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Pudendal nerve versus lower limb nerves electrophysiological abnormalities in diabetics with erectile dysfunction in Baghdad

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Abstract:

Background: Erectile dysfunction (ED) is the persistent inability to perform and maintain penile erection strong enough for fulfilling sexual interaction. It is caused by autonomic neuropathy, vasculogenic causes, endocrine deficit, drug-induced, psychosocial problems, or a combination of these causes.

Objective: This study aims to compare pudendal neuropathy against limb neuropathy in diabetics complaining of erectile dysfunction through electrophysiological studies.

Methodology: Eighty-four diabetic males were enrolled in this analytic cross-sectional study presented with erectile dysfunction. All participants were assessed by electrophysiological studies using Bulbocavernosus Induced Reflex to assess the competence of the pudendal nerve. Other nerve studies were used to assess lower limb nerve competence. The study was conducted in Ghazi Al-Hariri Surgical Teaching hospital in Baghdad for the period from October 2021 to June 2022.

Results: Nerve assessments revealed earlier involvement of the peripheral lower limb nerves in comparison with pudendal nerve.

Conclusion: Electrophysiological assessment is a practical test which can be used in identifying neurologic deficit among diabetic patients with erectile dysfunction.

Keywords: Erectile dysfunction, Electrophysiological assessment, Diabetes Mellitus.

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Introduction:

Erectile Dysfunction (ED) is defined as the persistent inability to perform and maintain penile erection strong enough for fulfilling sexual interaction, according to the National Institutes of Health.(1)(2). It is related positively to older age. The worldwide prevalence averages from 1% - 10% for males less than 40 years, up to 15% for men 40 - 49, up to 30% for men 50 - 59, up to 40% men from 60 - 69, and 50% - 100% for men from 70 - 90.(3)(4) Many causes are deemed to be associated with ED and can be categorised as organic (vascular, neurogenic, hormonal, or medication-related side effects), and non-organic, mainly psychogenic factors.(5) (6) Among organic causes, diabetes is the most frequent cause of impotence with 52.5% incidence rate for diabetic men aged 48-64 years.(7)(8) Raised blood sugar (hyperglycaemia) induces molecular and cellular deterioration of vascular and neural structure and function primarily responsible for the development of chronic complications in diabetes. Another factor that significantly contributes to the development of long-term consequences of diabetes is oxidative stress. In addition, neuropathy and angiopathy caused by diabetes may result in malfunctioning of cells, tissues, and organs.(9) (10) Elevated intracellular glucose levels in the neurons oversaturates the usual glycolytic pathway.(11)(12)

Upon which the glucose takes the autonomic route and transforms into fructose and sorbitol. As a result, the permeability of the cell membrane (the Na+/K+-ATPase pump) is diminished leading to reduced action potentials of the cell. Oxidative stress depletes the oxygen supply to the nerve cells, inhibits their ability to proliferate, and causes cellular apoptosis, or cell death; this results in progressive neuropathy.(11)(13)(14) Several previous studies showed that 43% of autonomic neuropathy was among those > 47 years old and 51.2% with peripheral somatic neuropathy among those > 40 years. (15) (16) (17) In addition, the relationship between peripheral neuropathy and impotence, particularly in people with diabetes, is not well-established or proven yet. In other words, diabetic individuals with ED are believed to have underestimated peripheral neuropathy. (15)(18) Thus, the main objective of this study is to identify which neuropathy happens earlier, the peripheral or the pudendal.

Methods:

This cross-sectional study was performed in Ghazi Al-Hariri Surgical Teaching Hospital, affiliated with Baghdad Medical College, from

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October 2021 to June 2022 on 84 diabetic males between 30 – 70 years of age. Diabetic males who presented with impotence regardless the types of diabetes, with or without peripheral neuropathy, were included in the study. The cases underwent the same clinical, biochemical and electrophysiological evaluations for the pudendal and peripheral nerves only. Any case with a neurologically-related condition other than diabetes was excluded to avoid any interference with the results. Patient's data were collected through history taking, physical and neurological examination, and laboratory assessment. Two standard scoring system questionnaires were implemented, the Toronto Clinical Scoring System (TCSS) and the International Index of Erectile Dysfunction-5 (IIED-5), for clinical categorisation of peripheral neuropathy and erectile dysfunction, respectively. Electrophysiological tests were performed on all subjects at the electrophysiological department.(20) The Bulbocavernosus reflex (BCR) was considered a reliable method for measuring the pudendal nerve integrity by using a ring stimulating electrode placed on the penile shaft, with a distance of 2-3 cm between both active and reference electrodes, setting the former more distal than the latter, respectively.(21)(22) The BCR is recorded via a concentric electrode which is inserted into the bulbocarvenosus (BC) muscles, the insertion site is 2-3 cm anterior to the anal orifice in the midway between the scrotum and the anus with few millimetres lateral to the perineal raphe line on both sides. The depth of the insertion is around 1-2 cm which depends on the body build of the subject. The proper needle position was confirmed by the pelvic floor voluntary contraction, which was, elicited by squeezing the anal sphincter or coughing many times throughout the session, as well as squeezing the glans penis while observing the EMG wave on the monitor as illustrated in Figure 1 **- Sacral reflexes (28)**

.(23)(24) Stepwise rectangular pulses with durations of 0.1 and/or 0.2 msec and intensities starting at "0" up to 300 v were used to stimulate the penis glans. The sweep speed for recording ranged from 5 to 10 msec, while the stimulation sensitivity was set on 200 µV.(25) The psychosensory threshold for feeling in the penis mainly the glans was identified by a stepwise stimulation increment per l sec.(25) The latency was assessed by determining the distance from stimulus to the first upward wave direction (negative peak), and is considered abnormal when it was more than 42 msec or absent. Figure 2 shows the reflex single CMAP.(25)(26) (27) Furthermore, lower limb peripheral nerves were assessed by electrodiagnostic studies mainly motor and sensory nerves (common peroneal, sural and tibial nerves).

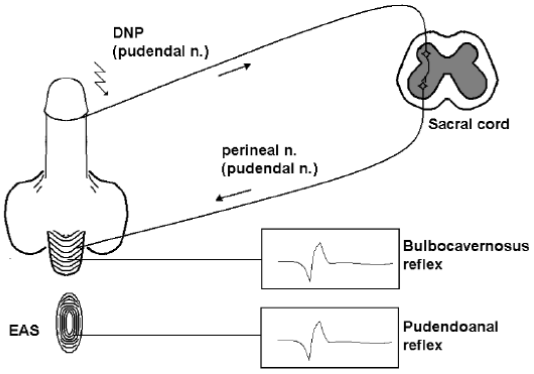

Figure 1 - Sacral reflexes (28)

Table 1 –BCR latency values

Group	Latency	
	Mean±SD msec.	(Range) msec.
Normal	38.4±3.87	31.1 - 42.05
Prolonged	48.8±2.56	43.1- 52.82
Absent	0	0

Figure 2– BCR response of one of the included cases

Statistical analysis: The data was processed by comparing differences between electrophysiological recording of the pudendal nerve and the lower limb nerves in diabetic subjects with impotence. The results were analysed using SPSS version 25, and the means ± SD were compared using an independent T-test. Association and the percentage using Pearson Chi-square tests whenever is applicable to test associations between variables. A P-value of <0.05 is considered statistically significant.

Result:

Of all the 84 diabetic males with impotence included in this study, 73.8% had ED with peripheral neuropathy while 26.2% had ED without peripheral neuropathy.

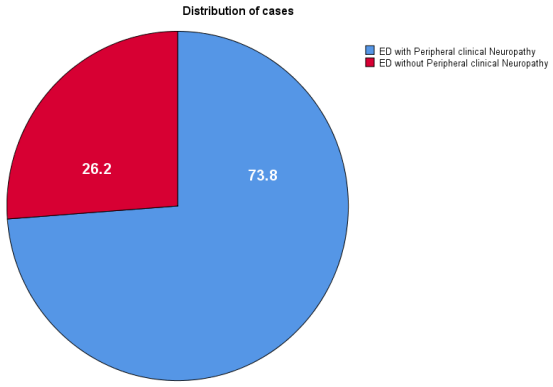

Figure 3 - Distribution of the study group by neuropathy

The mean age of the cases was (45.4 ±6.60) ranging from 32 to 62 years, 52.3% of the cases were between 41-50 years of age. The mean duration of diabetes was (8.4±2.81 years) with a range of 4 - 15 years. The mean duration of ED was (2.6±1.92) ranging from 1 - 8 years. HBA1c showed a mean value (9.2±1.94) ranging from 6.5 - 14. BMI had a mean value of (27.5±2.67) ranging from 22 - 32. Clinical scoring was performed to assess ED and peripheral neuropathy by using IIED-5 and TCSS, respectively. The results revealed that 45.2% of the cases complained from a moderate degree of clinical ED, and 31% suffered from moderate degree of clinical peripheral neuropathy.All 84 diabetic males were evaluated using the BCR method to assess the pudendal nerve integrity and neurological functionality. The results revealed that 40.5% were with normal latency of pudendal nerve of < 42 msec, with a mean value of (38.4±3.87). Although 4.8% showed absent response, the majority of the subjects 54.7% revealed a prolonged latency of > 42 msec (48.8±2.56) as shown in

Table ***1***. Table 2 shows the BCR results for the Pudendal nerve and lower limbs peripheral nerves through the Nerve Conduction Studies (NCS) latency to test for association of lower limb nerves in comparison with pudendal nerve latencies, which were statistically significant for all nerves (motor and sensory). Most patients had abnormal NCS findings with 59.5% for the pudendal nerve (prolonged or absent latency) and 40.5% had normal pudendal nerve NCS result. Both motor and sensory nerves of the lower limbs NCS revealed that 69% had abnormal findings and 31% had normal findings. There was a clear difference between clinical evaluation and electro-diagnostic study as shown in (**Error! Reference source not found.**) which revealed that all cases had various degrees of ED according to IIED-5 assessment. However, the electro-diagnostic study of the pudendal nerve by BCR showed that 59.5% have abnormal findings. The same steps were conducted on the lower limbs peripheral nerves, through clinical evaluation using TCSS which showed that the majority of the cases (73.8%) had some degree of peripheral neuropathy. The electro-diagnostic study showed that only 69% of the cases had either motor or sensory involvement or both. This demonstrates the association between diabetes mellitus, peripheral neuropathy and erectile dysfunction duration, almost all of the cases had peripheral neuropathy symptoms earlier than erectile dysfunction.

Table 2 – Contingency table testing the association between NCS of pudendal nerve and other lower limb nerves

Variable	Category	Pudendal Nerve Latency (NCS) No, (%)				P-value
		Absent	Prolonged	Normal	Total	
Peroneal N. Latency	Normal	0 (0.0)	6 (7.1)	26 (31.0)	32 (38.1)	0.001
	Prolonged	4 (4.8)	30 (35.7)	12 (14.3)	46 (54.8)	
	Absent	0 (0.0)	6 (7.1)	0 (0.0)	6 (7.1)	
Tibial N. Latency	Normal	0 (0.0)	12 (14.3)	32 (38.1)	44 (52.4)	0.001
	Prolonged	4 (4.8)	24 (28.6)	6 (7.1)	34 (40.5)	
	Absent	0 (0.0)	6 (7.1)	0 (0.0)	6 (7.1)	
Sural N. Latency	Normal	0 (0.0)	2 (2.4)	14 (16.7)	16 (19.0)	0.009
	Prolonged	2 (2.4)	18 (21.4)	20 (23.8)	40 (47.6)	
	Absent	2 (2.4)	22 (26.2)	4 (4.8)	28 (33.3)	

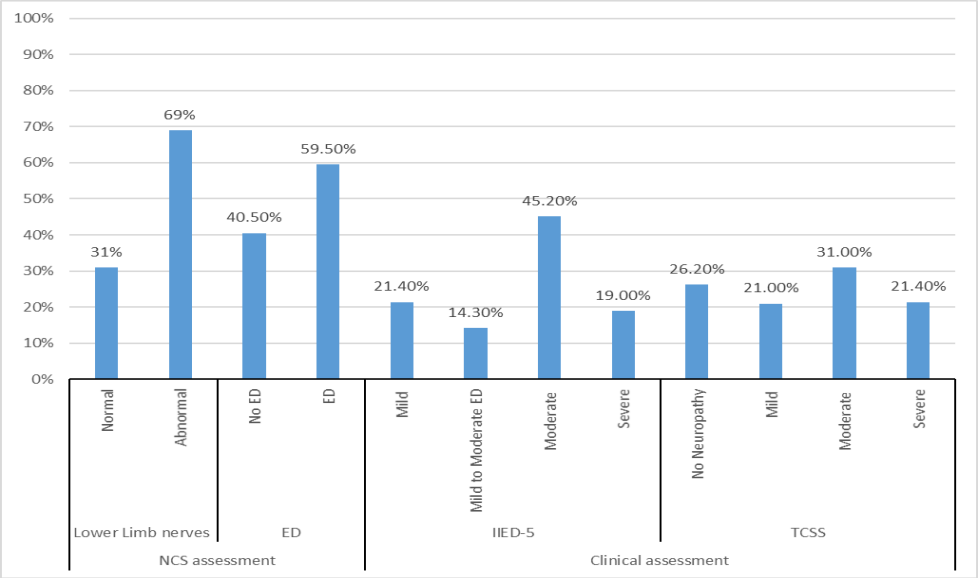

Figure 4 – Distribution of the cases based on NCS and clinical assessments

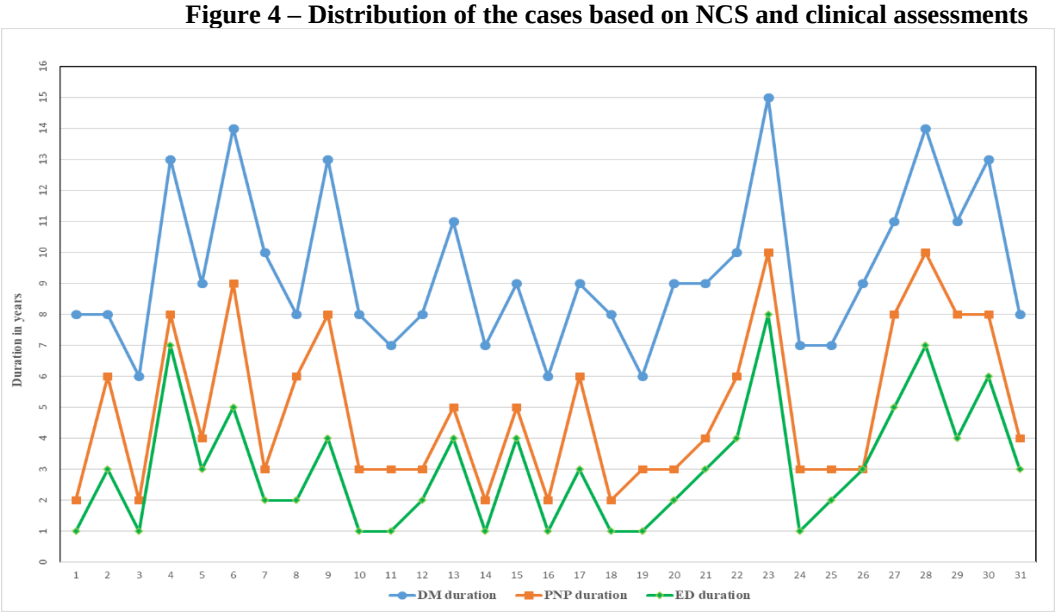

Figure 5– Duration of diabetes, peripheral neuropathy and erectile dysfunction

Discussion:

The erection process needs an active interaction between both parasympathetic and sympathetic autonomic systems to have a completed process, with the former playing an essential role in this process.(29) The somatic route is carried out by the pudendal nerve which ends by the penile dorsal nerve. It includes the afferent limb of the pudendal nerve (sensory), S2-S4 (sacral spine), and the efferent limb of the pudendal nerve (motor).(24) When the BCR arcs are damaged, no reaction is elicited, and when the afferent and efferent limbs are partially damaged, the BCR is prolonged. (30) The current study indicated that nerve conduction abnormality of the pelvic nerves was found in 59.5% of diabetic men with erectile dysfunction. This refers to 46 impotent diabetic subjects out of 84 patients; which is close to the results of previous studies.(25)(26)(27) Abnormal findings of prolonged or absent BCR latency indicates a neurological deficit, which plays an essential role in explaining the impotent status of the cases. These findings are in line with the results of previous study. (31) The electrodiagnostic studies of the peripheral nerves of the lower limbs demonstrated that 69% of the patients have confirmed peripheral neuropathy, in terms of sensory, motor or both. Additionally, IIED-5 was not sufficient to prove the link between clinical complaints of ED with the results of an electrodiagnostic study of BCR. There is a major contribution of peripheral neuropathy effect in those diabetic patients with ED, as well as it is consistent with the previous study regarding underestimation of peripheral neuropathy in ED. (15)(17)(18) Onuf's nucleus, located in the sacral ventral horn, is where most of the motoneurones (MNs) that control the pudendal nerve is found. Although the anterior horn cells assigned for pudendal nerve motor fibres are small in comparison with other motor neurones of the lower limb motor fibres, the conduction velocity of motor fibres of the pudendal nerve is similar to motor fibres of the lower limb

nerves.(32) This confirms the association of abnormal BCR latency with peripheral lower limbs nerves latency. The study explored the earlier onset and longer duration of peripheral neuropathy However, ED was sufficient to bring the patients to seek medical attention as early as possible. In our study, there were several limitations which can be summarized as follows: The small size of the study group, which might not be representative, and the short period of the study limiting the utilization of other relevant electrodiagnostic studies like Sympathetic Skin Response test (SSR) which may add a positive value in evaluating the autonomic nervous functionality. Another limitation is the unavailability of penile vascular assessment tools or instruments like penile Doppler to assess the vessels' vascular competency. This could exclude other causes for ED in diabetic patients who showed normal BCR latency.

Conclusion:

The study had shown a strong association between pudendal neuropathy and neuropathy of the peripheral nerves of the lower limbs.

Authors' Contributions: Authors' Contributions: Dr.Mohammed J. Al-Hadeethi: Student. Prof. Najeeb H. Mohammed: Supervisor

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التقييم الكهروفسلجي للعصب الفرجي لدى مرضى داء السكري المصابين بضعف الإنتصاب

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الخلاصة:
الخلفية: ضعف الإنتصاب هو عدم القدرة المستمرة على أداء الإنتصاب والحفاظ عليه بقوة كافية لتحقيق التفاعل الجنسي وهو ناتج عن اعتلال الأعصاب اللاإرادي، أو أسباب مرتبطة باعتلال الأوعية الدموية، أو عجز الغدد الصماء، أو بسبب أدوية معينة، أو المشاكل النفسية والإجتماعية.
الهدف: تهدف هذه الدراسة إلى مقارنة إعتلال العصب الفرجي مقابل إعتلال الأطراف العصبية لدى مرضى السكري الذين يشكون من ضعف الإنتصاب من خلال التقييم الكهروفزيولوجي.
المنهجية: تم تسجيل أربعة وثمانين رجلاً مصابًا بالسكري في هذه الدراسة المقطعية التحليلية المقدمة مع ضعف الإنتصاب. تم تقييم جميع المشاركين من خلال الدراسات الكهروفسلجية. أجريت الدراسة في مستشفى غازي الحريري الجراحي التعليمي في بغداد للفترة من تشرين الأول 2021 إلى حزيران 2022.
النتائج: كشفت تقييمات الأعصاب عن إعتلال مبكر لأعصاب الأطراف السفلية الطرفية بالمقارنة مع العصب الفرجي.
الاستنتاج: التقييم الكهروفزيولوجي هو إختبار عملي يمكن استخدامه في تحديد العجز العصبي لدى مرضى السكري الذين يعانون من ضعف الانتصاب.
الكلمات المفتاحية: ضعف الانتصاب, التقييم الكهروفيزيولوجي, داء السكري .