Original Article

Assessment of Serum Neudesin Levels in Type 1 Diabetic Iraqi Children

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Abstract

Background: Diabetes is a common chronic metabolic disorder. Symptoms of diabetes may occur suddenly, and its complications lead to severe pathological conditions. **Objectives:** This study aims to evaluate Neudesin as a novel secretory protein, in addition to determining other biochemical parameters in type 1 diabetic Iraqi children. **Materials and Methods:** Ninety Iraqi children from both genders fought the experiment (60 with type 1 diabetes and 30 without diabetes); their ages ranged from 8 to 17 years. The sampling tests included measurement of Neudesin as neurotrophic factor level, fasting serum glucose, glycated hemoglobin, C-peptide, homeostasis model assessment for insulin resistance-2, β-cell function, lipid profiles, and renal function test. **Results:** An increasing value was recorded for Neudesin level in patients according to age. A highly significant increase ($P < 0.0001$ and 0.001) for fasting serum glucose, glycated hemoglobin, total cholesterol, and low-density lipoprotein between type 1 diabetes mellitus patients and the control group. Our statistical analysis data disclose a highly significant increase ($P < 0.001$) of Neudesin levels among children with type 1 diabetes when compared to the control group. Neudesin had a strong positive correlation (r^2 =0.6, 0.7) with fasting serum glucose and glycated hemoglobin, respectively. **Conclusion:** The present study concluded from the data set the involvement of Neudesin as a regulating hormone for metabolic disorders. Thus, it was involved in one way or another for neuropathy peripheral generation in future cases by its high levels during patients' growing status. In addition, it indicates involvement through the inability of nerves to transmit nerve signals to the brain.

Keywords: C-peptide, insulin resistance, lipids profile, neudesin, type 1 diabetes mellitus

Introduction

Most cells need insulin for glucose phosphorylation, direct it to the cell membranes, obtain energy as adenosine triphosphate, and sustain cells.[1] Insulin also introduces excess glucose into adipose tissue or stimulates liver enzymes to store glucose as glycogen. When the beta cells of the pancreas are unable to produce insulin, an autoimmune reaction causes their demise. It is one of the hyperglycemia kinds called type 1 diabetes. Overall, 10% of people with type 1 diabetes have a genetic predisposition to make autoantibodies that destroy β cells. Health centers attempt to lower and normalize the elevated glucose level in these individuals by subcutaneous insulin injection to avoid ketoacidosis, diabetic coma, and then death.[1,2]

Neuropathy complications include diabetic polyneuropathy, such as common dysfunction that particularly targets sensory neurons with long axons, focal neuropathies, or mononeuropathies.[3] Peripheral neuritis is the most common complication in patients with diabetes. The severity of diabetes objectives the peripheral nervous system with various forms of injury. Peripheral neuropathy is nerve damage triggered by chronic hyperglycemia and diabetes.[4] It leads to loss of sensation and sometimes pain in the feet, legs, or hands, and it is the most common complication of diabetes. These damaged

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nerves cannot transfer messages between the brain and the rest of the body.

Increasing knowledge of regulatory peptides will enable the evaluation of their role in linking food intake processes, nutritional status, and body growth, primarily through the regulation of glucose metabolism and insulin resistance (IR).[5] Neudesin is a protein containing 172 amino acids and has a unique composition with neurotrophic activity. Neudesin neurotrophic factor is a secreted protein that is necessary for various biological processes, comprising neuronal function, adipogenesis, and tumorigenesis.[6] Studies confirm that Neudesin secreted from the hypothalamus is a protein that regulates food intake.[7] Numerous reports revealed that Neudesin is a significant factor for accurate neuronal progress and function. Nevertheless, Neudesin was found and expressed in different peripheral tissues comprising adipose tissue, skeletal muscle, heart, and kidney.[8] Neudesin is implicated as a nerve hormone that sends activation signals into phosphatidylinositol-3 kinase (PI3K) and mitogen-activated protein kinase (MAPK) pathways.[9] Neudesin has a role in the phosphorylation reactions of the extracellular signal-regulated kinase 1/2, while the activations were inhibited by the pertussis toxin,[10] an inhibitor of the Gi/Go-protein, suggesting that its activity is intermediated by activation of the MAP and PI3K pathways, which are possibly combined with the Gi/Go-protein-coupled signaling pathway. The classification of the MAPR family has been inserted Neudesin as an organ[11] showing multifunctional roles in understanding neuronal development and evaluation, and it is such a unique protein with a preserved heme/steroid binding domain similar to cytochrome 5. This protein has neurotrophic activity; it is thus similar to fibroblast growth factor, epidermal growth factors, and insulin-like growth and plays important roles in synaptic plasticity.[12] The current research aims to evaluate serum Neudesin levels for early diagnosis of peripheral neuritis in children with type 1 diabetes mellitus (T1DM).

Materials and Methods

Patients and control

Sixty Iraqi patients with T1DM (30 boys and 30 girls) participated in this study; they were compared with 30 healthy subjects in the control group (15 boys and 15 girls); their ages ranged from 8 to 17 years. They attended the National Diabetes Center (NDC), Mustansiriyah University, during the period from October to December 2022. All subjects underwent full clinical examination to determine the existence of other diseases. Demographic characteristics such as sex, age, height, and weight of all participants were noted.

Methods

Blood samples were taken for laboratory investigations, which comprised the following examinations: fasting serum glucose (FSG), total cholesterol (TC), triglyceride (TG), high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), serum urea, and creatinine were evaluated using an automated analyzer (Cobas e111). The Bio-Rad VARIANT hemoglobin A1C employs automated and precise ion-exchange high-performance liquid chromatography principles to separate glycated hemoglobin (Hb1Ac). Also, C-peptide level was estimated, and homeostasis model assessment for insulin resistance-2 (HOMA2-IR), HOMA2-sensitivity%, and β-cell function were deliberated using HOMA2-Calculator software downloaded freely from the website http://www.dtu.ox.ac.uk/homacalculator/download.php. Neudesin level was determined by an enzyme immunoassay for quantitative ELISA *in vitro* diagnostic assessment using a kit of Fine (Catalog-EH4312). In addition, BMI-for-age was calculated by programs at https://www.cdc.gov/healthyweight/bmi/calculator.html.

Statistical analysis

All data are shown as means ± SD. The *t* test and ANOVA were deliberated to compare between the trial groups. A *P* value of less than 0.05 was revealed as significant.

Ethical approval

The study was reflected in harmony with the Declaration of Helsinki. It was performed with patients' verbal and analytical consent before sample collection. The study protocol, subject information, and consent form were reviewed and approved by the local ethics committee (no. 367 on January 10, 2022).

Results

The results of the current study are in Table 1, including a comparison of a group of biochemical parameters that illustrate the difference between type 1 diabetics and healthy children. The obtained mean values were analyzed statistically, giving a very highly significant increase ($P < 0.0001$) for FSG, Hb1Ac, TC, and LDL had highly significant differences ($P < 0.01$) between T1DM patients and the control group, while the values indicated a significant difference ($P < 0.05$) for C-Peptide, HOMA2-IR, and TG. The B-cell, HOMA2-Sensitivity %, and HDL-C are significantly decreased ($P < 0.05$) in T1DM patients as compared to the control. Table 2 shows highly significant differences ($P < 0.01$) in Neudesin values as a comparison between T1DM patients and control.

Figures 1 and 2 provide details of Neudesin levels according to gender and age of the patients participating in the study; it was found that the rate of Neudesin is equal when comparing boys and girls, while it was increased among patients over 12 years old. Furthermore, Neudesin has a positive correlation with FSG, Hb1Ac, C-peptide, and HOMA2-IR, respectively ($r^2 = 0.6, 0.7, 0.51, 0.53$), as

Table 1: Comparison of biochemical parameters between T1DM patients and control

Parameters	Mean ± SD		*P*-value
	T1DM patients	Control	
Number	60	30	-
Sex (boy/girl)	(30/30)	(15/15)	-
Age (years)	13.65 ± 3.09	13.83 ± 1.08	0.115
BMI (kg/m^2)	20.05 ± 3.60	18.65 ± 4.12	0.137
FSG (mg/dL)	259.18 ± 81.23	82.83 ± 4.60	0.0001
HbA1C%	11.92 ± 12.14	4.83 ± 031	0.0001
C-Peptide (ng/mL)	3.63 ± 1.05	1.82 ± 0.33	0.05
HOMA2-IR	3.50 ± 1.10	1.37 ± 0.22	0.05
B-cell%	37.14 ± 13.28	90.27 ± 23.23	0.05
HOMA2-S %	30.77 ± 17.93	96.97 ± 15.07	0.05
TC (mg/dL)	183.15 ± 35.17	145.60 ± 20.65	0.01
TG (mg/dL)	91.78 ± 7.90	77.30 ± 8.67	0.05
HDL-C (mg/dL)	44.38 ± 8.67	52.26 ± 5.33	0.05
LDL-C (mg/dL)	120.41 ± 36.91	75.87 ± 3.30	0.01
S. urea (mg/dL)	25.58 ± 4.43	25.30 ± 3.33	0.128
S. creatinine (ng/mL)	0.72 ± 0.20	0.63 ± 0.16	0.142

n: number; T1DM: type 1 diabetes mellitus

Data are presented as mean ± SD; NS is no significant; *P*-value is significant at $P < 0.05$, and high significant at $P < 0.01$ and $P < 0.001$

Table 2: Neudesin levels between groups of study type 1 diabetes mellitus patients and control

Parameters	Mean ± SD		*P*-value
	Type 1 diabetes mellitus patients	Control	
Neudesin (ng/mL)	6.13 ± 2.57	1.37 ± 0.55	0.001

n: number

Data are presented as mean ± SD; *P*-value is high significant at $P < 0.001$

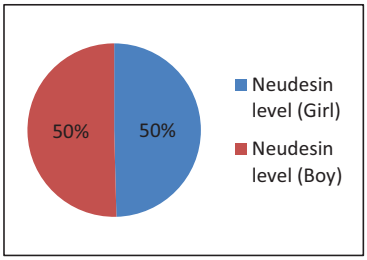

Figure 1: Comparison of Neudesin according

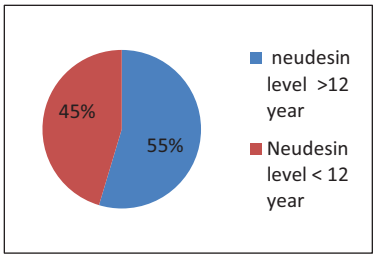

Figure 2: Comparison of Neudesin according to gender in type 1 diabetes mellitus (T1DM) patients ages in T1DM patients

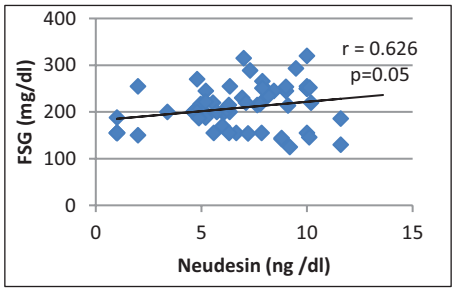

Figure 3: Correlation coefficient of Neudesin

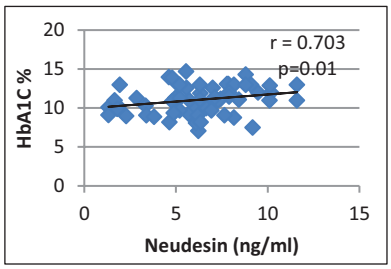

Figure 4: Correlation coefficient of Neudesin with FSG in type 1 diabetes mellitus (T1DM) Iraqi patients with HbA1c% in T1DM Iraqi patients

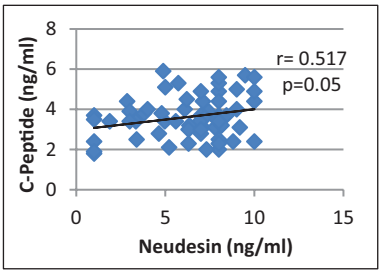

Figure 5: Correlation coefficient of Neudesin

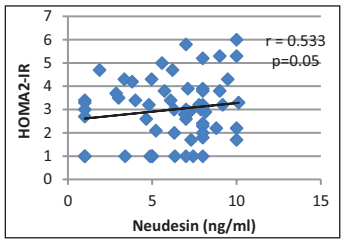

Figure 6: Correlation coefficient of Neudesin with C-Peptide in type 1 diabetes mellitus Iraqi patients with HOMA2-IR in T1DM Iraqi patients

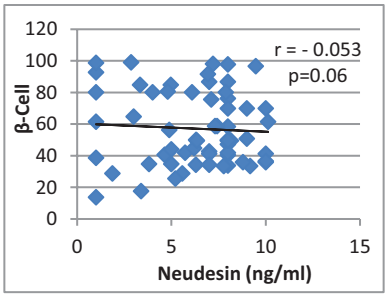

Figure 7: Correlation coefficient of Neudesin

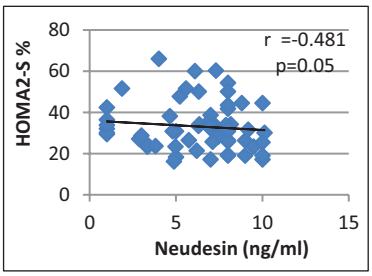

Figure 8: Correlation coefficient of Neudesin with β-cell in type 1 diabetes mellitus (T1DM) Iraqi patients with HOMA2-Sensitivity % in T1DM Iraqi patients

shown in Figures 3–6. In contrast, there was no correlation relation with the other parameters in Figures 7 and 8.

Discussion

The present study hypothesized that Nuedesin is a primary predictor in general for metabolic disorder and a special factor to show the complications of peripheral neuropathy before any other complications such as nephropathy, retinopathy, or cardiovascular symptoms.[13]

In indicating its sensitive role in the emergence of peripheral neuropathy problems in the near future, this is the first study that provides information about those factors. An important note was shown: a study suggests that Neudesin may be involved in weight loss and improved glucose control.[14] This was confirmed by the positive association between serum Nuedesin and insulin, which is particularly significant compared to the other effector pathways comprising activation of MAPK and PI3K signaling cascades.[7]

The correlation of Neudesin with a set of parameters was determined to represent a basic criterion for the repercussions of T1DM. Besides, Neudesin has a positive correlation with HOMA2-IR values and C-peptide levels in the present work. These data appearance how Neudesin dysregulation may have a role in the pathogenesis of carbohydrate metabolism illnesses in humans. Neudesin has been reported to be expressed in hypothalamic paraventricular and arcuate nuclei and is known to be complicated in food intake and energy metabolism. Neudesin has homeostasis modeling assessment feature metabolic disorder; the study of Byerly *et al.*[15] shown Neudesin involvement in reducing food intake and weight loss reported in a mice model fed with Neudesin composed from the cerebral ventricle. Then, followed a high-fat diet, thus found that the effect of Neudesin on food intake disappeared due to changed melanocortin signals. Therefore, this study proposed that was one of the reasons for the thinness in type I diabetic patients. Neudesin has a neural precursor cell that directly effect on the phosphorylation of serine-threonine protein kinase (AKT) and cyclic adenosine monophosphate (cAMP) response element binding protein.[16] The c-AMP levels had been increased in neural precursor cytosols by Neudesin activity, indicating that its potentially exerted activity was by the Gs protein-coupled signaling pathway, and its mechanism action in cytosols is distancing from that in the neurons.[17]

The Neudesin-heme binding is necessary for activation of this neurotrophic factor, where the activity of Neudesin appeared in primary cultured neurons, while it has disappeared in primary cultured astrocytes, so it confirms that it has a neural activity.[18]

Moreover, patients with T1DM and T2DM are hugely influenced by IR due to uncontrolled clinical factors and metabolic pathways.[19,20] Children with T1DM have higher IR levels in comparison to their healthy peers.[21]

A number of clinical and experimental studies defend the regulatory role of Neudesin management in glucose metabolism and insulin sensitivity. Kimura *et al.*[5] was consistent with the current data, which was examining serum Neudesin concentrations among children with T1DM, it was found a higher significant increase in children with T1DM compared to the control group. Neudesin has a positive correlation coefficient with lipids profile, especially with TC, TG, and LDL in children with T1DM. The reason is due to the high level of Nuedesin, which is directly associated, generally, with metabolism regulation and particularly in carbohydrate metabolism.[22]

Conclusion

Neudesin is a neurohormone, so its elevation can accelerate the onset of peripheral neuritis symptoms before the rest of other complications of diabetes. Through the current results, the following conclusions were recorded. Age has an effect on increasing Neudesin secretion, especially after puberty. An increase in lipid profiles as a result of raised

insulin resistance and positive correlation with Neudesin. There are no differences in Neudesin levels between boys and girls.

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Nil.

Conflicts of Interest

There are no conflicts of interest.

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