Original Article

Correlation of Serum Irisin Level with Nerve Conduction Study in Diabetic Patients

Zaid Talib Saleh Alfahham and Falah Mahdi Dananah

ABSTRACT

Objective: To assess irisin hormone in diabetic peripheral neuropathy and to assess the relation between irisin hormone and nerve conduction study.

Study Design: Meta-analysis of observational study

Place and Duration of Study: This study was conducted at the Marjan Teaching Hospital in Babil City in Endocrinology and Diabetes Center from 1st January 2025 to 31st March 2025.

Methods: Forty one diabetic patients divided into two groups, 22 patients with diabetic peripheral neuropathy and 19 patients without diabetic peripheral neuropathy. Patients with diabetic peripheral neuropathy are diagnosed based on history and clinical examination with assistance of Michigan Neuropathy Screening Instrument scoring system. Serum irisin, nerve conduction study of sural nerve (amplitude, velocity) and sural/radial amplitude ratio are doing for all patients.

Results: Irisin hormone level was significantly lower in patients with diabetic peripheral neuropathy (143.18 pg/ml) than patient without diabetic peripheral neuropathy (203.29 pg/ml), (p=0.0001) and the relation between irisin hormone and sural nerve conduction study and sural/radial amplitude ratio in both groups show no significant correlation.

Conclusion: The irisin hormone level is significantly decreased in DPN patients. There is no significant correlation between irisin and nerve conduction study of sural nerve and sural/radial amplitude ratio.

Key Words: Type 2 diabetes mellitus, Diabetic neuropathy, Irisin hormone, Nerve conduction study, Sural nerve

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INTRODUCTION

Type 2 DM is one of the most common noncommunicable disease in the world, it accounts for about 90% of diabetes cases globally. It's prevalent about 580 million in 2024 and 635 million at risk to develop diabetes.[1]

The complications of diabetes are serious and impact on the health and quality life of the patients. It includes vision loss, CAD, kidney failure and lower limb amputation.[2] One of the major complication is diabetic peripheral neuropathy that affects 50% of diabetes patients. In addition, approximately half of these cases may be present without symptoms, this led to serious complication like foot ulcer that may lead to limb amputation.[3]

Department Medical Physiology, Faculty of Medicine, University of Kufa, Iraq.

Correspondence: Zaid Talib Saleh Alfahham, Department Medical Physiology, Faculty of Medicine, University of Kufa, Iraq.
Contact No: 07813323385
Email: zaidalfahaam@hotmail.com

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The most common type of diabetic peripheral neuropathy is diabetic distal symmetrical polyneuropathy that constitutes about 80-90% of diabetic neuropathy.[4]

Irisin hormone is a myokine derived from FNDC5 protein in proteolytic mechanism by PGC1α named referring to the "Iris" a Greek messenger of the Gods. It discovered in 2012 by Boström and his colleagues as an exercise-induced hormone. The first description of its role is converting white adipose tissues to brown adipose tissues by what is called beiging, and this conversion aid by irisin via increase thermogenesis gene expression in white adipose tissues. Activation of brown adipose tissues dissipates energy as a heat; this can help in weight loss in obesity and T2DM patients.[5] After that, it was found that irisin also regulates glucose homeostasis by preventing gluconeogenesis and enhancing glycogen synthesis in the liver and helps in improving insulin resistance. For that, the interest is increased in researchers over all world to explore more effects of this hormone in physiological and pathological aspects.[6]

Later, it was found beneficial effect on the nervous system by enhancing memory, cognition and learning after brain injury such as stroke and cerebral ischemia.[7] Additionally, it can induce skeletal muscles hypertrophy by activating stem cell in the muscle (satellite cell) and so helping in protein synthesis.

Moreover, in model of muscle denervation, irisin can save muscle from atrophy.[8] In addition, there is a suggestion about irisin may induce neuronal differentiation and proliferation but need further studies to confirm it.[9]

The level of irisin in T2DM patients is controversy, most studies show decrease level of irisin[10]; conversely, some studies report increase level of irisin[11]; also, a few studies find no link between irisin and diabetes mellitus.[12]

Regarding irisin level in diabetic complications, the studies also report controversial result, most of them report lower irisin levels in patients with diabetic complication than without complications.[13] Regarding diabetic neuropathy, there are limited studies that correlate irisin hormone with it. However, two studies report a significant decrease in irisin hormone in diabetic neuropathy in comparison with diabetics without neuropathy.[14,15]

Nerve Conduction Study considers the gold standard tools to diagnosis the DPN. Moreover, it can be used for severity determination, follow up and screening of DPN.[16] The vast majority of polyneuropathy is axonal degeneration; it includes nearly all diabetic patients. On NCS it is demonstrated by decreasing amplitude and normal or slightly decrease in latency and conduction velocity.[17] Diabetic peripheral neuropathy can also be diagnosed with other tools like single fiber electromyography (SFEMG).[18]

The most sensitive nerve for evaluating DPN is the sural nerve. It is preferred because of many reasons related to the anatomical and pathophysiological features of DPN. Many authors agree for the first impairment appears in sural nerves. On the other hand, some authors suggest the NCS of the further distal nerves than sural, such as planter nerves, may be an early detector for DPN.[19] Up to know, there is no study correlating irisin hormone with nerve conduction study in diabetic patients.

The purpose of this study is to assess the level of irisin hormone in diabetic peripheral neuropathy patients. Also, to find the correlation between irisin hormone and nerve conduction study in diabetic patients.

METHODS

This study was conducted at Marjan Teaching Hospital in Babil City in Endocrinology and Diabetes Center from 1st January 2025 to 31st March 2025 vide letter No. MEC-101 dated 22/12/2024. This study involves 41 diabetic patients divided into two groups, 22 patients with diabetic peripheral neuropathy (10 male and 12 female) and 19 patients without peripheral neuropathy (12 male and 7 female). All of them are diagnosed with T2DM by physician according to American Diabetes Association criteria. They included if they are T2DM and aged lower than 60 years old. Patients with type 1 diabetic mellitus, chronic kidney disease or renal failure, hepatic failure, inflammatory diseases such as systemic lupus erythematosus, rheumatoid arthritis and inflammatory bowel disease, neoplasia, pregnancy and Hypothyroidism or hyperthyroidism are excluded.

Diabetic peripheral neuropathy is diagnosed based on signs and symptoms and clinical examination. Signs and symptoms include pain (burning, painful cold, electric shock), numbness, tingling, pins and needle symptoms, itching and loss of temperature sensation. The physical examination is done with assistance of MNSI system score that includes 5 parts in physical examination include appearance of feet, foot ulceration, ankles reflexes, vibration perception at great toe by 128 Hz tuning fork and 10 g monofilament, scoring of 2 of 10 and more of MNSI score consider diabetic neuropathy.

Venous blood sampling about 4 mL in gel tube and left it about 10 minutes before centrifugation, then separate the serum by centrifuge for 10-15 minutes in set of 4000 round per minute. Then the serum is divided into 2 Eppendorf tubes and stored in refrigerator at -20 Celsius. One of the Eppendorf tubes is thawed after all samples collection is complete to use for analysis. Irisin hormone assay was measured by using Human Irisin ELISA Kit (Elabscience/China) by ELISA reader (Biotec/USA) for all participants, by following the manufacture's protocol.

NCS is done for all patients in this study by a specialist examiner in EMG/NCS unit in Marjan Teaching Hospital by using EMG/NCV systems of Nihon Kohden company. The nerves that examined divided into motor and sensory nerves. The motor nerves that examined include peroneal and tibial nerves bilaterally. The sensory nerves include sural nerves bilaterally, radial and ulnar nerves. However, we include only the sural nerve parameter and sural/radial amplitude ratio (SRAR) in this study.

All statistical analyses were performed using the SPSS-26 and compared across groups using one-way analysis of variance (ANOVA). The normality of data distribution was assessed using the Shapiro–Wilk test. Variables that did not meet the assumptions of normality were expressed as median and interquartile range (IQR) and analyzed using the Mann–Whitney U test. Chi-square test or Fisher's exact test was used as appropriate. Pearson's correlation coefficient was used to determine the association between serum irisin levels and continuous variables, including age, body mass index (BMI), duration of diabetes, and nerve conduction parameters. A p-value of less than or equal 0.05 was considered statistically significant for all analyses.

RESULTS

The mean age of patient in diabetic patients with and without PDN are 53.5±6.6 and 51.9±5.2 respectively, which are not significantly different between groups.

The mean of BMI in diabetic patients without PDN show (28.5±2.9) and it is significant different (p=0.009) in comparison with diabetic PDN (31.1±5.3). The mean duration of DM shows borderline significant differences (p=0.05) between two groups. The mean duration of DM shows borderline significant differences (p=0.05) between two groups. The mean HbA1c is higher in diabetic PDN in comparison with patients without PDN with high significant differences (0.0001) [Table 1].

The mean level of irisin hormone in diabetic patients with PDN is (143.18 pg/ml) and it is lower than the mean level of the hormone in diabetic patients without PDN (203.29 pg/ml) with highly significant difference between them (p=0.0001) [Fig. 1].

The comparison of nerve conduction study in diabetic without and with PDN shows significant differences in sural nerve amplitude and SRA ratio between two groups (IQR=13.2(3.9), IQR=8.95(12), p=0.04), (IQR=0.8 (0.2), IQR=0.5(0.5), p=0.001) respectively. While there is no significant difference between sural nerve velocity between two groups (p=0.06) [Table 2].

Correlation of irisin with nerve conduction study: In both group of diabetic patients with and without PDN there is no significant correlation between irisin hormone and sural nerve amplitude, sural nerve velocity and sural to radial amplitude ratio (Table 3).

Table No.1: General characteristics of patient in study groups

Characteristics		Diabetic(n=19)	Diabetic Neuropathy(n=22)	p-value
Age		51.9±5.2	53.5±6.6	0.2
Body mass index		28.5±2.9	31.1±5.3	0.009
Duration of DM (years)		8.7±4.7	12±5.6	0.05
HbA1c		8.7±1.8	9.6±1.5	0.0001
Gender	Male	12 (63.2%)	10 (45.5%)	0.5
	Female	7 (36.8%)	12 (54.5%)	

Table No.2: Comparison of median (IQR) of sural nerve amplitude, sural nerve velocity and SRA ratio between diabetic patients with and without PDN

NCS	Diabetic (n=19) Median (IQR)	Diabetic neuropathy (n=22) Median (IQR)	P-Value
Sural nerve amplitude	13.2(3.9)	8.95(12)	0.04
Sural nerve velocity	46.8(9.2)	40.2(20.3)	0.06
SRA ratio	0.8 (0.2)	0.5(0.5)	0.001

Table No.3: Correlations of irisin with NCS

NCS	Irisin hormone			
	Diabetic		Diabetic Neuropathy	
	Pearson Correlation	Sig. (2-tailed)	Pearson Correlation	Sig. (2-tailed)
Sural N. Amp.	0.205	0.399	0.159	0.479
Sural N. Velocity	-0.092	0.709	0.012	0.957
SRA Ratio	0.089	0.716	0.192	0.393

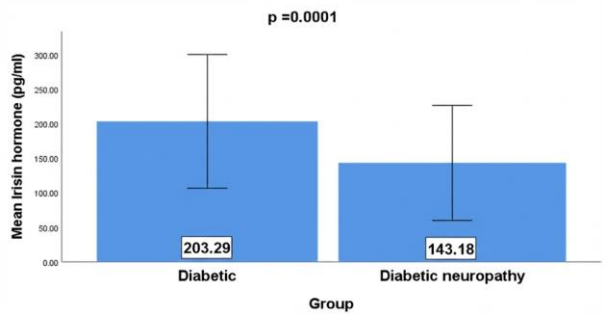

Figure No. 1: Irisin hormone level (pg/ml) among study groups

DISCUSSION

This study shows that irisin hormone level in patients with PDN is lower than patient without PDN. This agrees with other studies that also show decreases in irisin hormone in patients with PDN.[14,15]

Irisin is important in glucose homeostasis by facilitating glucose uptake by muscle.[20] For that, the increased irisin in diabetic group without PDN perhaps the normal physiological response to hyperglycemia to restore the normal condition in the body.

However, in disease progression and the condition worsens with development of complication because uncontrolled the disease, there may be exhaustion in this prosses that lead to decreased irisin[14], as shown in this study with group of PDN when compared with group of diabetics without PDN. The decreased in irisin concentration may further contribute to developing diabetic complications.

Another explanation for increased irisin in diabetic patients without PDN is irisin receptors resistance, the

increased irisin is to overcome this resistance. However, this prosses reach to point of exhaustion, resulting in decline in irisin level that may cause complications that appear in the patients[12]; this is shown in group of diabetic with PDN in this study when the concentration of irisin is lower than group of diabetics without PDN.

NCS in this study shows significant differences in sural amplitude and SRA ratio between diabetic patients with and without PDN as shown in table 2. This indicated a marked damage to the nerves in patients with neuropathic symptoms compared without symptoms.[16] Also, reduced sural amplitude indicated axonal degeneration in the nerve, it considers the major type of nerve injury in polyneuropathy especially in diabetes patients.[17] There is a significant difference between study groups in the duration of diabetes mellitus which significantly affects the severity of DPN and may confound the results of this study.[21]

To date, this is first correlation between irisin and NCS in diabetes patients. It is known that NCS consider an invasive procedure to the patient, the goal of this correlation is testing the possibility of irisin to be a biomarker indicator for neuropathy in diabetic patients. NCS in this study depends on sural nerve velocity and amplitude to assess the PDN as its accessibility more than others sensory nerves[19] and, in addition, the sural/radial amplitude ratio is measured.

The result in this study shows no correlation between irisin and sural nerve amplitude, sural nerve velocity and SRA ratio in both groups of diabetics as shown in table 3. This may be due to differences in the time of nerve damage and the control of the disease. The damage to the nerve when occurring in advanced stage is poorly reversed[17]; after while maybe the patient restores his glycemic control and improve the irisin level but the nerve damage persists.

However, more investigation is needed between irisin and NCS with more sample size, involved more nerves and may benefit to include newly diagnosed PDN.

CONCLUSION

The irisin hormone level was lower in diabetic peripheral neuropathy than diabetic patient without PDN. There is no significant correlation between irisin hormone and nerve conduction study of sural nerve, regarding amplitude and velocity, and RSA ratio.

Author's Contribution:

Concept & Design or acquisition of analysis or interpretation of data:	Zaid Talib Saleh Alfahham, Falah Mahdi Dananah
Drafting or Revising Critically:	Zaid Talib Saleh Alfahham, Falah Mahdi Dananah
Final Approval of version:	All the above authors
Agreement to accountable for all aspects of work:	All the above authors

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