Tawfik *et al.*
Egyptian Rheumatology and Rehabilitation (2022) 49:51
https://doi.org/10.1186/s43166-022-00149-7

Egyptian Rheumatology and Rehabilitation

RESEARCH Open Access

Patterns of facial and blink reflex abnormalities in type 2 diabetes mellitus patients with short disease duration: a clue to subclinical cranial neuropathy

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Abstract

Background: Cranial neuropathies occur in 3 to 14% of diabetic patients. Motor conduction study of the facial nerve and blink reflex study are electrophysiologic techniques used to assess the facio-trigeminal pathway in diabetic patients. The patterns of facial and blink reflex abnormalities are inconsistent among studies. This study aimed to assess the subclinical facial nerve and blink reflex abnormalities patterns in short-duration type 2 diabetes mellitus patients. This cross-sectional study included 30 type 2 diabetic patients with disease duration $\leq$ 5 years. We included only patients with the Toronto clinical neuropathy score $\leq$ 5. We enrolled 30 age- and sex-matched healthy subjects as a control group. We performed facial nerve motor conduction and blink reflex studies. Patients with prior history of cranial nerve lesions, stroke, or any other disease-causing polyneuropathy or drug-induced neuropathy were excluded from the study.

Results: Thirty diabetic patients were included, 20 females (66.7%) and ten males (33.3%). Their mean age was 52.63 $\pm$ 8.94 years. None of the patients had clinical evidence of neuropathy. There were significant differences between patients and controls in the distal latencies and amplitudes of facial nerve compound muscle action potentials and contralateral R2 late response latencies of the blink reflex. We detected subclinical cranial abnormalities in 6 diabetic patients (20%). One of them (3.3%) had facial nerve conduction abnormalities, four of them (13.4%) had blink reflex abnormalities, and one of them (3.3%) had both facial nerve and blink reflex abnormalities.

Conclusion: Subclinical cranial neuropathy can occur in short-duration type 2 diabetes mellitus patients. We detected different blink reflex patterns and facial conduction study abnormalities. We recommend blink reflex and facial nerve conduction studies as simple tests for the early evaluation of neurological subclinical affection in patients with short disease duration of T2DM as they may appear in the absence of peripheral neuropathy.

Keywords: Subclinical diabetic neuropathy, Cranial neuropathy, Electrophysiological studies

Background

Diabetes mellitus (DM) has reached epidemic international proportions, particularly in developing countries [1]. In the Eastern Mediterranean region, DM prevalence was 3.5–25% in 2003 and is expected to rise to 9–30% by 2025 [2, 3]. Diabetic neuropathies (DN) are the most prevalent chronic microvascular complications

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of diabetes (50 to 90%) [4, 5]. Diabetic neuropathies are classified into generalized and focal neuropathies [6, 7]. Generalized neuropathies include diabetic sensorimotor polyneuropathy (DSPN), acute painful polyneuropathy, and autonomic neuropathy. Focal/multifocal neuropathies include cranial neuropathy, mononeuritis, mononeuritis multiplex, radiculoplexus neuropathy, and entrapment neuropathy [6, 7].

Diabetic cranial neuropathies manifest as mononeuropathies. Multiple cranial neuropathies are less common [8], although they can occur concurrently in diabetic patients and may be the presenting symptom of newly diagnosed diabetes or glucose intolerance [8].

Diabetic patients have a ten-time increase in the incidence of cranial nerve palsies [8], and the occurrence of cranial nerve affection (painful or painless) varies between 3 and 14% [9]. The facial and oculomotor nerves are among the most commonly affected nerves, while the trochlear, trigeminal, glossopharyngeal, and vagus nerves are less frequently affected [8–11]. The prognosis is favorable for most patients recovering spontaneously within 3 to 5 months [8].

Diabetic neuropathies not only are a late complication but also can develop during the disease [7]. Facial nerve motor conduction and blink reflex (BR) studies are electrophysiologic techniques used for the assessment of the facial nerve and the facio-trigeminal pathway in diabetic patients, including those with early diagnosed type 2 diabetes (T2DM) [9].

Different studies [11–15] showed significant prolongation in distal latency (DML) and reduction of the amplitude of facial compound muscle action potential (CMAP) in diabetic patients compared to controls. In addition, a significant delay in the early response (R1), ipsilateral late response (R2I), and contralateral late response (R2C) of the BR were detected in diabetic patients compared to controls [11–17]. Facial nerve abnormalities were reported in 5 to 23.9% [10, 11] and BR abnormalities in 26 to 55% of diabetic patients [10, 11, 15].

Few studies, however, presented patterns of facial and BR abnormalities at individual levels. These patterns delineate sites of involvement along the cranial nerves pathway, both intra- and extra-axial, and may help to reveal the underlying pathophysiologic mechanisms (vascular, inflammatory, and neurodegenerative) [18, 19].

This work aimed to detect the pattern of the subclinical BR and facial nerve conduction abnormalities in the early diagnosed T2DM. The main reference of the current study was detected by Aramideh and his colleagues [18], who used autopsy and magnetic resonance images in localizing the abnormalities of the BR in the facial-trigeminal pathway.

In contrast to manifestations in the distal portions of the body, particularly the lower extremities, the subclinical trigeminal and facial nerve complications in T2DM are not adequately investigated. However, patients' quality of life and well-being depend on proper trigeminal function (which includes efficient mastication, food enjoyment, communication, and intimacy) [20] and facial function (face expressions). That gives attention to screening and detection of the subclinical trigeminal and facial neuropathy in T2DM of short duration.

Methods

This study is a cross-sectional case-control study. We enrolled 30 diabetic patients from those attending the outpatient clinics of Physical Medicine, Rheumatology and Rehabilitation Department, Alexandria, and Main University Hospital. In addition, 30 healthy age- and sex-matched volunteers were enrolled as a control group. The clinical diagnosis of T2DM was according to the World Health Organization criteria for diagnosis of DM [21]. Patients with short-duration T2DM were included (disease duration from 6 months to 5 years). Demographic data were recorded. General and neurological examinations (cranial, motor, sensory, and reflexes) were performed. Moreover, laboratory investigations, such as fasting blood glucose level, 2-h postprandial, and glycated hemoglobin (HbA1C), were performed for them.

All cranial nerves were examined to assess any abnormalities, focusing on the trigeminal and facial nerves. Motor, sensory, and reflexes are components of the trigeminal nerve. We tested ophthalmic, maxillary, and mandibular sensory branches with cotton wool.

Regarding the motor component, masseter and temporalis muscles were inspected, and then, patients were asked to clench their teeth to test power. Patients were asked to open the jaw and keep it open against resistance to test pterygoid muscle power. The corneal and jaw jerk reflexes were done. Facial muscles were examined: facial movements (upper and lower face) using the Sunnybrook Facial Grading System (by comparing both sides of the face as regards eye movement, nasolabial fold, and mouth movement in the standard face expressions). The examination of the sensory branch of the facial was done by assessing the taste sensation over the anterior two-thirds of the tongue [22].

The Toronto clinical neuropathy scoring system (TCNS) [23] was used to measure changes in early DSPN pathophysiology because of its content validity [23]. The TCNS score of each patient was recorded out of 19. It was used to categorize the severity of neuropathy [24]. No neuropathy (0 to 5), mild neuropathy (6 to 8), moderate (9 to 11), and severe diabetic neuropathy (12 to 19).

We enrolled only patients with a score of ≤ 5 points (no clinical DSPN).

Electrophysiological assessment

Neuropack 2 electromyograph apparatus (MEB-7102K) and (MEB-9400) from the Nihon Kohden (Japan) were used to perform the electrophysiological studies of this work [25]. The temperature of the room was adjusted for standardized results.

We studied facial motor nerves bilaterally by measuring the DML and amplitude for nasalis and orbicularis oculi muscles. The stimulation site was just below the ear anterior to the tragus. An active recording electrode was placed lateral to the mid-nose and a reference electrode was placed on thecontralateral side of the nose at the same site for recording from the nasalis muscle. An active recording electrode was placed inferior and slightly lateral to the pupil at mid-position, and a reference electrode was placed just lateral to the lateral canthus for recording from the orbicularis muscle. We placed the ground electrode at the wrist of the patient. Abnormalities of the facial nerve conduction study were determined based on a comparison of normative data obtained from the control group. Values exceeding the cutoffs (mean ± 3SD in DML and mean ± 2SD in amplitude) obtained from the control group were abnormal [14].

Blink reflex recording was simultaneously performed on both sides of the face using a two-channel recording apparatus. We only needed a current of 15 to 25 mA to get supramaximal stimulation. We set the duration of the electrical pulse to 100 μs. We set sensitivity at 100 to 200 μV per division; we set the sweep speed at 5 to 10 ms per division, and the filter motor settings were 10 Hz and 10 kHz. The following BR parameters were recorded: ipsilateral early response (R1), ipsilateral late response (R2I), and contralateral late response (R2C) latencies. Abnormalities of the BR parameters were determined based on a comparison with normative data got from the control group. Values exceeding the cutoffs (mean ± 2SD) obtained from the control group were abnormal. Interpreting BR abnormalities for localization of the lesion across the BR arc pathway was done according to Aramideh et al. [18] and electromyography neuromuscular disorders [25]. Latency differences of over 1.2 ms between the right and left sides for the R1 responses, 5.0 ms for the R2I and 7.0 ms for R2C responses, were abnormal [25].

In addition, peripheral sensory and motor conduction studies of upper and lower limbs were done to detect associated subclinical DSPN. Antidromic sensory conduction studies of median, ulnar, superficial radial, and sural nerves were performed [25]. Motor conduction studies and F-wave responses of the median, ulnar, posterior tibial, and deep peroneal nerves were performed [25].

The local ethics committee of the Faculty of Medicine approved this current study at the Alexandria University. We got written consent from all the studied patients and controls.

Statistical methods

Data were analyzed using the Statistical Package for Social Science. Qualitative data were described using numbers and percentages. Quantitative data were described using the range, arithmetic mean, standard deviation, and median. The chi-square test (χ^2) was used to categorize variables and compare between different groups. Student *t*-test (t) was used for comparison of normally distributed quantitative variables, while the Mann-Whitney test (U) was used for comparison of abnormally distributed quantitative variables to compare the two studied groups. Kruskal-Wallis *H*-test (H) was used for comparison of more than two groups. Pearson correlation coefficient test (r) was used to measure the statistical association between two continuous variables. Spearman's correlation coefficient (rs) was used to measure the strength and direction of association between two variables on at least an ordinal scale.

Results

The study included 30 diabetic patients with a mean age of 52.63 ± 8.94 years, ranging from 31 to 65 years; 20 were females (66.7%), and 10 were males (33.3%). Thirty healthy subjects were enrolled as a control group; 19 were females (63%), and 11 were males (37%). Their age ranged from 40 to 65 years, with a mean of 51.07 ± 7.75 years. No significant differences were found between patients and controls regarding age and gender ($P = 0.305$ and 0.260, respectively). Duration of DM ranged from 8 months to 5 years, with a mean of 3.15 ± 1.43 years.

The fasting blood glucose level of diabetic patients ranged from 73 to 358 mmol/l with a mean of 181.5 ± 73.88 mmol/l. Two-hour postprandial glucose levels ranged from 120 to 550 mmol/l with a mean of 272.9 ± 108.6 mmol/l. On the other hand, the HbA1C of the studied patients ranged from 6.5 to 11.9 and had a mean of 8.9 ± 1.67. All patients were receiving oral hypoglycemic drugs.

None of the patients had subjective facio-oral complaints or objective evidence (signs) of cranial neuropathy on the clinical examination. The TCNS ranged from 0 to 5 points bilaterally with a median of 3.0 (2.0–4.0), indicating the absence of clinical neuropathy.

Table 1 Comparison between the diabetic and control groups regarding facial nerve parameters

	Facial nerve	Diabetics ($n = 30$)	Controls ($n = 30$)	Test of sig.	*P*
Orbicularis oculi	**DL**	3.06 ± 0.58 (2.50–6.80)	2.87 ± 0.25 (2.20–3.30)	$U = 1299.0$*	0.008*
	Amplitude	1.84 ± 0.48 (1.10–3.0)	2.73 ± 1.32 (0.30–7.0)	$U = 831.0$*	< 0.001*
Nasalis	**DL**	3.60 ± 0.52 (2.50–5.50)	3.20 ± 0.54 (2.50–4.70)	$t = 4.177$*	< 0.001*
	Amplitude	1.54 ± 0.28 (1.20–2.50)	2.88 ±1.34 (0.60–8.0)	$t = 7.634$*	< 0.001*

Data are presented as mean ± SD (minimum-maximum). *t*, Student *t*-test; *U*, Mann-Whitney test; *n*, number; *DL*, distal motor latency; *P*, *P*-value for comparing between the studied groups. *Statistically significant at $P \leq 0.05$

Table 2 The cutoff values of the electrophysiological parameters of the studied facial nerves branches (orbicularis oculi & nasalis)

	Orbicularis oculi	Nasalis
Distal latency (ms)	3.6	4.8
Amplitude (mv)	0.75	0.9

Table 3 Comparison between the diabetic and control groups regarding blink reflex latencies

Blink reflex	Diabetics	Controls	*t*	*P*
R1	10.70 ± 1.09 (8.40–13.80)	10.76 ± 1.08 (9.10–13.0)	0.337	0.737
R2I	35.30 ± 4.10 (25.0–42.90)	34.30 ± 3.03 (30.0–42.0)	1.505	0.135
R2C	37.16 ± 4.38 (27.30–48.60)	34.89 ± 3.53 (32.20–44.0)	3.093*	0.002*

Data are presented as mean ± SD (minimum-maximum). *t*, Student *t*-test; *BR*, blink reflex; *R1*, early response; *R2I*, ipsilateral late response; *R2C*, contralateral late response; *P*, *P*-value for comparing between the studied group. *Statistically significant at $P \leq 0.05$

Table 4 Cutoff values of the electrophysiological parameters of the studied blink reflex

Blink reflex	Latency (ms)
Early response	12.9
Ipsilateral late response	41.4
Contralateral late response	44.3

Electrophysiological results

Regarding the electrophysiological study of the facial nerve, the DML was significantly prolonged, and the amplitude was significantly reduced in the diabetic group compared to controls (Table 1). Abnormalities in facial nerve conduction study were values exceeding the cutoffs (mean ± 3SD for the DML and mean ± 2SD for the amplitude) got from the control group (Table 2).

The BR showed statistically significant prolongation of the mean latency of R2C in patients compared to controls ($P = 0.002$) with no difference regarding the mean latencies of R1 and R2I, as shown in Table 3. Abnormalities of the BR were values exceeding the cutoffs (mean ± 2SD) got from the control group (Table 4).

Individual data analysis

We found subclinical cranial neuropathy in 6 patients (20%). One patient (3.3%) had abnormal facial nerve conduction study, 4 patients (13.4%) had abnormalities in BR study, and one patient (3.3%) had both facial nerve conduction study and BR abnormalities.

The facial nerve conduction study was abnormal (exceeding the cutoff value) in 2 patients (6.7%) (one female & one male). The diabetic female patient had prolonged DML and diminished amplitude in the right facial nerve with involvement of both branches (to orbicularis oculi & nasalis) (Fig. 1). The diabetic male patient had prolonged DML in the left facial nerve involving only the branch to orbicularis oculi muscle, as well as having right trigeminal neuropathy abnormality in the BR (absent right R1, R2I, and R2C).

We detected abnormalities of the BR in 5 patients (16.7%) (4 males & one female). Figures 2, 3, 4, 5 and 6 show patterns of BR abnormalities in those patients. These represented four patterns:

1. Absence of right R1, R2I, and R2C in one patient (3.3%) which localizes the lesion at the peripheral pathway (right trigeminal neuropathy). This patient has left facial neuropathy as well.
2. Delayed left R2I and R2C (lesion of the spinal complex of the left trigeminal nerve) were detected in two patients.
3. Delayed left R1 (left mid-pontine lesion) found in one patient.

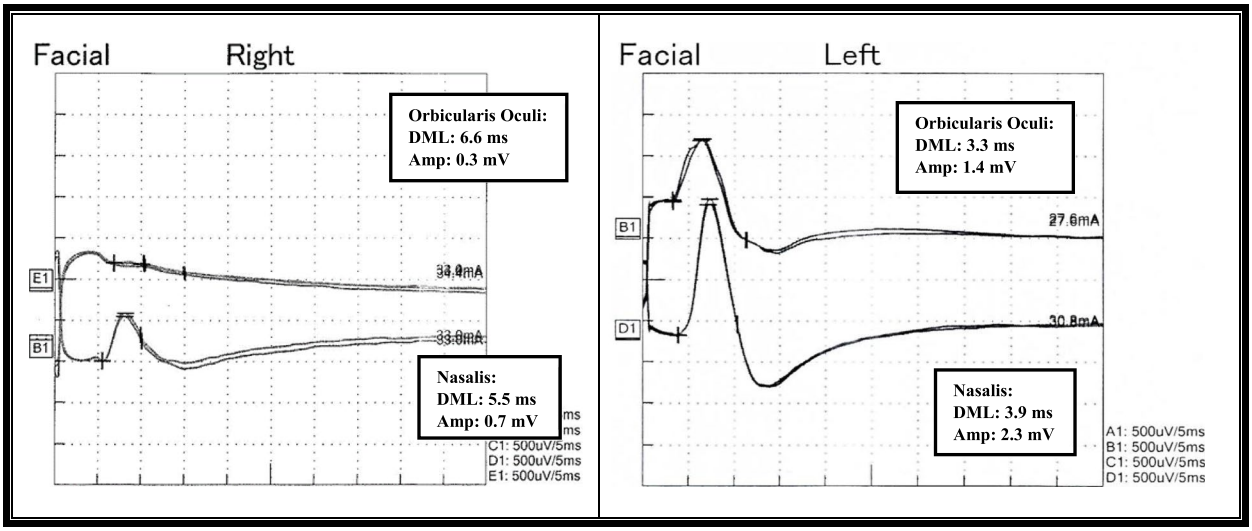

Fig. 1 Bilateral facial nerve conduction study of a 63-year-old diabetic female patient showing mixed demyelinating-axonal degeneration neuropathy of the right facial branches: orbicularis oculi and nasalis. DL, distal latency; Amp, amplitude

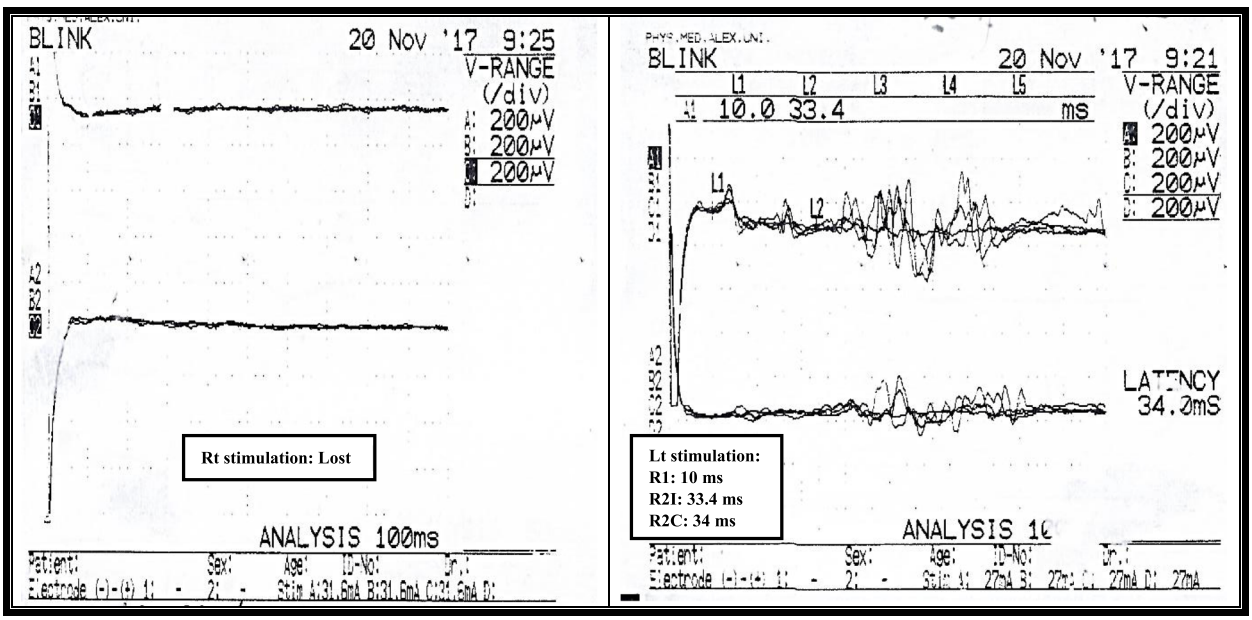

Fig. 2 BR study of a 60-year-old diabetic male patient showing right trigeminal neuropathy (absent right R1, ipsilateral R2, and contralateral R2). R1, early response; R2I, ipsilateral late response; R2C, contralateral late response

4. Delayed left R2I and absent R2C bilaterally (left trigeminal spinal complex and crossed interneuron fibers lesion) were detected in one patient.

Patterns 2, 3, and 4 are consistent with lesions in the central pathway (13.4%).

We presented a comparison between patients and controls in parameters of sensory and motor nerve conduction studies of the upper and lower limb nerves (Table 5). We found electrophysiological evidence of subclinical DSPN in 7 patients (23.3%). Only two patients (28.6%) out of 7 patients with subclinical DSPN had subclinical cranial neuropathy (both had BR abnormalities). Four

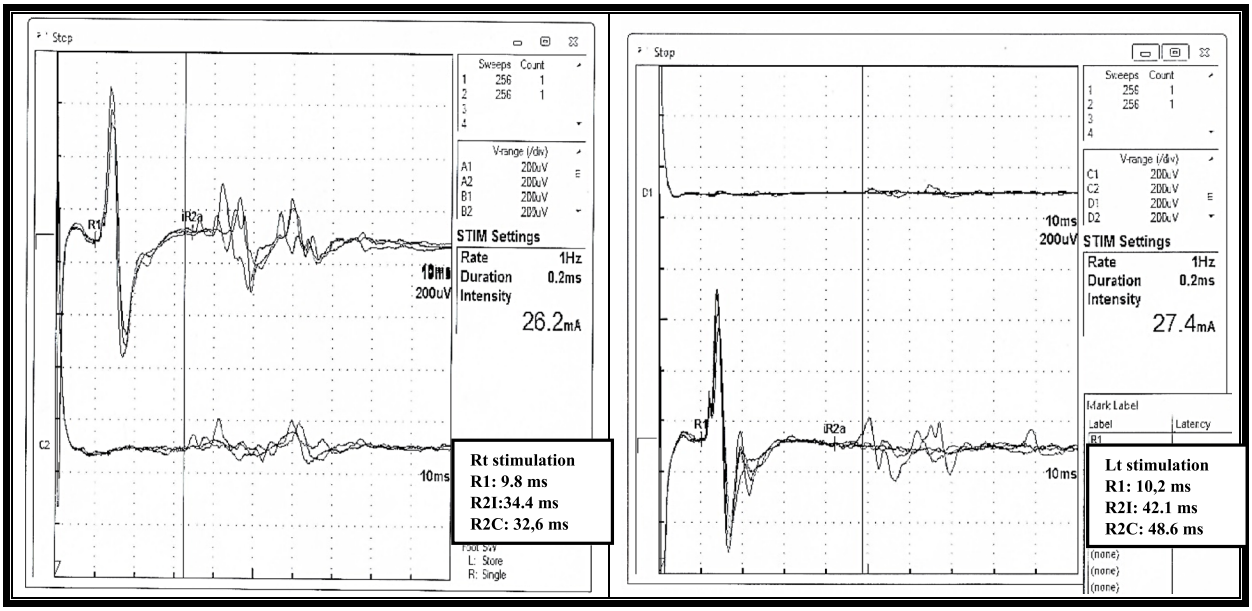

Fig. 3 Blink reflex study of a 65-year-old diabetic male patient A showing left trigeminal spinal complex neuropathy (delay left R2I and R2C). R1, early response; R2I, ipsilateral late response; R2C, contralateral late response

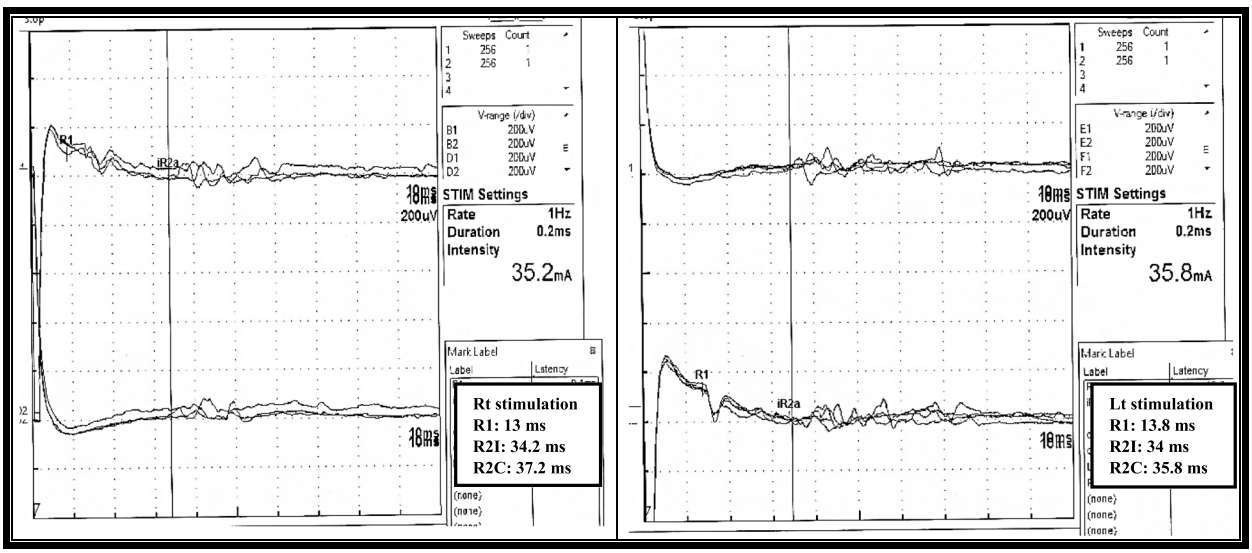

Fig. 4 Blink reflex study of a 37-year-old diabetic male patient A showing left mid-pontine fibers neuropathy (delay left R1). R1, early response; R2I, ipsilateral late response; R2C, contralateral late response

patients (17.4%) out of 23 patients without DSPN had subclinical cranial neuropathy.

Facial nerve conduction and BR abnormalities had positive correlation with age ($r = 0.389$, $P = 0.002$) and no correlation with disease duration ($rs = -0.082$, $P = 0.532$), HbA1C ($r = -0.123$, $P = 0.349$), or subclinical DSPN ($rs = 0.036$, $P = 0.79$) (Table 6).

Discussion

Diabetic cranial neuropathies are less common than peripheral neuropathies, and the exact incidence is unknown [9, 26]. Subclinical cranial neuropathy (trigeminal & facial involvement) was reported to be 7.5-fold more frequent in T2DM patients than in the nondiabetics [27].

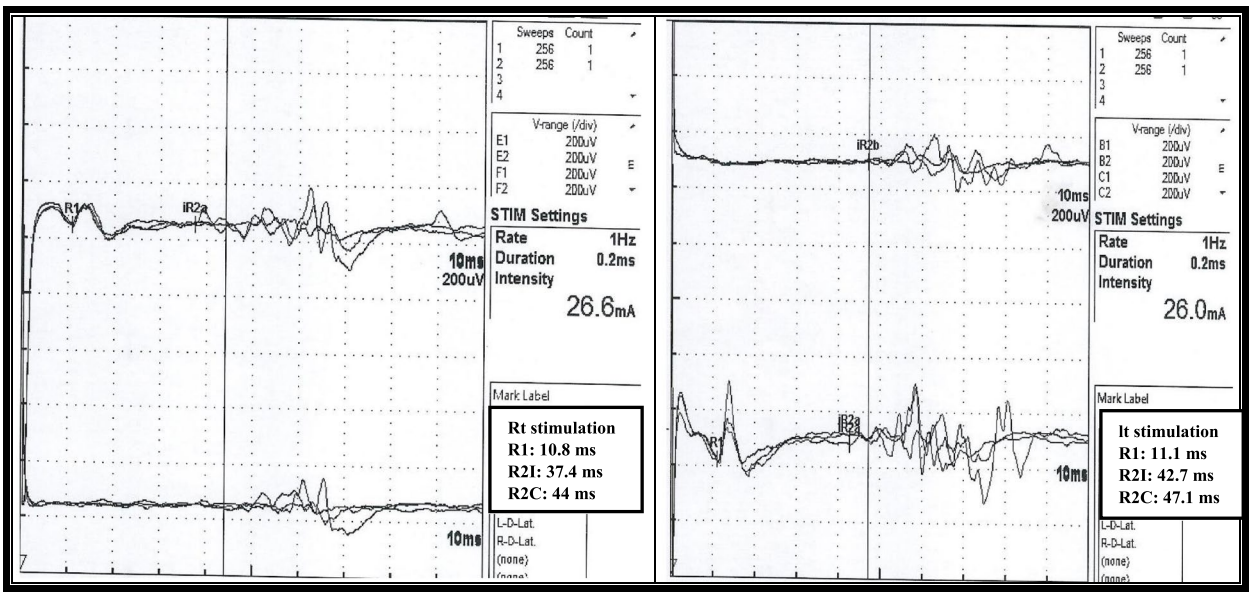

Fig. 5 Blink reflex study of a 63-year-old diabetic female patient showing left trigeminal spinal complex neuropathy (delay left R2I and R2C). R1, early response; R2I, ipsilateral late response; R2C, contralateral late response

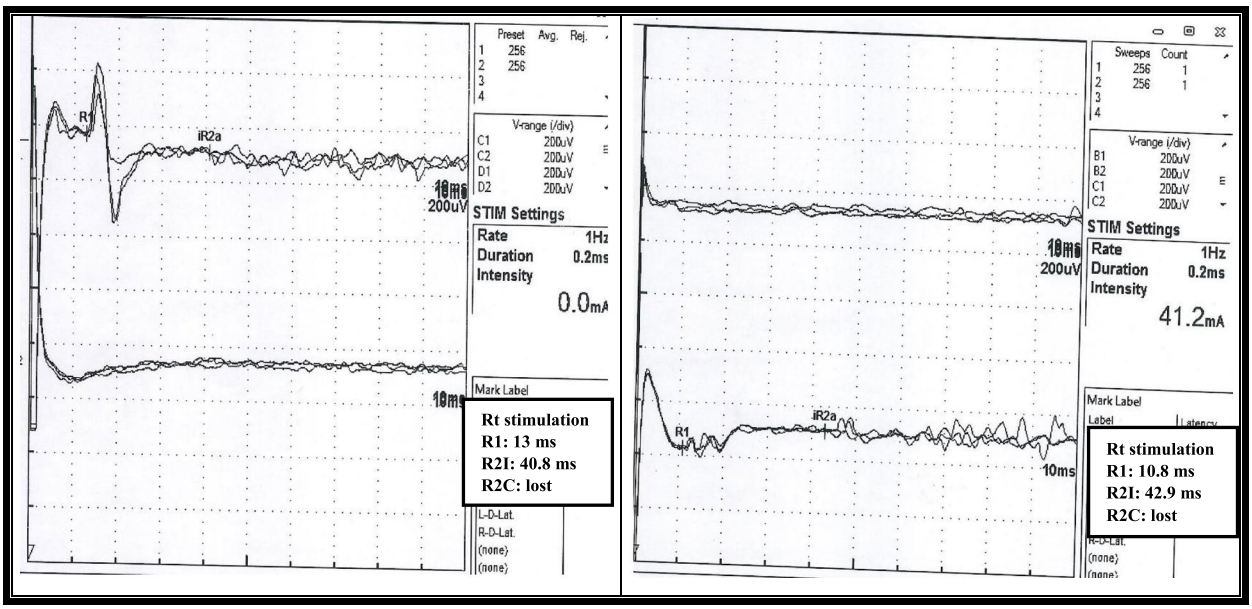

Fig. 6 Blink reflex study of a 63-year-old diabetic male patient A showing left trigeminal spinal complex and crossed interneuron fibers lesion (delay left R2I and absent R2C bilaterally). R1, early response; R2I, ipsilateral late response; R2C, contralateral late response

In the current study, 20% of the studied diabetic patients had abnormalities in facial nerve and BR studies, which indicates that subclinical cranial neuropathy is not uncommon in short-duration T2DM patients. Mean DML of facial nerve was significantly prolonged, and mean amplitude was significantly diminished in diabetic patients compared to controls. Leventoğlu et al. (2009) [28], and Metwally et al. (2014) [9], showed significantly delayed facial nerve DML in early diagnosed diabetic patients compared to controls with no significant difference in facial nerve CMAP amplitude. They concluded that the evaluation of facial nerve DML may improve

diagnostic yield and should be included in the routine evaluation of diabetic patients [28].

Unilateral subclinical facial neuropathy was found in 2 of the currently studied patients (6.7%). Similarly, Urban et al. (1999) [27] found subclinical facial neuropathy in 6.2% of diabetic patients indicating that subclinical facial nerve involvement is not infrequent in T2DM.

As regards blink reflex, the present work showed significant prolongation of mean latency of R2C in patients compared to controls, with no significant change regarding the mean latencies of R1 and R2I. This can be explained by the fact that R1 is conducted by oligo-synaptic exteroceptive intermediate thickness myelinated A-beta fibers, while R2 is conducted by polysynaptic nociceptive thin myelinated A-delta fibers [16, 29]. Thin myelinated fiber pathology is thought to occur before large fiber early involvement in the prediabetic and newly diagnosed T2DM [30]. Moreover, the prolongation of R2 latencies is secondary to altered conduction of the central polysynaptic circuits in diabetic patients.

Similarly, both Guney et al. (2008) [17] and Elkholy et al. (2014) [16] found a significant prolongation of R2C response in patients compared to controls and reported that the R2C is the most sensitive response in the BR. It aids in the identification of subclinical cranial neuropathy in T2DM, indicating sensory dysfunction and neural hyper-excitability [17]. Xiao et al. (2021) [31] explained that the reflex arc of R2 and the intermediate neurons of the reticular structure have a multisynaptic connection that is vulnerable to many circumstances, including thalamic and brain lesions [31].

Additionally, the current study detected subclinical abnormalities of the BR in 16.7% of the studied diabetic patients. These results suggest that BR can be helpful as a tool for evaluating and diagnosing diabetes patients with subclinical cranial neuropathy [31]. In line with these results, Elkholy et al. in (2014) [16] found that 20% of diabetic patients with a disease duration of 6.75 ± 4.30 years had abnormal BR manifested as delayed mean latency of R2C.

Regarding patterns of BR and facial nerve abnormalities, they are quite variable among studies. In the present study, the BR pattern abnormalities localized the subclinical cranial neuropathy along the BR arc in the trigeminal nerve either in the peripheral pathway (3.3%) or in the central pathway (13.4%). Accordingly, it was suggested that BR can be used as an indicator of cranial neuropathy whether central or peripheral, as well as the conduction channels that connect them [31]. Several authors [10, 11, 15, 17, 18, 32, 33] suggested that BR is a highly sensitive approach for pinpointing lesions of the trigeminal or facial nerves, as well as lesions of the brain stem, even at an early stage.

The absence of facial neuropathy in the BR results highlights the importance of performing a facial nerve

Table 6 Correlation between age, disease duration, the HbA1C level, and subclinical DSPN with cranial neuropathy in the diabetic group

Parameter	Cranial neuropathy	
	Test	*P*
Age (years)	$r = 0.389$*	0.002*
Disease duration	$r_s = -0.082$	0.532
HbA1C	$r = -0.123$	0.349
Subclinical DSPN	$r_s = 0.036$	0.79

r, Pearson coefficient; r_s, Spearman coefficient; *P*, *P*-value for comparing between the studied categories. *Statistically significant at $p \leq 0.05$. *HbA1C*, glycated hemoglobin; *DSPN*, distal symmetrical sensorimotor polyneuropathy

Table 5 The significant sensory and motor conduction study parameters of the upper and lower limbs

Nerve	Parameters	Diabetic ($n = 30$)	Control ($n = 30$)	*U*	*P*
Sural nerve	CV (m/s)	44.62 ± 8.74	46.75 ± 2.68	11142.5*	0.007*
Superficial radial nerve	Amplitude (μV)	20.67 ± 8.36	21.92 ± 3.51	1131.0*	0.001*
Sensory median nerve	CV (m/s)	46.63 ± 8.50	54.62 ± 2.35	575.5*	< 0.001*
Sensory ulnar nerve	CV (m/s)	53.58 ± 4.28	58.49 ± 3.99	710.0*	< 0.001*
Common peroneal nerve	Amplitude (μV)	3.17 ± 1.73	5.05 ± 1.27	673.1*	< 0.001*
	CV at the leg (m/s)	43.43 ± 4.48	50.62 ± 3.29	353.0*	< 0.001*
Posterior tibial nerve	CV at the leg (m/s)	41.77 ± 4.56	46.17 ± 2.38	616.0*	< 0.001*
Motor median nerve	DML (ms)	4.38 ± 1.15	3.66 ± 0.42	853.5*	< 0.001*
	CV at the forearm (m/s)	52.71 ± 5.22	55.55 ± 2.59	986.0*	< 0.001*
	F-wave minimum latency (ms)	27.91 ± 2.77	25.86 ± 2.61	1036.5*	< 0.001*
Motor ulnar nerve	DML (ms)	2.88 ± 0.37	2.69 ± 0.25	1128.5*	0.001*
	CV at the forearm (m/s)	54.88 ± 4.73	59.21 ± 3.86	861.5*	< 0.001*

Data are presented as mean ± SD (minimum-maximum). *DML*, distal motor latency; *U*, Mann-Whitney test; *CV*, conduction velocity. *P*, *P*-value for comparing between the studied group. *Statistically significant at $p \leq 0.05$

conduction study in screening for subclinical facial neuropathy in T2DM. This could be explained by the distal to proximal neural damage as a character of DN [34]. In addition, the changes (prolonged latency reflecting conduction slowing) in the facial nerve conduction study in the current work are mild and mostly diluted by the long pathway and multiple synapses along the BR pathway. Unfortunately, we did not measure BR amplitude to detect the abnormalities related to axonopathy.

The frequency of subclinical cranial neuropathy in patients with subclinical DSPN (28.6%) was higher than that in patients without DSPN (17.4%). These results agreed with Elkholy et al. (2014) [16] who found that 35% of diabetic patients with DSPN have abnormal BR compared to 5% of diabetic patients without PN. In addition, Lai et al. (2020) [35] and Xiao et al. (2021) [31] found that R1, R2I, and R2C latencies were all longer in patients having DSPN. They concluded that patients with DSPN have a higher risk of cranial nerve abnormalities than diabetic patients without clinical DSPN [16, 31, 35]. Moreover, Fadhil et al. in (2017) [15] concluded that DSPN increases the risk of cranial neuropathy. This can be explained through the fact that the microvascular complications of T2DM can cause damage to somatic cranial nerves by a similar mechanism to peripheral nerves (metabolic, vascular, and other causes) [16].

In the current study, there were 5 patients with subclinical DSPN who had no cranial neuropathy. In addition, there was no significant correlation between subclinical cranial neuropathy and subclinical DSPN. This indicates that cranial neuropathy can occur in isolation with the absence of peripheral neuropathy in diabetic patients [26]. The relation between DSPN and the occurrence of cranial neuropathy was variable in the literature. Kazamel et al. (2015) [26] reported that cranial nerves may be affected in T2DM in isolation without DSPN. Fadhil et al. (2017) [15] suggested that peripheral neuropathy raises the possibility of cranial nerve neuropathy. There was no explanation for this so far. Accordingly, BR and facial nerve conduction studies are effective methods for detecting subclinical cranial nerve abnormalities in diabetic patients with short duration.

We found that subclinical cranial neuropathy was not correlated with disease duration and HbA1C. These results agree with the results of Irkeç et al. (2001) [14] who found no correlation between facial nerve conduction study parameters and both duration of diabetes and HbAlC values. Additionally, Trujillo-Hernández et al. (2003) [29] reported that BR abnormalities can occur even in patients with a short period of T2DM. However, Shahine (2013) [36] found no correlation between BR abnormalities and diabetic disease duration. El-Bardawil et al. (2019) [37] found no correlation between BR abnormalities and HbA1C. On the other hand, this study showed that cranial neuropathy had a positive significant correlation with age that can be explained by age-related reduction of dopamine production by dopaminergic neurons in the substantia nigra, which can affect trigeminal-facial stimulation [13].

Conclusions

In conclusion, subclinical cranial neuropathy can occur in short-duration T2DM patients even in the absence of DSPN. We detected different patterns of abnormalities in blink reflex and facial nerve conduction studies. We recommend blink reflex and facial nerve conduction studies as simple tests for the early screening of cranial neuropathy in diabetic patients.

Limitations

The limitation of the current study includes a small number of studied patients. We need more extensive assessment techniques for abnormalities detection in the central trigeminal-facial pathway as magnetic resonance imaging.

Abbreviations

HbA1C: Glycated hemoglobin; BR: Blink response; CMAP: Compound muscle action potential; DML: Distal motor latency; DN: Diabetic neuropathy; DSPN: Distal symmetrical sensorimotor polyneuropathy; R1: Early response; R2C: Contralateral late response; R2I: Ipsilateral late response; T2DM: Type 2 diabetes mellitus; TCNS: Toronto clinical neuropathy scoring system.

Acknowledgements

Not applicable.

Authors' contributions

Conception and design of the study, HS, GY, and GT. Recruitment of patients, GT. Electrophysiology of the patients, WE. Data collection, GT. Analyzing and interpreting data, GT and WE. Manuscript preparation and revision, HS, GY, WE, and GT. The authors read and approved the final manuscript.

Funding

The present work was not funded.

Availability of data and materials

The data that support this study are available at Gihan Abd EL-Fattah Tawfik (the corresponding author) on reasonable request.

Declarations

Ethics approval and consent to participate

Approval of study conduction was obtained from the Ethical Committee at the Faculty of Medicine Alexandria University FAW 00018699/020951. All patients included in this study gave written informed consent to participate in this research.

Consent for publication

Not applicable

Competing interests

The authors declare that they have no competing interests.

Received: 10 June 2022 Accepted: 29 August 2022
Published online: 26 September 2022

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