

Does Peripheral Neuropathy Associate with Cranial Nerves Neuropathy in Type 2 diabetes Patients?

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Abstract

Diabetic peripheral neuropathy (DPN) is the most common complication of type 2 diabetes mellitus. Cranial neuropathies is usually presenting as mononeuropathies coexist with DPN either presented clinically or in subclinical form. The aim of this study is to detect cranial neuropathy in diabetic patients. Eighty three patients with type 2 diabetes mellitus (T2DM) with an age range of 30-69 years were included in the study. The study also involved normal healthy persons whose age and gender are harmonized with that of our patients that were deliberated as control group (60 persons). Diabetic patients with DPN had significant difference in age, highly significant difference in the duration of the disease and highly significance difference in BMI had poor glycemic control reflected by high FBS and HbA1c, while lipid profile picture showed insignificant difference when compared with diabetic patients without DPN. Nerve conduction study (sensory and motor) showed a significant difference regarding latency, amplitude, and conduction velocity between diabetic patients with DPN and those without DPN. The results of blink reflex showed highly significant difference between diabetic patients and controls.

Keywords: Diabetic peripheral neuropathy, Cranial neuropathy, nerve conduction study.

الخلاصة

الاعتلال العصبي المحيطي السكري هو أكثر المضاعفات شيوعا لداء السكري من النوع الثاني اعتلال الأعصاب القحفية عادة تظهر مع الاعتلال العصبي المحيطي السكري إما سريريا أو في شكل تحت الإكلينيكي. الهدف الرئيسي من هذه الدراسة هو تقييم لدور منعكس الطرفية في التشخيص المبكر لاعتلال الأعصاب القحفية لدى مرضى السكري من النوع الثاني مع أو بدون اعتلال الأعصاب. شملت الدراسة 83 مريضا ممن يعانون من داء السكري النوع الثاني ضمن الفئة العمرية من 35-69 سنة. وجدت الدراسة أن مرضى السكري مع اعتلال الأعصاب المحيطية لديهم رابطة كبيرة مع زيادة العمر ، و كبيرة للغاية مع مدة المرض، وأهمية عالية مع الفرق في مؤشر كتلة الجسم بالمقارنة مع مرضى السكري من دون اعتلال الأعصاب المحيطية بينت دراسة التوصيل العصبي (الحسية والحركية) فرق كبير بين الكمون، والسعة، وسرعة التوصيل بين مرضى السكري مع اعتلال الأعصاب المحيطية والذين لا يعانون من هذه الحالة. وأظهرت نتائج منعكس الطرفية فرق هام للغاية. **الكلمات المفتاحية:** اعتلال الاعصاب المحيطي السكري، اعتلال الاعصاب القحفي، دراسة التوصيل العصبي

Introduction

Diabetes Mellitus (DM) is a morbid disease worldwide, with increasing incidence as time passes. It has macro-vascular and micro-vascular complications. The main cause of these complications is poorly controlled postprandial hyperglycemia. The chronic hyperglycemia associated with diabetes contributed to the long last damage of body organs that happen in DM (ADA, 2015). The complications that arise from diabetes mellitus are numerous but generally its can full in to two categories: Macro vascular type of complications in form of cerebrovascular, cardiovascular and peripheral vascular diseases and micro vascular complications which is more common than former, include nephropathy, retinopathy and neuropathy and it result from chronic hyperglycemia (Aaberg *et al.*, 2008).

Regarding diabetic neuropathy (DN) , It is the most common micro vascular complication of DM with prevalence rate reaching 45-50% (Holiner *et al.*, 2013).

Diabetic peripheral neuropathy (DPN) is by far the most mutual type of diabetic neuropathy and in clinical practice, it's synonymous with diabetic neuropathy

(Jack *et al.*, 2012). Hyperglycemia regarded as the main causative factor accused for the developments and progression of diabetic neuropathy along with other micro vascular complications of diabetes (Van Dam *et al.*, 2013).

In addition to damaging effects of diabetes on peripheral nervous system (PNS), somatic cranial neuropathy in form of mono neuropathies also occur although it is rare (Nazliel *et al.*,2001; Shakouri & Davoudi 2006).

Aims of the study

Detecting cranial neuropathy in diabetic patients is the core of this study. The study designed to roll out the value of blink reflex in diagnosis of cranial neuropathy in diabetic patients with or without polyneuropathy.

Materials and Methods

This study was conducted in the unit of neurophysiology of merjan medical city in Babylon governorate through the period from *Jan.* 2014 till *Aug.* 2014.

In this case control study eighty three patients (39 males and 44 females) with an age range between 30-69 years conformed to have T2DM were included as patient group.

The patients were selected according to inclusion criteria, and were divided in to two groups according to presence or absence of peripheral neuropathy.

Additional 60 adults (24 males and 36 females) were also included as the control group whom their age was consistent with that of the patient group (30-69 years).

All the participants were subjected to same procedures as history, physical examination and investigations. Full history were taken from each patient regarding personal data, medical history focusing on history of diabetes, signs and symptoms of diabetes mellitus and peripheral neuropathy as well as history to exclude overt cranial nerves involvement and other causes of peripheral neuropathy. General examination to assess blood pressure, weight, height, and systemic examination was done including neurological examination. The neurological assessment included cranial nerves examination to evaluate any abnormalities focusing on trigeminal and facial nerve. **Biochemical Evaluation** done to verify the exclusion criteria to omit causes of PN other than diabetes mellitus, these were: red blood corpuscles count (RBCs count), hemoglobin Concentration, platelet Count, total white blood cells count (WBCs count), differential leukocyte count, determination of serum aspartate aminotransferase, determination of serum alanine aminotransferase, determination of serum alkaline phosphatase (ALP), determination of serum creatinine and quantitative determination of urea.

Furthermore, the patients and controls were submitted to other types of investigations in order to assess disease morphology like glycosylated hemoglobin (HbA1c), serum glucose measurement and serum lipid profile. **Electrophysiological testing** in form of conventional nerve conduction study (NCS) was done for each participant including at least four motor nerves tested (median, ulnar, tibial and peroneal), and three sensory nerves (median, ulnar and sural nerves). Limb temperatures is measured using adhesive skin patch and were maintained between 31-32C° by exposing the patient to radiant heater when needed, and the preparation of the skin done by cleaning the area by coarse skin detergent (Kimura, 2013).

Maximal responses were gained using electrical stimuli. Numerous parameters were measured for each nerve, these are distal latency, conduction velocity and waveform amplitude, duration and shape were stated and documented for each nerve at each stimulus site (Daube and Rubin, 2009).

Blink reflex

The procedure of blink reflex explained to patients and controls. The examining room was quiet and the patients were asked to closed their eyes slightly while the recording was done by putting the active electrodes above the eye. The procedure was done for both eyes and the obtained latency expressed by R1, ipsilateral R2 and contralateral R2 were measured and compered with standard value ((Preston & Shapora, 2013).

Statistical Analysis (Data Analysis)

Computerized SPSS program software 22 was used to analyze data which were expressed by means \pm stander deviation (SD). ANOVA was used to examine the differences between different groups and within groups. Comparison between control and patients and comparison between patients were performed also. The statistical difference considered to be significant when p value < 0.05 (Daniel, 1999).

Results**Socio Demographic data of the diabetic patients with or without diabetic peripheral neuropathy**

As shown in table 1 most diabetic patients aged between 50-59 years, most of them were female, uneducated, had positive family history of diabetes and urban.

Table 1: Socio Demographic data of the patients

Characteristics	groups	Patients
Age, year	30-39	6
	40-49	18
	50-59	35
	60-69	24
Gender	male	39
	female	44
Occupation	educated	28
	Non-educated	55
Residence	rural	30
	urban	53
Family history	Positive	64
	Negative	19

Blink Reflex

The results of blink reflex for diabetic patients with and without DPN and control group are shown in table (2). There are a significant ($p < 0.01$) differences between patients and control in latency which expressed as right R1(RTR1), left R1(LTR1), right ipsilateral R2 (RTipsiR2), left ipsilateral R2(LTipsiR2), right contralateral R2 (RTcontraR2) and left contralateral R2 (LTcontraR2).

Table (2): The results of blink reflex of diabetic patient with or without peripheral neuropathy and control

	Patients with DPN	Patients without DPN	Control subject	P value
RTR1	9.84±2.14	9.09±1.01	8.20±.60	0.001**
RT ipsi R2	30.37±7.80	28.22±6.01	23.70±2.50	0.001**
RT contraR2	30.08±8.49	29.48±6.33	24.30±3.30	0.001**
LTR1	10.02±2.79	9.32±1.30	8.20±.60	0.001**
LTipsiR2	30.45±7.92	28.22±5.86	23.50±2.70	0.001**
LTcontraR2	30.22±7.31	29.32±6.00	24.80±3.10	0.001**

**p value < 0.01 is highly significant; RTR1=right R1 ; RTipsiR2=right ipsilateral R2 RTcontraR2=right contralateral R2 ; LTR1=left R1 ; LTipsiR2=left ipsilateralR2 LTcontraR2=left contra lateralR2

Frequency of Diabetic Peripheral Neuropathy and Abnormal Blink in the Studied Groups

Figure 1 showed the percentage of DPN in the studied groups. Nearly 73.5% of diabetic patients had peripheral neuropathy while, 26.5% of the diabetic patients were normal.

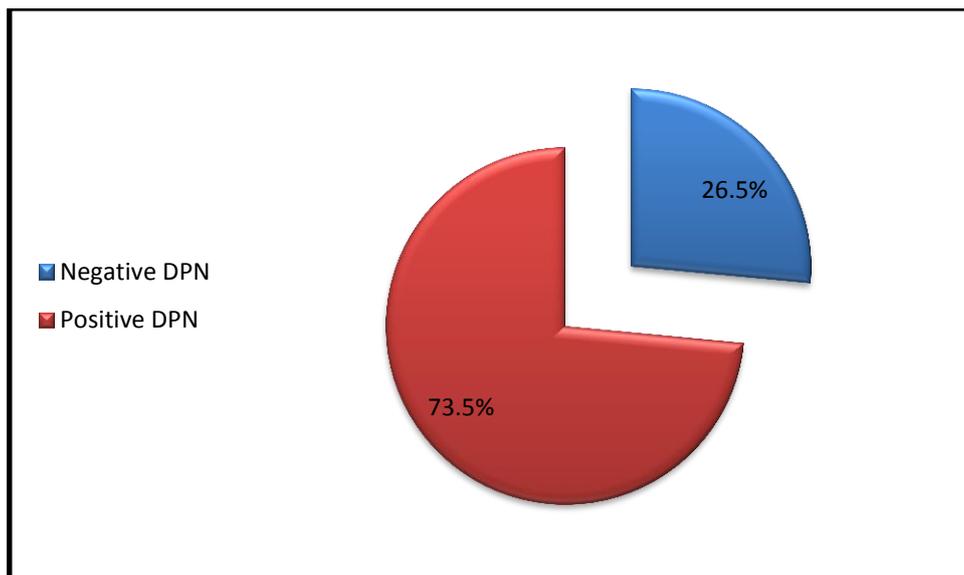


Figure 1: The frequency of diabetic peripheral neuropathy in the studied groups

The rate of abnormal blink reflex express in (figure 2). It was found that 55.4% of the patients had normal blink reflex. Meanwhile 44.6% of the patients had abnormal blink reflex.

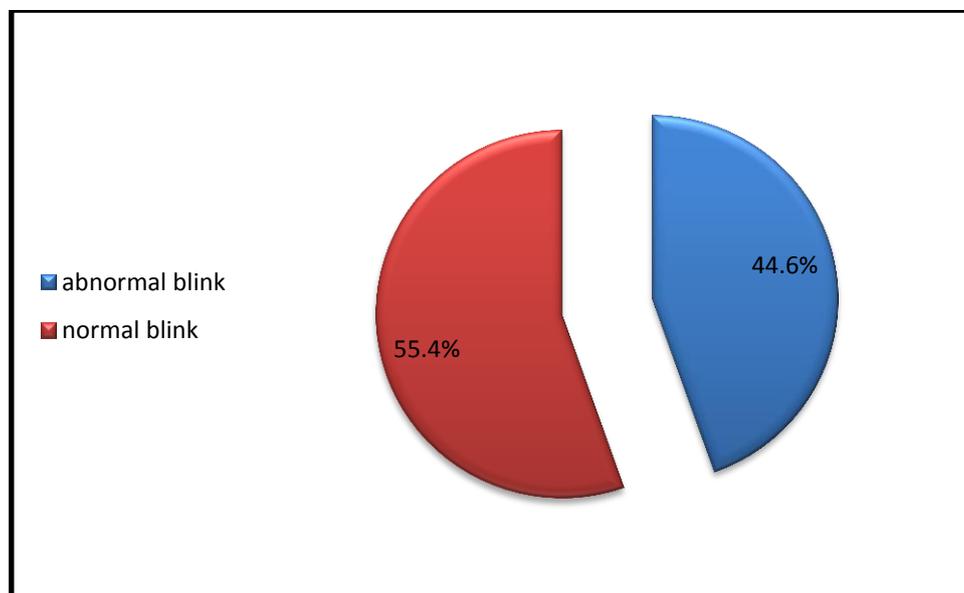


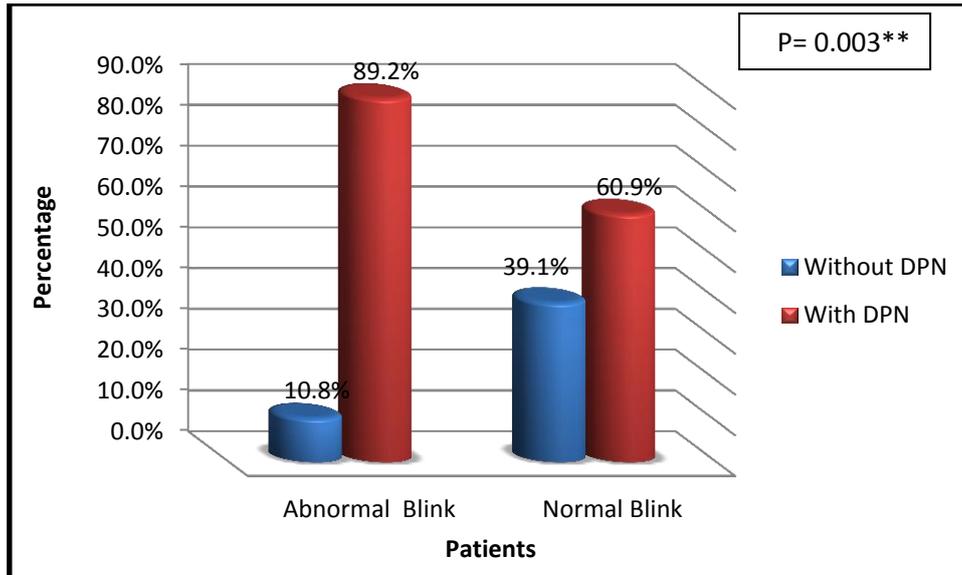
Figure 2: Frequency of abnormal blink reflex in the studied groups

Relation Between Blink Reflex and Diabetic Peripheral Neuropathy

The blink rate was compared in the studied group according to the presence and absence of DPN (Figure 3 and Figure 4). Most of the patients with abnormal blink had DPN (89.2%). There was a significant ($P < 0.05$) difference in blink in relation to DPN.

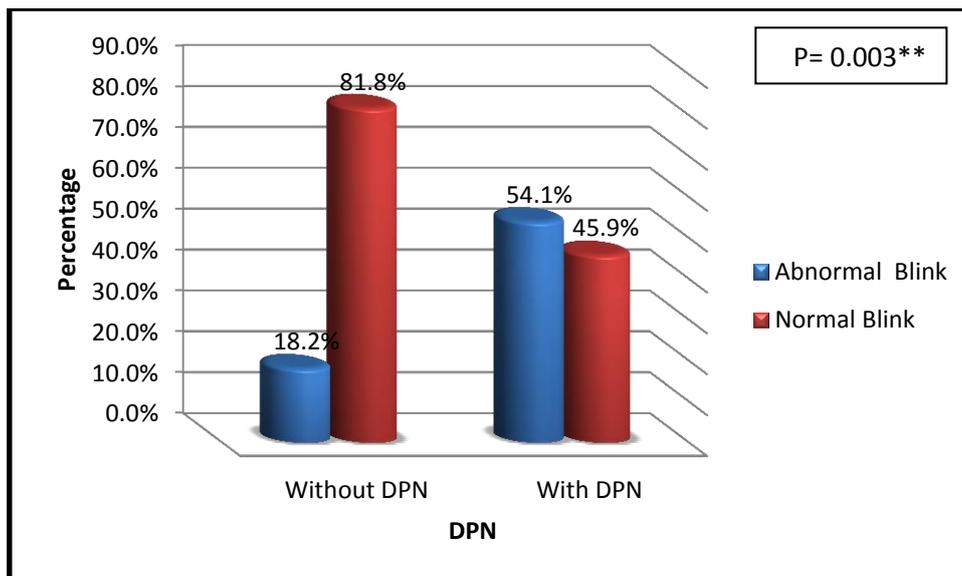
The odds ratio for the of blink was about five time more in diabetic patients with DPN when compared with diabetic patients without DPN (Odds ratio = 5.29; CI= 0.057- 0.623, p-value = 0.003).

This result means if a diabetic patient had diabetic peripheral neuropathy he will have five times more risk to develop cranial nerves neuropathy which is either avert or subclinical reflected by abnormal blink reflex.



**p value < 0.01 is highly significant

Figure 3: Relation between blink reflex and peripheral neuropathy



**p value < 0.01 is highly significant

Figure 4: Relation between peripheral neuropathy and blink reflex

Discussion

The Interpretation of Blink Reflex (Table 2)

According to this study blink reflex shows highly significant ($p < 0.01$) differences in latency expressed by RTR1, LT R1, RTipsiR2, LTipsiR2, RTcontraR2 and LTcontraR2 between patients and controls (table 2). These results indicate that blink reflex is highly sensitive procedure in detecting subclinical craniopathy. This results agree with (Kennelly, 2006; Guney *et al.*, 2008).

Also this study agree with Guney, (2012) who stated that both R1, ipsilateralR2 and contralateralR2 latencies in all diabetic patients with or without polyneuropathy

were prolonged relative to controls and the differences were statistically significant ($p < .001$), also R1 latencies in diabetic patients with polyneuropathy were prolonged relative to diabetic patients without polyneuropathy and the differences were statistically significant ($p < .001$). These findings presumably reflect that facial nerve is severely involved in diabetic polyneuropathy. At last (Guney, 2012) stated that blink reflex can be useful tool for detection of clinically silent intra axial brainstem functional abnormalities or extra axial lesions in patients with polyneuropathy.

The Study of the Frequency of Diabetic Peripheral Neuropathy and Abnormal Blink in the Studied Groups (Figure 1, 2)

According to this study abnormal blink reflex founded in 44.6% of the studied group while 55.4% of the patients had normal blink reflex (Figure 2). Nazliel *et al.*, (2001) stated that abnormal blink reflex responses were found in 55% of patients studied. Also Kazem & Behzad (2006) studied blink reflex in diabetes in which Abnormalities were found in 54.4% of diabetic patients.

This high percent of abnormal blink reflex suggests that blink reflex testing is a useful method for obtaining early diagnosis of cranial nerve compromise in diabetic patients who do not show any clinical symptoms or signs of cranial nerve involvement.

The Study of the Relationship between Blink Reflex and Diabetic Peripheral Neuropathy (Figure 3, 4)

According to this study most patients with abnormal blink reflex had DPN (89.2%) and only (10.8%) of the patients did not had DPN (Figure 3).

Furthermore, 60.9% of the patients who had normal blink reflex were founded to have DPN while 39.1% of them did not show DPN (Figure 3). The blink reflex study in patients with DPN abnormal in 54.1% and the rest had normal (Figure 4). Patients without DPN exhibit 81.8% of normal blink reflex and only 18.8% of them showed abnormal blink reflex. There was a significant ($P < 0.05$) difference in blink in relation to DPN.

All these data collectively showed that peripheral neuropathy increases the risk of cranial nerves neuropathy which was reflected by abnormal blink reflex. This in agreement with other study (Pawar *et al.*,2012) who stated that all the latencies of blink reflex in diabetic patients with polyneuropathy were significantly prolonged relative to diabetic patients without polyneuropathy. This finding also consistent with the results of Elkholy and her coworkers (2014) who stated that diabetic patients with peripheral neuropathy showed significantly prolonged distal latency and reduced amplitudes of the blink response as compared to patients without peripheral neuropathy.

Conclusions

1. Sub clinical cranial nerve neuropathy coexists with DPN.
2. Diabetic peripheral neuropathy increases the risk of cranial neuropathy.
3. Nerve conduction study is a valuable method to diagnose DPN.
4. Blink reflex is appreciated noninvasive and useful method for the evaluation and diagnosis of subclinical cranial nerve involvement in diabetic patients.

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