and 5,8% in study done in Sweden, and United States of America(3). The prevalence of carpal tunnel syndrome in study carried out in Egypt was 32,7% for male and 39,7% for female among a group of computer professionals (4). Co-morbidities associated with the occurrence of CTS include obesity and diabetes (5).

On the other hand, the estimated global prevalence of migraine is 14.7% it is the third most common disease in the world (following dental caries and tension-type headache) (6). Also, affects more than 35 million people in the United States of America, and 10% of the

population in the world (7). According to the location of the study the prevalence of migraine is variable and ranges from 10 to 18%, (8). In Egypt, a study done in Assuit Governorate showed that prevalence of migraine was 10,51% (9).

Recent findings on the pathogenesis of frontal migraine headache support, besides a central vasogenic cause, an alternative peripheral mechanism involving compressed craniofacial nerves (10). This led to introduction of surgical intervention in the treatment of migraine in spite of the fact that this issue remains controversial (11). Moreover, one large epidemiological study suggested an association between CTS and migraine headache (12).

CTS and migraine are both common conditions that cause chronic ache that are commonly seen in the society. The aim of this study is to evaluate whether these two chronic conditions, are related in any way.

Patients and methods:

The present study is a cross-sectional case control study. It was conducted at Mansoura University Hospitals in the period from July, 2017 through Nov, 2018. The study protocol was approved by the local ethical committee and an informed consent was taken from all included subjects participate in the study.

SUBJECTS

The study included 120 patients with CTS in addition to age and sex matched 120 healthy controls. Patients were selected according to certain inclusion and exclusion criteria.

Inclusion criteria:

Patients already diagnosed with idiopathic carpal tunnel syndrome by electrophysiology who follow up in Mansoura University Hospital outpatient clinic.

Exclusion Criteria:

- Patients have any disease which have a tendency to cause CTS.
- Patients who have no definitive diagnosis of CTS by electrophysiological study.
- Patients who have any cause of headache except primary headache.
- Patients who have any neurological disorder besides CTS.

METHODS

All participants were subjected to:

Detailed history taking: To detect the common risk factors between CTS and primary headache.

Detailed medical examination: To exclude any signs indicating systemic disease that may cause CTS like diabetes mellitus, rheumatoid arthritis, and hyper/hypothyroidism. And to exclude systemic causes of secondary headache.

Detailed neurological examination: To exclude any signs indicating the presence of other neurological disorder with stressing on other neuropathy which can cause CTS except idiopathic CTS. To exclude any reason for headache except primary headache.

Nerve conduction velocity on median nerve bilaterally.

Assessment of the clinical severity of CTS by six- stage scale as follows;

- Stage (0) no CTS
- Stage (1) only nocturnal paresthesia
- Stage (2) diurnal paresthesia
- Stage (3) sensory deficit
- Stage (4) muscle weakness
- Stage (5) atrophy or muscle paralysis (13-14).

Evaluation of headache by the IHS criteria: According to International Headache Society this classification primary headache is classified to; migraine, tension type headache, clusters headache with other trigeminal autonomic cephalgia, and other primary headaches (International Headache Society, third edition, beta version, 2016).

Calculation of body mass index(BMI) (15): This is done by dividing weight in kilogram by height in meter square. The WHO regards a BMI as (<18.5= under weight, from 18.5 :24.9 =normal weight, from 25:29.9= over weight, from 30:34.9 =obese class 1 (moderate), and 35: 39.9 = obese class 2 (severe), 40:44.9 = obese class 3(very severe obese).

Beck Depression Inventory(BDI): Aaron T Beck created the Beck Depression Inventory which, is a self-report inventory, used to assess the intensity of depression.

The first versions of the BDI was published in 1961 and later revised in 1978 as the BDI-1A, and the BDI-II, published in 1996. In its new version, the BDI-II is composed of 21 items of question (multiple choice), each item is a list of four statements arranged in increasing severity about a particular symptom of depression such as hopelessness and irritability, cognitions such as guilt or feelings of being punished, as well as physical symptoms such as weight loss, fatigue, and lack of interest in sex(16-19).

Boston questionnaire form(BQF) (20,21): composed of two parts, the first is Symptom Severity Scale (SSS) and the second is Functional Status Scale (FSS). SSS composed of 11 questions and responses may be scored according (0=none or never, 1= mild, 2=moderate, 3= severe, 4=very severe).

While, Functional Status Scale (FSS) is composed of eight questions to assess the difficulty in performing selected activity, the overall score for FSS and responses may be scored according to(0=none or never, 1=mild, 2=moderate, 3=severe, 4=very severe score).

The higher the symptoms severity and functional status score indicates worse symptoms and dysfunction.

Statistical analysis

Data obtained from the present study were computed using SPSS version 22. Continuous data were expressed in the form of mean \pm SD while categorical data were expressed in the form of count and percent. Comparison of continuous data were performed utilizing student t test, while categorical comparisons were performed using Chi-square test. Univariate logistic regression analysis was performed to detect predictors of any relationship between CTS and migraine. P value less than 0.05 was considered statistically significant.

Results:

Table-1 shows no statistically significant differences between the studied groups regarding the reported demographic data. A significantly higher rates of cosmetic obesity and obesity in patients as compared to controls Fig (1). Also, there is a significantly higher nerve affection according to NCS in patients' group Fig (2). Moreover, patients had significantly higher frequency of moderate to severe and very severe nerve affection as compared to controls Fig (3).

	Patients (n=120)	Control (n=120)	P value
Age (year)	37.3 ± 7.7	36.2 ± 6.3	0.22
Sex (%)			
Male	40 (33.3%)	46 (38.3%)	0.42
Female	80 (66.7%)	74 (61.7%)	
Socioeconomic standard in Egy pounds n (%)			
> 1200	63 (52.5%)	64 (53.3%)	0.9
< 1200	57 (47.5%)	56 (46.7%)	
Education n (%)			
> 8 years	88 (73.3%)	92 (76.7%)	0.55
< 8 years	32 (26.7%)	28 (23.3%)	
Occupation n (%)			
House wife	41 (34.2%)	42 (35%)	0.34
Professional worker	34 (28.3%)	41(34.2%)	
Manual worker	31 (25.8%)	20 (16.7%)	
Unemployed	14 (11.7%)	17 (14.1%)	
Obesity n (%)			
Normal (18,5: 24,9)	20 (16.7%)	67 (55.9%)	0.001*
Over weight (25:29,9)	57 (47.5%)	28 (23.5%)	
Obese class I (30:34,9)	37 (30.8%)	23 (19.3%)	
Obese class II (35: 39,9)	6 (5%)	2 (1.3%)	
NCS findings			
Normal	-	114 (95%)	0.001*
Right CTS	53 (44.2%)	3 (2.5%)	
Left CTS	18 (15%)	2 (1.7%)	
Bilateral CTS	49 (40.8%)	1 (0.8%)	
NCS severity			
Mild	29 (24.2%)	6 (5%)	0.001*
Moderate	61 (50.8%)	-	
Sever	28 (23.3%)	-	
Very sever	2 (1.7%)	-	

Fig. (1) The reported BMI in the studied patients

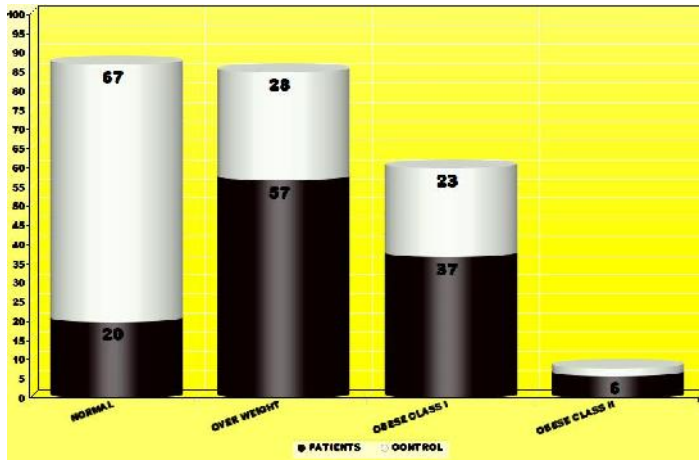


Fig. (2) NCS findings in the studied groups

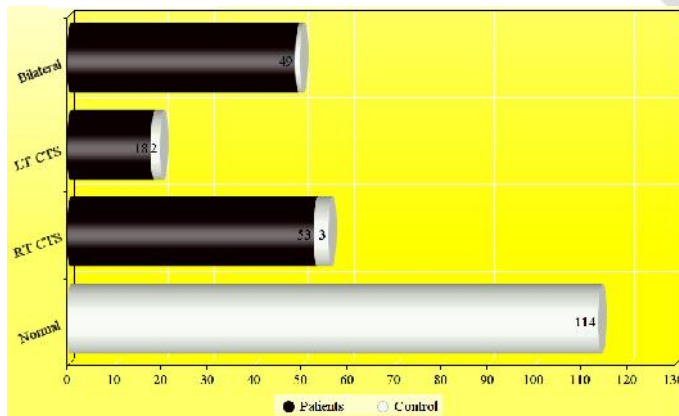


Fig. (3) NCS severity in the studied groups

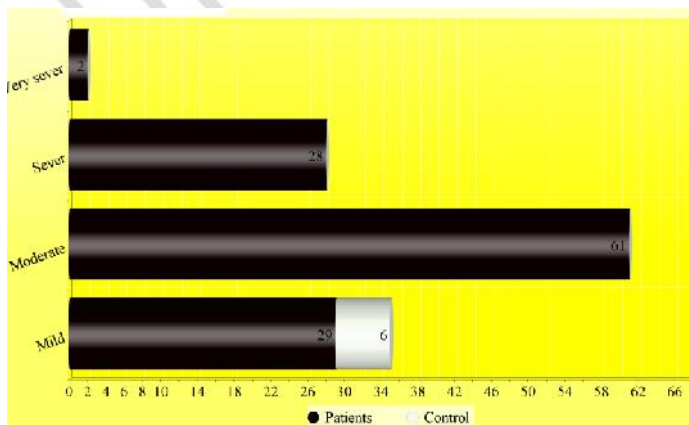


Table-2 shows that patients had significantly higher rates of migraine headache (28.3 %) either alone (17.5 %) or combined with tension headache (10.8 %) when compared to controls Fig (4). No statistically significant differences were found between the studied groups regarding the frequency of isolated tension headache. However, the total rate of cases with tension headache (n=43) including those in association with migraine is significantly higher in patients when compared to controls. Patients had significantly higher rates of various grades of symptoms severity. All patients but 17 are functionally affected while none of the controls group is affected Fig (5). Patients had significantly higher rates of borderline and moderate depression when compared to controls Fig (6).

	Patients (n=120)	Control (n=120)	P value
Type of headache			
None	56 (46.7%)	86 (71.6%)	P < 0.05*
Migraine	21 (17.5%)	10 (8.4%)	
Tension headache	30 (25%)	20 (16.7%)	
Both tension & migraine	13 (10.8%)	4 (3.3%)	
Symptoms severity scale			
None	-	114 (95 %)	P < 0.05*
Mild	30 (25.0 %)	6 (5 %)	
Moderate	61 (50.8 %)	-	
Sever	28 (23.4 %)	-	
Very sever	1 (0.8 %)	-	
Functional severity score			
None	17 (14.2 %)	120 (100.0 %)	P < 0.05*
Mild	51 (42.5 %)	-	
Moderate	36 (30.0 %)	-	
Sever	15 (12.5 %)	-	
Very sever	1 (0.8 %)	-	
Beck Depression Inventory findings			
Normal ups and downs	53 (44.2 %)	79 (65.8 %)	P < 0.05*
Mild mood disturbances	39 (32.5 %)	36 (30.0 %)	
Borderline depression	18 (15.0 %)	5 (4.2 %)	
Moderate	10 (8.3 %)	-	

Fig. (4) The reported headache types in the studied groups.

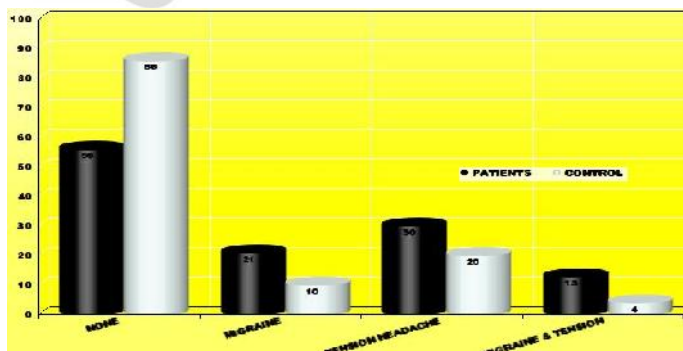


Fig. (5) Functional affection in the studied groups

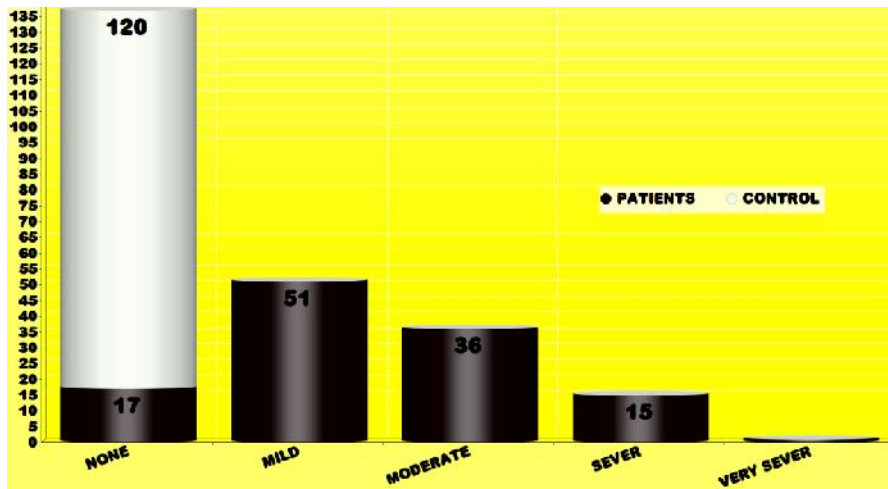


Fig. (6) BDI in the studied groups

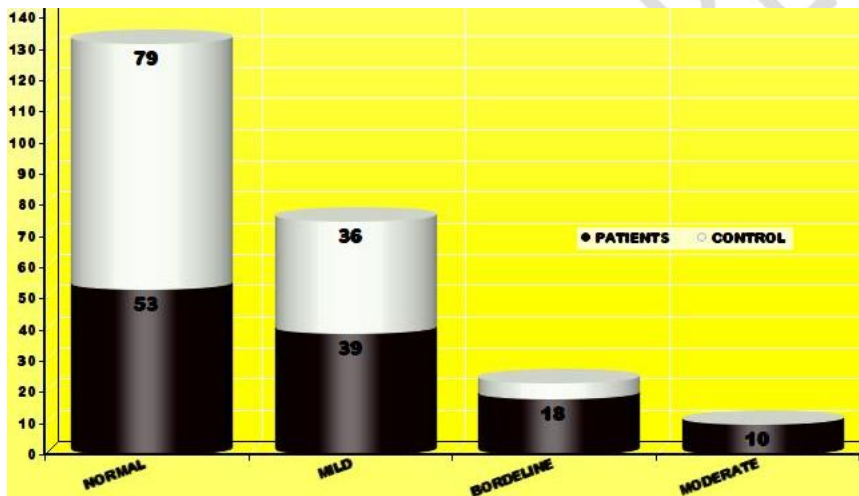


Table-3 : shows that patients with headaches are significantly older than those without. Also, it was noted that patients with migraine headache are significantly older than patients with tension headache. In addition, it was found that there is significantly higher frequency of females in patients with migraine when compared with patients without. Also, this table shows significantly higher rates of obesity in patients with headaches when compared with patients without Fig (7). However there was no significant association between presence of various types of headaches and NCS findings and severity.

	Migraine N= 21	Migraine + Tension N = 13	Tension headache N = 30	None N = 56	P value
Age (year)					
	42.0 ± 6.7*#	42.7 ± 4.5*#	37.7 ± 8.6*	34.1 ± 6.6	P<0.05*
Sex (%)					
Male	2 (9.5 %)	2 (15.4 %)	11 (36.7 %)	25 (44.6 %)	0 . 0 1 4
Female	19 (90.5 %)	11 (84.6 %)	19 (63.3 %)	31 (55.4 %)	
Socioeconomic standard in Egy pounds n (%)					
> 1200	13 (61.9 %)	6 (46.2 %)	11 (36.7 %)	33 (58.9 %)	0 . 1 8
< 1200	8 (38.1 %)	7 (53.8 %)	19 (63.3 %)	23 (41.1 %)	
Education n (%)					
> 8 years	17 (81.0 %)	10 (76.9 %)	18 (60.0 %)	44 (78.6 %)	0 . 2 3
< 8 years	4 (19.0 %)	3 (23.1 %)	12 (40.0 %)	12 (21.4 %)	
Occupation n (%)					
House wife	9 (42.9 %)	8 (61.5 %)	7 (23.3 %)	17 (30.4 %)	0 . 0 8
Professional worker	6 (28.6 %)	4 (30.8 %)	8 (26.7 %)	16 (28.6 %)	
Manual worker	2 (9.5 %)	1 (7.7 %)	13 (43.3 %)	15 (26.8 %)	
Unemployed	4 (19.0 %)	-	2 (6.7 %)	8 (14.2 %)	
Obesity n (%)					
Normal (18,5: 24,9)	2 (9.5 %)	1 (7.7 %)	2 (6.7 %)	15 (26.8 %)	0.016*
Over weight (25:29,9)	8 (38.1 %)	5 (38.5 %)	13 (43.3 %)	31 (55.4 %)	
Obese class I (30:34,9)	9 (42.9 %)	5 (38.5 %)	13 (43.3 %)	10 (17.9 %)	
Obese class II (35: 39,9)	2 (9.5 %)	2 (15.4 %)	2 (6.7 %)	-	
NCS findings					
Normal	-	-	-	-	0.28
RT CTS	9 (42.9 %)	4 (30.8 %)	11 (36.7 %)	29 (51.8 %)	
LT CTS	4 (19.0 %)	2 (15.4 %)	2 (6.7 %)	10 (17.9 %)	
Bilateral CTS	8 (38.1 %)	7 (53.8 %)	17 (56.6 %)	17 (30.3 %)	
NCS severity					
Mild	5 (23.8 %)	3 (23.0 %)	5 (16.7 %)	16 (28.6 %)	0.14
Moderate	13 (61.9 %)	5 (38.5 %)	12 (40.0 %)	31 (55.4 %)	
Sever	3 (14.3 %)	4 (30.8 %)	12 (40.0 %)	9 (16.0 %)	
Very sever	-	1 (7.7 %)	1 (3.3 %)	-	

Fig. (7) BMI categories in patients' subgroups

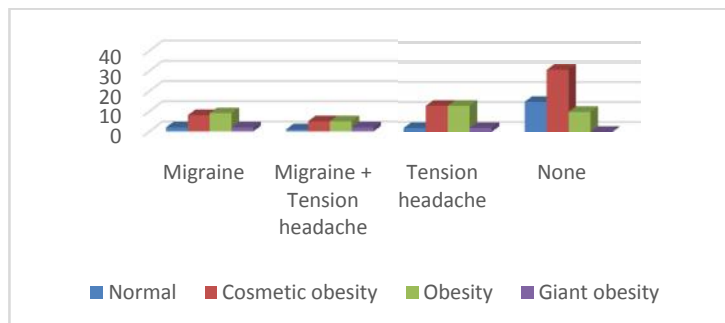


Table-4 shows significant association between CTS symptoms severity score and presence of headaches. Most patients with headaches experienced moderate to very severe symptoms (Fig 8) and worse functional severity score when compared with patients without (Fig 9). Moreover, patients with headaches had significantly higher rates of borderline and moderate depression when compared with patients without headaches.

	Migraine N= 21	Migrain+ Tension N = 13	Tension headache N = 30	None N = 56	P value
Symptoms severity scale					
Mild	5 (23.8 %)	1 (7.7 %)	5 (16.7 %)	19 (33.9 %)	P<0.05*
Moderate	9 (42.9 %)	5 (38.5 %)	12 (40.0 %)	35 (62.5 %)	
Sever	7 (33.3 %)	7 (53.8 %)	12 (40.0 %)	2 (3.6 %)	
Very sever	-	-	1 (3.3 %)	-	
Functional severity score					
None	2 (9.5 %)	-	4 (13.3 %)	11 (19.6 %)	P<0.05*
Mild	7 (33.3 %)	4 (30.8 %)	9 (30.0 %)	31 (55.4 %)	
Moderate	5 (23.9 %)	4 (30.8 %)	13 (43.4 %)	14 (25.0 %)	
Sever	7 (33.3 %)	5 (38.4 %)	3 (10.0 %)	-	
Very sever	-	-	1 (3.3 %)	-	
Beck Depression Inventory findings					
Normal ups and downs	8 (38.1 %)	1 (7.7 %)	11 (36.7 %)	33 (58.9 %)	P<0.05*
Mild mood disturbances	4 (19.0 %)	5 (38.5 %)	13 (43.3 %)	17 (30.4 %)	
Borderline depression	4 (19.0 %)	5 (38.5 %)	3 (10.0 %)	6 (10.7 %)	
M o d e r a t e	5 (23.9 %)	2 (15.3 %)	3 (10.0 %)	-	

Fig. (8) Relation between types of headaches and symptoms severity score

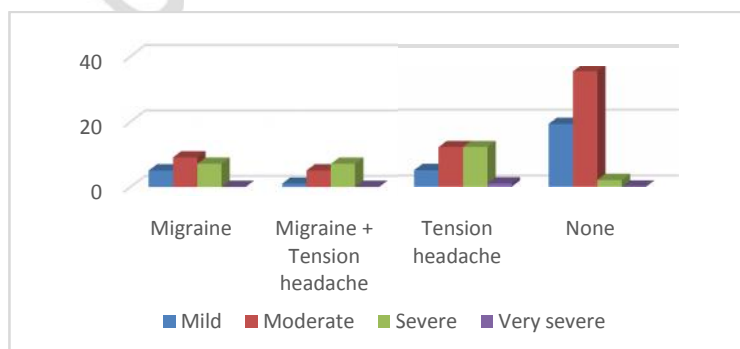


Fig. (9) Relation between presence and types of headaches and functional severity score

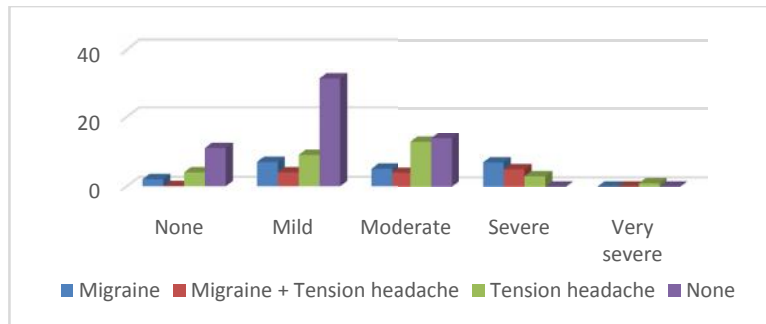


Table-5 Logistic regression analysis for predictors of migraine headache in the studied patients shows that using univariate logistic regression analysis, older age (P value = **0.0001**), female sex (P value = **0.003**), being manual worker (P value = **0.005**), obesity class 11 (P value = **0.023**), very severe functional severity scale (P value = **0.001**), borderline and moderate depression (P value = **0.008** and **0.002** respectively) were significant predictors of migraine.

		Univariate analysis		
		OR	P	CI
Age		0.87	0.0001	0.82-0.93
Sex	Male	Ref.		
	Female	5.5	0.003	1.8-17.0
SES	> 1200 LE	Ref.		
	< 1200 LE	1.2	0.6	0.56-2.8
Education	> 11 years	Ref.		
	< 11 years	0.66	0.39	0.25-1.7
Occupation	Housewife	Ref.		
	Professional worker	1.8	0.45	0.7-4.7
	Manual worker	6.9	0.005	1.8-26.5
	Unemployed	1.8	0.36	0.5-6.9
BMI	Normal	Ref.		
	Over weight	0.6	0.46	0.15-2.4
	Obese class 1	0.28	0.07	0.07-1,1
	Obese class 11	0.09	0.023	0.01-0.7
NCS findings	Right side	Ref.		
	Left side	0.5	0.67	0.21-2.1
	Bilateral	0.76	0.53	0.32-1.8
NCS Severity	Mild	Ref.		
	Moderate	0.89	0.82	0.33-2.4
	Severe	1.1	0.83	0.35-3.7
	Very severe	0.38	0.51	0.02-6.8
Symptoms Severity Scale	Mild	Ref.		
	Moderate	0.0	1.0	0.0-
	Severe	0.0	1.0	0.0-
	Very severe	0.0	1.0	0.0-
Functional Severity	Mild	Ref.		

Score	Moderate	0.47	0.37	0.09-2.4
	Severe	0.4	0.28	0.08-2.1
	Very severe	0.03	0.001	0.005-0.2
Beck Depression Inventory	Normal ups and downs	Ref.		
	Mild mood disturbances	0.66	0.43	0.23-1.9
	Borderline depression	0.21	0.008*	0.06-0.7
	Moderate depression	0.09	0.002*	0.02-0.41

Discussion

In this study, females markedly outnumbered males (2:1) in the CTS patients' group. This is line with previous Egyptian studies including that of El Miedany et al., 2008, Elsaman et al., 2015, and Razek et al., 2017 (22,23,24).

Regarding the reported BMI, the current study found significantly higher rates of cosmetic obesity and obesity in patients as compared to controls. This is in agreement with the study of Mansour et al., 2017 who found high prevalence of obesity among CTS patients (25). Also, in the studies of Bhanderi et al., 2017 and Pourmemari et al., 2018, obesity was identified as a risk factor for CTS (26-27).

As expected, the present study found significant differences between patients and controls regarding nerve conduction studies, clinical symptoms score and functional severity score.

Regarding to depression, CTS patients had significantly higher rates of borderline and moderate depression when compared to controls. The association between CTS and depression was reported by many studies. de Azevedo et al., 2015 noted that CTS is significantly associated with depression (28). This association applied to diabetic and non-diabetic patients as reported by the study of Tanik et al., 2016 (29).

Also, the present study found that patients with headaches had significantly higher rates of borderline and moderate depression when compared with patients without headaches. These data are in harmony with the study of Moisset et al., 2017 on patients with inflammatory bowel disease, migraine was associated with higher depression scores

(30). Moreover, In the study of Jat et al., 2018 that assessed the prevalence of migraine among patients of depressive disorder, it was found that migraine was linked more with those having severe depressive disorder (31).

Khan et al., 2017 highlighted that the subjective symptoms of CTS are well correlated with psychological factors, and their correlation with objective electrophysiological severity (32). Also, studies restricted to female patients reported high rates of depression with significant association with pain intensity (Fernández-de-las-Peñas et al., 2015 and Fernández-Muñoz et al., 2016 (33-34). Even in pregnant women, higher depression scores were noted in women with CTS (35).

The prevalence of migraine in the control group was 11.7 %. This is in accordance with many other studies. Migraine was reported in 11.8 % of participants in the large American study of Buse et al., 2013(36). In a subsequent study from the same country, the prevalence of migraine and severe headache was 14.2 % (37).

In another study (38), Woldeamanuel and coworker 2014 analyzed the prevalence of migraine in African studies and found that among 21 community-based studies included 137,277 subjects, pooled migraine prevalence was 5.61% while in a Canadian study, the prevalence of migraine was 8.3 % (39). However, in a recent Saudi study by Muayqil et al., 2018, migraine was present in 26.97% of the studied population (40).

In the present study, patients had significantly higher rates of migraine headache (28.3 %) either alone (17.5 %) or combined with tension headache (10.8 %). This high rate of migraine headache is in agreement with the large study of 952 CTS patients by Law et al., 2015 (41). In their' study, migraine prevalence was 34% in those with CTS compared with 16% in those without CTS. However, in the study of Yucel 2015, the prevalence of migraine in the 261 CTS patients' study was only 10.8 % (42). This difference between various studies is due to multiple factors including the severity of the disease and associated co-morbidities.

Regarding tension headache, there were 24 patients (20.0 %) in the control group. This is agreement with Cvetković et al., 2013 (43) who reported a prevalence of 20.6 % in the Croatian population and Al-Hashel et al., 2017 from Kuwait who diagnosed tension headache in 29.0 % of a large 15,523 patients' study (44).

Comparison between CTS patients with various types of headache revealed that patients with migraine headache are significantly older and included significantly higher frequency of females. This is in agreement with the study of Almalki et al., 2018 who concluded that Gender was significantly correlated with migraine prevalence (45).

Moreover, the present study found significantly higher rates of obesity in patients with headaches when compared with patients without. This is in line with the study of Miri et al., 2018 who investigated the probable association between obesity and migraine (46).

While the present study failed to prove any association between migraine and or tension headache development in CTS patients and their nerve conduction study findings, it report a significant association between both symptom and functional severity scores and having migraine headache in this set of patients. However, this conclusion may find support in studies assessing the association between migraine headache and other morbidities characterized by painful symptoms or functional limitations. For example, Gozubatik-Celik and co worker 2014 found a significant association between severity of restless leg syndrome and migraine headache (47). In addition, Ashina et al., 2015 reported a high frequency of chronic neck pain among migraine patients (48).

Conclusion:

- There is a significant association between CTS and migraine headache. This association suggests the possibility of a common risk factors for development of migraine headache include older age, female gender, obesity, low functional and high symptoms scores and depressive symptoms.

- While the present study failed to prove any association between migraine development in CTS patients and their nerve conduction study findings, it reports a significant association between both symptom and functional severity scores and having migraine headache in this set of patients. However, this conclusion may find support in studies assessing the association between migraine headache and other morbidities characterized by painful symptoms or functional limitations.

Recommendations

- A larger longitudinal study is recommended to confirm results of the present study.
- This opens the door for another study to find out the effect of CTS treatment on migraine headache.
- Patients with migraine should be screened for subclinical CTS. In addition, migraine headache may be an early warning sign of an increased risk of future carpal tunnel syndrome.

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