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# Estimation of Apelin Levels in Iraqi Patients with Type II Diabetic Peripheral Neuropathy

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## Abstract:

Diabetes mellitus type 2 (T2DM) is a chronic and progressive condition, which affects people all around the world. The risk of complications increases with age if the disease is not managed properly. Diabetic neuropathy is caused by excessive blood glucose and lipid levels, resulting in nerve damage. Apelin is a peptide hormone that is found in different human organs, including the central nervous system and adipose tissue. The aim of this study is to estimate Apelin levels in diabetes type 2 and Diabetic peripheral Neuropathy (DPN) Iraqi patients and show the extent of peripheral nerve damage. The current study included 120 participants: 40 patients with Diabetes Mellitus, 40 patients with Diabetic peripheral Neuropathy, and 40 healthy persons as control, the age range of 34-66 years, matched in age and sex. For all groups, fasting blood sugar, lipid profile (Cholesterol, Triglyceride, High-density lipoprotein, Low-density lipoprotein, and very-low-density lipoprotein), HbA1c, serum total Apelin levels, BMI, and Waist to Hip Ratio were calculated. The results showed highly increase in Apelin levels in neuropathy patients 670.4 ± 41.67 pg/ml compared to diabetes patients 247.6 ± 20.37 pg/ml and healthy people 208.02 ± 8.30 pg/ml with a P value=0.001. Body Mass Index showed increase in diabetic and neuropathy patients compared with control group 31.05 ± 1.01 kg/m$^2$, 31.05 ± 0.73 kg/m$^2$, versus 23.92 ± 0.16 kg/m$^2$, respectively, with a P value=0.001. The result showed a significant increase in lipid profile with $p \leq 0.05$, except HDL which showed a significant decrease $p \leq 0.05$. The present study concluded that incremented Apelin levels have an important role in Neuropathy pathogenesis and could determine the extent of peripheral nerve damage by the high levels in the blood due to their presence in the central nervous system. Also, increasing BMI, excessive lipid, and duration of disease showed a progressive role in DM and neuropathy and cause damage to the nerves, and play roles in the development of complications.

**Keywords:** Apelin, Body Mass Index, Diabetic Peripheral neuropathy, Glycosylated hemoglobin, Lipid profile, Type 2 Diabetes mellitus

## Introduction:

Type II diabetes mellitus (T2DM) is defined by different degrees of pancreatic beta-cell failure along with inadequate insulin activity (insulin resistance).

The proportional importance of the two pathophysiological developmental pathways of diabetes differs from person to person and ethnic group to ethnic group [1, 2]. Long-term blood glucose elevation causes serious complications such as retinopathy that may cause vision loss, nephropathy that can cause kidney failure and vascular complications which cause cardiovascular diseases, and peripheral neuropathy [3,4]. Peripheral Neuropathy in diabetic patients (DPN) is the most widespread type of neuropathy in people around the world. It is estimated that nearly half of persons with DM have it, and 10% to 20% have symptoms severe enough to require therapy [5]. The DPN is primarily a sensory nerve disorder, and patients often experience both positive and negative sensory signs, which include pain, tingling, prickling sensations (paresthesia), and other negative

symptoms, such as numbness, in their feet. When the feet are touched, improper sensory processing may cause discomfort (allodynia) and increase susceptibility to noxious stimuli (hyperalgesia) [6]. Poor time-dependent glucose management may impact diabetes complications. Therefore, long-term glycemic variation, as measured by variations in HbA1c, may be a risk factor for the development of microvascular problems such as DPN [7].

Apelin, a bioactive peptide, was discovered in a bovine stomach tissue extract for the first time. Apelin and its receptor are expressed in addition to the central nervous system (CNS), adipocytes, placenta, and in avariety of organs [8]. Apelin is Adipocytokine that serves as a ligand of the G protein-coupled receptor known as APJ. [9]. Apelin is synthesized from pre-propeptide with a 77-amino-acid precursor with several basic amino acid residues (Arg-Lys and Arg-Arg ) which are hydrolyzed by proteolytic enzymes to form active Apelin peptides of 36, 17, and 13 amino acids, and also the post-translation modified (Pyr1)apelin-13 [10]. According to previous studies, Apelin is an adipokine that regulates a variety of biological activities, including body energy homeostasis and glucose metabolism, water balance, and immunity [11,12]. In diabetic patients, Apelin may represent endothelial dysfunction, microangiopathic alterations, and inflammatory processes, which all have a role in the etiology of diabetic peripheral neuropathy (DPN). Apelin may be used as a DPN marker [13]. Interestingly, Apelin has been studied in other diseases; previous studies investigated the effect of Apelin-36 and Apelin -13 as a predictor of heart disease in women with polycystic ovary syndrome (PCOs) and found a high level of Apelin-36 in obese PCOs patients [14,15]. In most studies, the focus is on the effect of high blood sugar on the nerves. In the current study, Apelin was studied as a marker to show the extent of nerve damage. To the best of our knowledge, there is no study to assess the level and the role of total Apelin in Iraqi patients with type 2 diabetes with peripheral neuropathy. Apelin, an adipokine can be used as a predictor of cardiovascular disease and its relationship to obesity and effects on the development of complications. Thus, the current study aimed to estimate Apelin levels in T2DM and DPN in Iraqi patients and determine the extent of peripheral nerve damage.

## Materials and Methods:

### Subject

The study was conducted at the National Diabetes Center \ Mustansiriyah University \ Baghdad \ Iraq.

A total of 120 participants under treatment with metformin and sulfonylurea drugs were involved in this research depending on the results of the medical examination they were 40 healthy persons and 80 patients, 40 patients with T2DM and 40 patients with Diabetic Neuropathy. The age range was 34-66 years. The groups were matched in both age and sex. Anthropometric and biochemical characteristics for all groups are presented by questionnaire. Diabetic patients with peripheral neuropathy were diagnosed by a neurologist using Toronto clinical scoring that consisted of three components: symptoms score, sensory score, and reflex score. Score ≥ 6 diagnosed as Neuropathy. Based on their clinical history, physical examination, and routine laboratory results, the exclusion criteria were patients with hepatic, renal, and cardiac failure, type 1 diabetes diseases, and pregnancy, the inclusion criteria were patients with type 2 diabetes mellitus with and without peripheral neuropathy complication.

### Methods

A 10 mL disposable syringe was used to collect venous blood from each participating individual (patient and control). The blood was divided into two parts: one was drawn in a gel tube to collect serum (after clotting, blood was centrifuged at 3000 rpm for 10 minutes at room temperature, and then serum was separated, distributed into aliquots in an Eppendorf tube, and stored at -20°C until assayed), and the other was drawn in an EDTA tube and analyzed for HbA1c assay. Human total serum Apelin was measured by enzyme-linked immunoassay (ELISA), using a kit supplied by My BioSource- U.S.A. Fasting blood sugar (FBS) and lipid profile were determined by Biolabo kit-France using Kenza (240TX) instrument. HbA1c was determined by high-performance liquid chromatography using the (HLC-723GX) Tosoh analyzer. Body Mass Index was determined by using [weight in kilograms / height in square meter] equation [16] Waist to Hip ratio ($waist\ cm \div hip\ cm$) [17].

### Statistical Analysis

Statistical Packages for Social Sciences (SPSS) version 26 was used to analyze the data. The result was expressed as mean ± SE. ANOVA was used to determine the difference between three independent variables, post hoc, correlation coefficient (r) between parameters, and T-test The statistical significance is determined by the probability value, which showed a significant difference at $p \leq 0.05$and no significant difference at $p>0.05$.

## Results and Discussion:

The mean value of biochemical parameters in Table. 1, showed a significant difference p≤ 0.05 between control and patient groups (diabetic and Neuropathy) in FBS 92.07 ±1.61, 176.05 ± 9.77, 209.37± 12.22 respectively. The current study agrees with Abdulahi *et al.* [18] and Fasil *et al.* [19] which showed common poor glycemic control and DM complications, indicating that effective intervention is needed to enhance glycemic control and avoid or control complications in diabetic patients[19]. Grisold *et al.*[20]study showed that hyperglycemia has a critical and life-threatening role in the development of DPN in diabetic patients. Also, HbA1c showed a significant difference p≤ 0.05, between control, diabetic, and Neuropathy groups 5.005 ± 0.05, 8.56 ± 0.27, and 9.20 ± 0.30 respectively. Our findings are in agreement with Sangeetha and Manikandan [21] who reported that 41.5% of diabetes individuals had peripheral neuropathy, with age above 50 years and poor HbA1C management as the main factors. Other relevant research [22] has shown a significant link between hyperglycemia and the development of diabetes complications (micro and macrovascular problems), which may result in high-risk diabetic foot and cardiovascular disorders. As a result, utilizing HbA1c to monitor blood glucose control has the added advantage of identifying diabetics who are at risk of acquiring such complications [23]. Furthermore, Table. 1 shows that the results of Cholesterol, Triglyceride, low-density protein (LDL), and very low-density lipoprotein (VLDL) significantly increased while there was a significant decrease in high-density lipoprotein (HDL) in patients groups (DM, DPN) compared to control.

**Table 1. Comparison of biochemical parameters in all groups**

| Parameters | Control Group (1) No. (40) | Diabetes Mellitus (DM) Group (2) No. (40) | Neuropathy Group (3) No. (40) | P-value | LSD between groups (1,2) | LSD between groups (1,3) | LSD between groups (2,3) |
|---|---|---|---|---|---|---|---|
| **Age (year)** | 51.07 ± 1.15 (51) | 52.08 ± 1.18 (53.5) | 53 ± 1.18 (54.5) | 0.513 | 0.549 | 0.249 | 0.579 |
| **BMI (kg/m$^2$)** | 23.92 ± 0.16 (24.03) | 31.05 ± 0.73 (30.4) | 31.05 ± 1.01 (28.92) | 0.001** | 0.001** | 0.001** | 1.00 |
| **W/H ratio** | 0.88 ± 0.01 (0.895) | 0.95 ± 0.01 (0.94) | 0.967 ± 0.014 (0.94) | 0.001** | 0.001** | 0.001** | 0.243 |
| **FBS (mg/dL)** | 92.07 ±1.61 (92.5) | 176.05 ± 9.77 (157) | 209.37± 12.22 (198.5) | 0.001** | 0.001** | 0.001** | 0.011* |
| **HbA1C %** | 5.005 ± 0.05 (5) | 8.56 ± 0.27 (8) | 9.20 ± 0.30 (9) | 0.001** | 0.001** | 0.001** | 0.55 |
| **Cholesterol (mg/dL)** | 153.92 ± 1.66 (154.5) | 169.01 ± 5.85 (172.5) | 181.97 ± 5.45 (176.5) | 0.001** | 0.026* | 0.001** | 0.055 |
| **TG(mg/dL)** | 104.28 ± 3.26 (109.95) | 140.62 ± 5.51 (34.85) | 159 ± 11.72 (146.5) | 0.001** | 0.001** | 0.001** | 0.091 |
| **HDL-C (mg/dL)** | 48.24 ± 0.70 (47) | 26.07 ± 1.21 (24.5) | 26.02 ± 0.98 (25.5) | 0.001** | 0.001** | 0.001** | 0.972 |
| **LDL-C(mg/dL)** | 84.82 ± 1.68 (85.7) | 114.81 ± 5.63 (122) | 124.11 ± 5.98 (122.3) | 0.001** | 0.001** | 0.001** | 0.177 |
| **VLDL-C (mg/dL)** | 20.85 ± 0.65 (21.99) | 28.12 ± 1.10 (28.4) | 31.84 ± 2.34 (29.3) | 0.001** | 0.001** | 0.001** | 0.091 |

- Data were presented as Mean ± SE (Median)
- LSD: Least significant Difference
*Significant difference between means using ANOVA -test at 0.05 level.
** Highly Significant difference between means using ANOVA -test at 0.05 level.

Our findings are in agreement with Selvi *et al.* [24] The results are an increase in small dense LDL, which is one of the hallmarks of diabetic dyslipidemia and is also linked with cardiovascular disease risk. Zhang *et al.* [25] showed high Triglyceride and low (HDL) in diabetic patients. The current study agrees with Al-Fartosy *et al.* [26] Hyperinsulinemia and hyperglycemia are all stimulators of VLDL-C synthesis in the liver. Plasma VLDLC particle turnover may be enhanced, the result could be an increase in plasma VLDL-C concentrations and a decrease in plasma HDL-C concentrations. The BMI and W/H ratio also showed a significant increase in DM and DPN groups in comparison to the control**.**

Duration of DM and hyperglycemia may cause complications like Neuropathy. Table 2 shows that 87.5% of DPN patients have more than 5 years of duration and 67.5% of DM patients have less than 5 years.

**Table 2. Comparison of Duration between diabetic and Neuropathy groups**

| | | Diabetes Mellitus (DM) Group No. (40) | | Neuropathy Group No. (40) | | p-value |
|---|---|---|---|---|---|---|
| | | **No.** | **%** | **No.** | **%** | |
| **Duration of disease (years)** | **less than 5 years** | 27 | 67.5 | 5 | 12.5 | 0.001** |
| | **More than 5 years** | 13 | 32.5 | 35 | 87.5 | |
| | **Mean ± SD** | 3.85 ± 0.45 | | 7.32 ± 0.30 | | |

**Highly Significant difference at 0.05 level.

Table. 3 shows the distribution of age and BMI mean values for all the studied groups in the current study. The mean values in this table revealed that there were no significant differences in age between the patient and control groups p>0.05. In this study, the age of the healthy and patient groups was matched. The BMI exhibited a significant difference p≤ 0.05, between the studied groups, when compared to the control group.

Both patient groups showed a significant increase p≤ 0.05, but there was no significant difference p>0.05,identified between patient groups. The current study showed that high BMI is related to T2DM and may develop neuropathy which agrees with Tesfaye *et al.* [27] who found that higher BMI levels were linked to the cumulative incidence of neuropathy.

**Table 3. Distribution of Age and BMI between patients and control groups**

| **Parameters** | | **Control Group No. (40)** | | **Diabetes Mellitus (DM) Group No. (40)** | | **Neuropathy Group No. (40)** | | **p-value** |
|---|---|---|---|---|---|---|---|---|
| | | **No.** | **%** | **No.** | **%** | **No.** | **%** | |
| **Age (Year)** | **≤ 50** | 20 | 50 | 14 | 35 | 14 | 35 | 0.513 |
| | **> 50** | 20 | 50 | 26 | 65 | 26 | 65 | |
| **BMI (kg/m$^2$)** | **Healthyweight (18.5-24.9)** | 35 | 87.5 | 2 | 5 | 6 | 15 | 0.001** |
| | **Overweight (25-29.9)** | 5 | 12.5 | 17 | 42.5 | 17 | 42.5 | |
| | **Obese (30-34.9)** | ---- | ---- | 12 | 30 | 8 | 20 | |
| | **ExtremelyObese (>35)** | ---- | ---- | 9 | 22.5 | 9 | 22.5 | |

**Highly Significant difference by using One-Way ANOVA test at 0.05 level.

The mean values of Apelin in pg/ml for all the studied groups in the current study were recorded in Table. 4 and Fig 1. Table 4 indicates a highly significant increase p ≤0.05, in Apelin level in the neuropathy group compared to the control while no significant p>0.05, difference was found between DM and control groups. Also, a highly significant increase p ≤0.05, was found in the neuropathy group compared to the DM group. According to the location of Apelin in the central nervous system (CNS), Apelin expression levels in the CNS changed significantly with nervous system damage caused by different neurological illnesses [28].
Castan-Laurell *et al.* [29] showed that Apelin Type 2 diabetes patients have the highest values compared to healthy people, suggesting that the Apelin/Apj receptor system may be a good target for Type 2 diabetic therapy .The increase in Apelin levels in neuropathy patients may be due to compensatory functions such as its role as an anti-inflammatory in diabetic neuronal cells by reducing (nuclear factor kappa-light-chain enhancer of activated B cells) NF-κB activation because activation of NF-κB in neuronal cells upregulates the expression of pro-inflammatory cytokines that cause nerve damage under hyperglycemic stress and by eliminating Reactive Oxygen Species (ROS) generation in neurons to slow the development of diabetic neuropathy [30].
Moreover, a previous study by Abo El-Hassan *et al.* [31] supports our findings that Apelin is significantly higher in neuropathy diabetic patients compared to DM patients and both were higher than the healthy group.

**Table 4. Apelin levels in patient and control groups**

| Parameter | Control Group (1) No. (40) | Diabetes Mellitus (DM) Group (2) No. (40) | Neuropathy Group (3) No. (40) | P-value | LSD between groups (1,2) | LSD between groups (1,3) | LSD between groups (2,3) |
|---|---|---|---|---|---|---|---|
| **Apelin (pg/ml)** | 208.02 ± 8.30 (207.5) | 247.6 ± 20.37 (217.5) | 670.4 ± 41.67 (672.5) | 0.001** | 0.306 | 0.001** | 0.001** |

- Data were presented as Mean ± SE (Median)
- LSD: Least significant Difference
** Highly Significant difference between means using ANOVA -test at 0.05 level.

On the contrary Erdem *et al.* [32] showed that in newly diagnosed and untreated T2DM patients, plasma Apelin levels are low. Zhang *et al.* [33] also showed the same result. Al-Kuraishy et al. [34] showed that compared to healthy controls, people with T2DM had higher serum Apelin levels. In numerous animal models and people, Apelin (acute and chronic therapy) has been demonstrated to have beneficial impacts on the pathophysiology of cardiovascular system CVS and T2DM. Certainly, further research is required, particularly in humans, to establish that targeting the Apelin/APJ system is more than beneficial when other problems or complications connected with diabetes are taken into account [35]. Helmy *et al.*[36] also showed high Apelin levels in DM patients. So Apelin has a role in the pathogenesis of diabetes and its complications. Al-Zaidy and Ahmed [37] reported an increase in Apelin levels in diabetic patients.

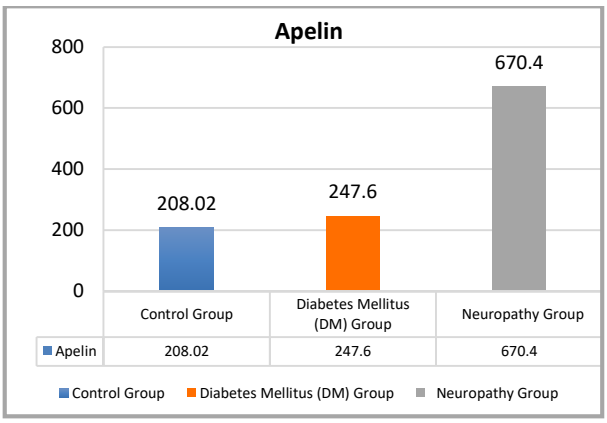


**Figure 1. Apelin levels between the groups**

**Table 5. The correlation of Apelin with all parameters**

| | | Apelin (pg/ml) | | |
|---|---|---|---|---|
| | | **Control Group No. (40)** | **Diabetes Mellitus (DM) Group No. (40)** | **Neuropathy Group No. (40)** |
| Age (years) | r | 0.191 | -0.102 | 0.058 |
| | P | 0.237 | 0.532 | 0.721 |
| Weight (kg) | r | 0.088 | 0.048 | 0.086 |
| | P | 0.589 | 0.767 | 0.598 |
| Length (cm) | r | 0.068 | -0.106 | -0.137 |
| | P | 0.677 | 0.515 | 0.399 |
| BMI | r | 0.97 | 0.171 | 0.134 |
| ($Kg/m^2$) | P | 0.553 | 0.291 | 0.408 |
| W/Hratio | r | 0.064 | -0.151 | -0.060 |
| | P | 0.695 | 0.352 | 0.714 |
| FBS (mg/dL) | r | 0.054 | 0.100 | 0.053 |
| | P | 0.742 | 0.538 | 0.744 |
| HbA1C % | r | -0.051 | -0.036 | 0.170 |
| | P | 0.754 | 0.825 | 0.295 |
| Cholesterol (mg/dL) | r | 0.153 | 0.156 | 0.134 |
| | P | 0.346 | 0.338 | 0.410 |
| TG(mg/dL) | r | 0.104 | 0.274 | -0.054 |
| | P | 0.522 | 0.087 | 0.741 |
| HDL-C(mg/dL) | r | -0.019 | 0.007 | -0.299 |
| | P | 0.906 | 0.965 | 0.061 |
| LDL-C(mg/dL) | r | 0.119 | 0.106 | 0.193 |
| | P | 0.466 | 0.513 | 0.234 |
| VLDL-C(mg/dL) | r | 0.104 | 0.274 | -0.054 |
| | P | 0.522 | 0.087 | 0.741 |
| Duration of disease | r | | -0.094 | 0.279 |
| | P | | 0.563 | 0.081 |

*Correlation is significant at the 0.05 level.

Table. 5, shows there was no correlation of Apelin with other parameters in the study while the study showed high Apelin levels in neuropathy patients.

## Conclusion:

The current study showed that the extent of peripheral nerve damage can be determined by the high levels of Apelin in the blood due to its presence in the central nervous system. Also, Apelin may have an effect on neuropathy pathogenesis. Apelin may affect other organs and tissue in other complications of diabetes. BMI, excessive lipid and duration of disease are risk factors for T2DM and the development of its complications which affect and damage the vessels and nerves.

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## The limitation of the Study:

The limitation of this study was the delay in obtaining samples for peripheral neuropathy patients because each patient was subjected to a precise medical examination by the neurologist, according to the Toronto clinical system, which diagnosed that each patient has peripheral neuropathy if the score after the examination ≥6. The other limitation of the study is the duration of the disease, where in our study the duration of the disease was determined to be 10 years in order to avoid the overlap of other complications of the disease and their impact on the results. Perhaps in future studies, the duration of the disease will be increased to show the effect of Apelin more clearly.

## Authors' declaration:

- Conflicts of Interest: None.
- We hereby confirm that all the Figures and Tables in the manuscript are mine ours. Besides, the Figures and images, which are not mine ours, have been given the permission for re-publication attached with the manuscript.
- Authors sign on ethical consideration's approval
- Ethical Clearance: The project was approved by the local ethical committee in University of Baghdad.

## Authors' contributions statement:

HKJ: acquisition of data, do laboratory analytics, interpretation, drafting the MS. FM K: Conception and design the idea of MS, interpretation, revision and proofreading the MS, and supervising. INS: Diagnosis of neuropathic and diabetes patients. BAA: Assisting and supervising some laboratoryanalyzes and proofreading the MS. Ethics approval: this survey was approved by the Scientific Committee of the College of Science for Women, and a verbal consent form was obtained from each participant enrolled in the study.

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# تقدير مستويات الأبلين في المرضى العراقيين المصابين باعتلال العصبي المحيطي السكري النوع الثاني

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**الخلاصة:**

داء السكري من النوع 2 (T2DM) هو حالة مزمنة ومتقدمة ، تصيب الناس في جميع أنحاء العالم. يزداد خطر حدوث المضاعفات مع تقدم العمر إذا لم تتم إدارة المرض بشكل صحيح. ينتج اعتلال الأعصاب السكري عن ارتفاع مستويات الجلوكوز والدهون في الدم، مما يؤدي إلى تلف الأعصاب .الابلين هو هرمون ببتيد يوجد في أعضاء بشرية مختلفة، بما في ذلك الجهاز العصبي المركزي والأنسجة الدهنية.الهدف من هذه الدراسة هو تقدير مستويات الابلين في مرضى السكري من النوع 2ومرضى الاعتلال العصبي المحيطي السكري ( DPN) لدى المرضى العراقيين واظهار مدى تلف الاعصاب المحيطية. تضمنت الدراسة الحالية 120مشارًكا : 40 مريضا يعانون من داء السكري ، و 40 مريًضا يعانون من اعتلال الأعصاب المحيطية السكري، و 40 شخصا يتمتعون بصحة جيدة كمجموعة تحكم ، تتراوح أعمارهم بين (34-66) عامًا ، متطابقة في العمر والجنس. بالنسبة لجميع المجموعات، تم حساب نسبة السكر في الدم الصائم ، ومستوى الدهون (الكوليسترول،والدهون الثلاثية ، والبروتين الدهني عالي الكثافة ، والبروتين الدهني منخفض الكثافة ، والبروتين الدهني منخفض الكثافة للغاية) و HbA1c ، ومستويات Apelin الكلية في الدم ، ومؤشر كتلة الجسم ، ونسبة الخصر إلى الورك .أظهرت النتائج زيادة عالية في مستويات الأبلين في مرضى الاعتلال العصبي 41.67pg/ml ± 670.4 مقارنة بمرضى السكري 20.37 pg/ml ± 247.6 والأشخاص الأصحاء pg / ml 8.30 ± 208.02 مع قيمة P = 0.001.أظهر مؤشر كتلة الجسم زيادة لدى مرضى السكري والاعتلال العصبي مقارنة بمجموعة التحكم 1.01 ± 31.05 (كجم / م$^2$ )، 0.73 ± 31.05 (كجم / م$^2$) مقابل 0.16 ± 23.92 ( كجم / م$^2$)على التوالي ، بقيمة = P . 0.001أظهرت النتائج زيادة معنوية في ملف الدهون مع $p \leq 0.05$ فيما عدا HDLأظهر انخفاضاً معنويا$p \leq 0.05$ خلصت الدراسة الحالية إلى أن مستويات الابلين المتزايدة لها دور مهم في التسبب في الاعتلال العصبي وتحديد مدى تلف الأعصاب المحيطية من خلال المستويات العالية في الدم بسبب وجوده في الجهاز العصبي المركزي ، كذلك اظهرت زيادة مؤشر كتلة الجسم، زيادة الدهون ومدة المرض دوًرا تقدميًا في مرض السكري والاعتلال العصبي وتسبب تلف الأعصاب وتلعب دوراً في تطور المضاعفات.

**الكلمات المفتاحية:** الأبلين، مؤشر كتلة الجسم، أعتلال الاعصاب المحيطية السكري، الهيموجلوبين الجليكوزيلاتي ملف الدهون، مرض السكري النوع الثاني .