Original Article

Association of Carpal Tunnel Syndrome with Diabetic Polyneuropathy

Sayeda Shabnam Malik¹, Mohammad Rezaul Karim Khan², MA Hannan³, SK Mahbub Alam ⁴ Received: 17 February 2021 Accepted: 30 March 2021 doi: https://doi.org/10.3329/jemc.v11i2.65189

Abstract

Background: Common thought is that diabetic neuropathy is a predisposing factor to entrapment syndromes. Carpal tunnel syndrome (CTS) is the most frequent entrapment neuropathy. **Objectives**: To find out association of carpal tunnel syndrome with diabetic polyneuropathy. Materials and Methods: During the period of March 2013 to September 2015, this cross-sectional study was carried out in the Department of Neurology, Bangabandhu Sheikh Mujib Medical University, Dhaka. A total of 100 adult patients having symptoms and signs of polyneuropathy were recruited as study population. Of them 50 patients grouped into diabetic polyneuropathy (DPN) and the rest 50 patients in non-diabetic neuropathy due to other causes. Results: Out of all patients, the mean age was found 49.60 (13.53) years with 42% female in diabetic neuropathy patients and mean age was 44.64 (15.72) years with 46% female in non-diabetic neuropathy patients. The duration of diabetes was found 8.44 (7.79) years. According to development of Carpal tunnel syndrome (CTS), in diabetic neuropathy patients, about 58% patients developed CTS while in non-diabetic neuropathy patients, that of 14% (p=0.0001). We found diabetic neuropathy patients have 8.48 times higher possibility of development of CTS than non-diabetic neuropathy patients. On adjusted model, age as confounding variable, diabetic neuropathy and female sex were found significantly associated with development of CTS with adjusted odd ratio 10.92 and 3.78 respectfully (p < 0.0001). Conclusion: In conclusion, we revealed the higher frequency of CTS in diabetics with DPN. As well we also found DPN and female sex were strongly associated with development of CTS. As DPN is a risk factor for CTS, priority should also be given to the treatment of DPN.

Key words: Diabetic neuropathy; Carpal tunnel syndrome

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Introduction

Diabetes mellitus is the most common chronic non communicable disease now-a-days. Peripheral neuropathy has been considered as the most troublesome complication of DM. Diabetes affects 382 million people worldwide and its prevalence is expected to increase to 592 million by the year 2035.¹ Diabetes mellitus is a clinical syndrome characterized by hyperglycemia caused by absolute or relative deficiency of insulin.² Diabetic neuropathy, a wellknown long term complication of diabetes, can affect almost half of the diabetic population³ and is associated with higher mortality and morbidity.⁴ The

Correspondence Sayeda Shabnam Malik, Email: sayedashabnam.malik@gmail.com

^{1.} Assistant Professor, Department of Neurology, Enam Medical College, Savar, Dhaka

^{2.} Professor, Department of Neurology, Bangabandhu Sheikh Mujib Medical University, Shahbag, Dhaka

^{3.} Department of Neurology Bangabandhu Sheikh Mujib Medical University, Shahbag, Dhaka

^{4.} Associate Professor, Department of Neurology, Bangabandhu Sheikh Mujib Medical University, Shahbag, Dhaka

overall prevalence of neuropathy is 66% for type 1 and 59% for type 2 diabetes.⁵ Prevalence of neuropathic symptoms increases at the time of diagnosis, the incidence increases to about 50% after 20–25 years of diabetic life.⁶

Painful diabetic neuropathy (PDN) is a common type of diabetic neuropathy and the most common cause of neuropathic pain.⁷ Neuropathic pain can be a prominent presenting symptom in a great number of peripheral neuropathy.⁸ DPN is insidious in onset and patient complains of tingling, pricking, burning sensation and numbness of mild to moderate severity.⁹ PDN is caused by the involvement of small nerve fibers, which may affect without objective clinical findings. The diagnosis of DPNP does not require evidence of a large-fiber abnormality.¹⁰ Other common causes of neuropathy, e.g., Guillaine Barre syndrome, CIDP, toxins and metabolic and nutritional diseases.⁵

Carpal tunnel syndrome (CTS) is a compressive neuropathy which is defined as a mononeuropathy or radiculopathy caused by mechanical distortion produced by a compressive force¹¹ and a symptomatic compression neuropathy of the median nerve at the level of the wrist.¹²

CTS is the most well-known and frequent form of median nerve entrapment, and accounts for 90% of all entrapment neuropathies¹³ and the second most important cause of diabetic neuropathy after distal symmetric sensory motor polyneuropathy.⁹ CTS is caused by entrapment of the median nerve at the level of the carpal tunnel, and delimitated by the carpal bones and by the transverse carpal ligament.¹² Physiological evidence indicates increased pressure within the carpal tunnel, and therefore decreased function of the median nerve at that level.¹² The prevalence of CTS is 15–25% in patients with DPN.¹⁴

The most typical symptoms are pain and paresthesia in the thumb, index, middle finger and the radial side of ring finger, occurring especially at night.¹⁴ The main conditions associated with carpal tunnel syndrome are diabetes, hypothyroidism, rheumatoid arthritis, osteoarthritis, obesity and pregnancy.¹⁵ Carpal tunnel syndrome and diabetic polyneuropathy are common conditions in patients with diabetes and therefore frequently occur concomitantly. Carpal tunnel syndrome has been reported in up to 20% of people with diabetes. The diabetic link is possibly due to the fact that when blood glucose levels are high the proteins in the tendons of the carpal tunnel become glycosylated, inflaming them and forming a sort of biological superglue that makes the tendon less able to slide freely.¹⁵

The two provocative tests most commonly used in the clinical settings are Phalen's and Tinel's tests. The sensitivity of Phalen's test is 67-83% and specificity is 40-98%. Tinnel's test has sensitivity of 48-73% and specificity is 30-94%.¹⁶

Nerve conduction study is considered to be gold standard in the diagnosis of CTS. This is the most sensitive and accurate technique, with a sensitivity of 80-92% and specificity of 80-99%.17 NCS criteria is used to diagnose CTS in diabetic subjects without distal peripheral neuropathy in the same manner as in the non-diabetic population. The standard method of diagnosis is comparing the latency and amplitude of a median nerve segment across the carpal tunnel to another nerve segment that does not go through the carpal tunnel, such as the radial or ulnar nerve.¹⁷ Prolonged motor and sensory latencies of the median nerve and reduced sensory and motor conduction velocities are accepted as diagnostic criteria for carpal tunnel syndrome.¹⁴ When CTS occurs due to entrapment then only distal latency is increased in both motor and sensory parts. If two stimuli are given in both proximal and distal to the wrist, entrapment can be identified. In diabetic mononeuropathy usually homogenous involvement of nerve (axonal and demyelinating) may occur both proximal and distal to wrist joint. It is important to determine whether median neuropathy is due to entrapment or it results from diabetic polyneuropathy. For future treatment planning it is important to determine whether CTS is an entrapment of the median nerve under the transverse carpal ligament or it results from diabetic polyneuropathy.

Materials and Methods

This cross-sectional analytical study was carried out in the inpatient and outpatient departments of neurology including neuropathy clinic of Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka from March 2013 to September 2015. Study population was adult patients having symptoms and signs of polyneuropathy. Then these patients were grouped into diabetic polyneuropathy and non-diabetic polyneuropathy due to other causes. Patients having symptoms of CTS were included in both groups by random sampling method 107 adult patients who were having symptoms and signs of polyneuropathy undergo meticulous history and physical examination. Then these patients were divided into diabetic polyneuropathy and non-diabetic polyneuropathy (due to other cause). 50 patients were in diabetic polyneuropathy group and 50 were in nondiabetic polyneuropathy group (due to other cause). Rest 7 patients did not give consent to take part in the study and had other diseases like hypothyroidism.

- The diagnosis of CTS was done by the presence of nocturnal and activity related pain or dyseshesia limited to hand. Patients having symptoms of CTS were included in both groups.
- Height and weight were measured and BMI was calculated as weight (kg)/height (m)².
- 2015 American Diabetes Association (ADA) diabetes guidelines criteria used for diabetes diagnosis, the values were HBA1c ≥6.5%, FPG ≥126 mg/dL (7.0 mmol/L), two-hr PG ≥200 mg/dL (11.1 mmol/L) during OGTT (75g).
- The diabetic and non-diabetic patients with a history and signs of polyneuropathy were evaluated by some routine investigations (CBC, ESR, FBS, PPBS, HBA1C, serum creatinine, RA Test, TSH) for exclusion of other diseases.
- For evaluation for presence of CTS distal latency, conduction velocity of sensory and motor component of medial nerve was measured.
- If the median motor latency exceed 4.4 ms or the difference between distal motor latency of median and ulnar nerve exceed 1.1 ms or the difference between distal sensory latency of median and

ulnar nerve exceed 0.2ms used as a parameter for diagnosis of CTS.

Data were collected by face to face interview or history taking of the patient. Clinical examination, laboratory investigations were collected by using structured data information sheet.

Data were analyzed by computer with the help of SPSS version 21.0 Software package. All data were recorded systematically in a preformed data collection sheet. Quantative variables are expressed as mean \pm SD. Analysis of the variables was done by using Chi square test and independent t-test. For all statistical tests, we considered p value <0.05 as statistically significant. Binary logistic regression was seen to reveal the association of CTS with diabetic polyneuropathy and nondiabetic polyneuropathy.

Results

This cross-sectional analytical study was carried out in the Department of Neurology, Bangabandhu Sheikh Mujib Medical University, Dhaka from March 2013 to September 2015. By random sampling method 107 adult patients who were having symptoms and signs of polyneuropathy were enrolled in this study. Seven patients who did not give consent to take part in the study and had other diseases like hypothyroidism were excluded. Finally, a total of 100 adult patients having symptoms and signs of polyneuropathy were recruited as study population. Out of these patients, 58% were male and 42% female. Fifty patients had diabetic polyneuropathy and 50 patients non-diabetic neuropathy due to other causes. All diabetics had type 2 DM and mean (SD) duration was 8.44 years. Table I shows the distribution of the patients by gender.

Table II shows comparison of patients according to nerve conduction velocity. In context of median nerve and ulnar nerve, all the parameters showed statistically significant difference between diabetic and non-diabetic neuropathy patients except the distal latency of ulnar nerve which was found statistically nonsignificant. Other nerve shows non-significant difference.

Gender	Туре	C1.:		
	Diabetic Neuropathy (n=50)	Non-Diabetic Neuropathy (n=50)	(df)	p value*
Male	29 (58.0%)	27 (54.0%)	0.041 (1)	0.840 ^{ns}
Female	21 (42.0%)	23 (46.0%)	0.041(1)	

ns=non significant; *Chi square test was done to measure level of significance #Figure within parenthesis denoted corresponding column percentage

	Diabetic neuropathy (n=50) Mean (SD)	Non-diabetic neuropathy (n=50) Mean (SD)	p values*
Median nerve			
Distal motor latency (ms)	5.02 (1.50)	3.84 (1.21)	<0.0001 ^s
Motor amplitude (mv)	8.29 (4.12)	5.13 (4.61)	<0.0001s
Sensory amplitude (µv)	11.40 (8.86)	29.22 (25.69)	<0.0001s
NCV (m/s)	32.96 (13.41)	40.22 (10.17)	0.003 ^s
Ulnar nerve			
Distal latency (ms)	2.84 (0.64)	3.21 (1.20)	0.067 ^{ns}
Motor amplitude (mv)	9.80 (6.10)	7.61 (5.24)	0.060 ^s
Sensory amplitude (µv)	12.85 (9.30)	30.63 (25.48)	<0.0001 ^s
NCV (m/s)	36.72 (12.82)	31.04 (12.27)	0.027^{s}
NCV (m/s) tibial nerve	31.79 (9.36)	32.88 (8.88)	>0.05 ^{ns}
NCV (m/s) peroneal nerve	33.33 (5.14)	33.75 (7.40)	>0.05 ^{ns}
NCV (m/s) sural nerve	39.09 (7.20)	42.03 (9.03)	>0.05 ^{ns}

Table II: Comparison of patients according to nerve conduction velocity (N=100)

ns=non significant; s=significant; *Independent sample t test was done to measure the level of significance

Table III shows distribution of patients according to development of carpal tunnel syndrome (CTS). In diabetic neuropathy patients, about 58% patients developed CTS while in non-diabetic neuropathy patients CTS was 14%. There was statistically highly significant difference between these groups in terms of CTS development.

Table III: Distribution of patients according to development of carpal tunnel syndrome (CTS) (N=100)

CTS	Diabeteic neuropathy (n=50)	Non-diabetic neuropa- thy (n=50)	p value*	
Present	29 (58.0)	7 (14.0)	<0.00018	
Absent	21 (42.0)	43 (86.0)	<0.0001°	

*Chi square test was done to measure the level of significance. Figure within parenthesis indicates percentage. s= significant

Table IV: Binary logistic regression model to see the association of carpal tunnel syndrome with diabetic neuropathy patients (Enter method)

	unadiOD	p value	95% CI	
	unaujOK		Lower value	Upper value
Non-diabetic neuropathy (Ref)	1			
Diabetic neuropathy	8.48	< 0.0001	3.195	22.523

unadjOR= unadjusted odd ratio

 Table V:
 Multiple logistic regression model to see the association of Carpal tunnel syndrome with age, sex and diabetic neuropathy (Forward conditional method)

	adjOR	p value	95% CI	
			Lower value	Upper value
Group				
Non-diabetic neuropathy (Ref)	1			
Diabetic Neuropathy	10.92	< 0.0001	3.76	31.74
Sex				
Male (Ref)	1			
Female	3.78	0.010	1.370	10.417

adjOR= adjusted odd ratio

Binary logistic regression was seen in enter method to reveal the association of carpal tunnel syndrome with diabetic neuropathy (Table IV). Here we found diabetic neuropathy patients have 8.48 times higher possibility of development of CTS than non-diabetic neuropathy patients which is statistically highly significant (p <0.0001). Table V shows multiple logistic regression model done in Forward conditional method. Here age was act as confounding variable. Diabetic neuropathy and female sex were found significantly associated with development of CTS with adjusted Odd Ratio 10.92 and 3.78 respectfully.

Discussion

Carpal tunnel syndrome (CTS) which is the most wellknown and frequent form of median nerve entrapment accounting for 90% of all entrapment neuropathies, remains a puzzling and disabling condition.^{13,18} One in every five subjects who complain of symptoms such as pain, numbness and a tingling sensation in the hands is expected to have CTS based on clinical examination and electrophysiological testing.¹⁸ An epidemiological study in UK reported that median number of days away from work due to CTS is amongst the highest in the UK at 27 days.¹⁹ Therefore, the underlying cause of CTS is necessary to detect for its better management.

The prevalence of diabetic polyneuropathy (DPN) has been reported as 5 to 60%.²⁰ It occurs thrice as frequently in a diabetic population compared with a normal healthy population.^{21,22} The increased prevalence in diabetes may be related to repeated undetected trauma, metabolic changes, accumulation of fluid or edema within the confined space of the carpal tunnel, and diabetic cheiroarthropathy.²³ CTS is found in up to one-third of patients with diabetes, when demonstrated electrophysiologically, but may only be symptomatic in 5.8%.²⁴

This cross-sectional study was carried out in the department of neurology, Bangabandhu Sheikh Mujib Medical University, Dhaka from March 2013 to September 2015. A total of 100 adult patients having symptoms and signs of polyneuropathy were recruited as study population. Of them 50 patients were diabetic polyneuropathy and 50 patients non-diabetic neuropathy due to other causes.

There are substantial numbers of publications

demonstrating the prevalence and association of CTS with diabetic neuropathy patients. We compared our study findings with result of some other published articles elsewhere in the world to verify our results.^{25–27}

Analysis of gender distribution showed that out of all patients, 58% were male and 42% female in diabetic neuropathy diagnosed patients and in non-diabetic neuropathy patients, 54% were male and 46% female. But in unadjusted odd ratio model, we found female were 2.5 times more prone to develop CTS than male and that was statistically significant (p<0.05). Our study findings are consistent to some other studies done in the world. Aybin et al²⁸ studied on 100 patients, 16 patients developed CTS and among them 11 were female and 5 were male.

According to development of Carpal Tunnel Syndrome (CTS), in diabetic neuropathy patients, about 58% patients developed CTS while in non-diabetic neuropathy patients it was 14% which is statistically highly significant (p<0.0001). CTS was present in 16% of all diabetic patients and of these 93% were found to have DPN (p<0.001). A review was done Comi et al²⁹ on carpal tunnel syndrome (CTS) in patients with diabetes mellitus. The prevalence of CTS is higher in diabetic patients with peripheral polyneuropathy compared to patients with diabetes, who do not have diabetes-related late complications (30% vs. 14%). One of the study observed the prevalence of carpal tunnel syndrome (CTS) in diabetic polyneuropathy (DPN) patients in a cross-sectional design in a total of 478 subjects.²⁵ On the basis of nerve conduction study, the prevalence of clinical CTS was 2% in the reference population, 14% in diabetic subjects without DPN, and 30% in those with DPN. Moreover reported the prevalence of symptomatic CTS in those with diabetes as 11 and 6% in type 1 and type 2 diabetic patients, respectively.25

On the measuring of distal motor latency of median nerve, the mean (SD) of non-diabetic neuropathic patients with CTS was found 6.29 (1.54) m/sec which was statistically significant than NDPN without CTS, 3.45 (0.47). Meanwhile, statistical significant difference was also found in distal motor latency of median nerve between diabetic neuropathy with CTS and without CTS [6.03 (1.21) vs. 3.64 (0.11), p<0.0001].

Binary logistic regression was seen in enter method to reveal the association of Carpal tunnel syndrome with diabetic neuropathy patients. Here we found diabetic neuropathy patients have 8.48 times higher possibility of development of CTS than non-diabetic neuropathy patients which was statistically highly significant (p<0.0001). We also found age is not associated with development of CTS. But in case of female gender, we found female were 2.5 times more prone to develop CTS than male and that was statistically significant (p < 0.05). Diabetic neuropathy and female sex were found significantly associated with development of CTS with adjusted Odd Ratio 10.92 and 3.78 respectfully (p<0.0001). A similar study done by Galer et al³⁰ evaluated the prevalence of Carpal tunnel syndrome (CTS) in diabetics and associated risk factors. The strongest risk factors for CTS, in order of importance, were: female sex, older age and presence of neuropathy which is in accordance of our study findings, found that there were more CTS patients than control subjects who had diabetes (p=0.03; odds ratio, 3.02) which is in agreement of our study findings.²⁷ In other studies, DPN is found to be a major risk factor for developing CTS.^{21,22,31,32}

In our study, we recorded 58% patients developed carpal tunnel syndrome (CTS) in diabetic neuropathy patients while in non-diabetic neuropathy patients, that of 14% which was statistically highly significant. We also found diabetic neuropathy patients have 8.48 times higher possibility of development of CTS than non-diabetic neuropathy patients (p<0.0001). Diabetic neuropathy and female sex were found significantly associated with development of CTS with adjusted odd ratio 10.92 and 3.78 respectfully (p<0.05). Therefore, on our study findings CTS development is common in diabetic neuropathy patients in our country context. Examination of the hands and shoulders should be included in the evaluation of patients with diabetes. So, proper monitoring and advice may reduce the frequency of development of CTS in DPN patients.

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