

Studying Neudesin marker in Iraqi Thyroid Dysfunction Patients

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ABSTRACT

Thyroid dysfunctions (TDs) are the most common endocrine diseases, especially in women. Phrase "thyroid dysfunction" refers to a variety of diseases affecting the thyroid gland and its hormones. This study aims to compare serum neudesin levels and lipid profiles between people with and without thyroid dysfunction. Study involved 56 TDs patients from a medical laboratory and 28 healthy controls (HCs). Neudesin concentration in serum was assessed using an enzyme-linked immunosorbent test (ELISA), whilst triglycerides (TGs), total cholesterol (T. Cho), High-density lipoprotein cholesterol (HDL-C) and total cholesterol levels were measured using enzyme colorimetry. Serum level of neudesin was lower in thyroid dysfunction patients than in HCs ($P < 0.0001$), neudesin has an important negative correlation with TGs, HDL, and very low-density lipoprotein (VLDL) (mg/dL) ($P < 0.0001$), while it showed a positive correlation with low-density lipoprotein (LDL) (mg/dL) ($P < 0.0001$). Studied parameters showed of the areas under the receiver operating characteristic (AUROC) curve hypothyroidism and hyperthyroidism, respectively: Neudesin (0.8017 and 0.9043 ng/mL), HDL (0.677 and 0.5708 mg/dL), triiodothyronine (T3) (0.8578 and 1 nmol/L), thyroxine (T4) (0.9872 and 1 nmol/L), thyroid-stimulating hormone (TSH) (0.9847 and 0.757 mIU/mL), T. Cho. (0.909 and 0.6645 mg/dL), TGs (0.944 and 0.669 mg/dL), VLDL (0.942 and 0.669 mg/dL), and LDL (0.872 and 0.7526 mg/dL). Present study found serum levels of neudesin showed a negative correlation with T.Cho, and LDL in hyperthyroidism patients while showing a negative correlation with triglycerides and VLDL in hypothyroidism patients.

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1. INTRODUCTION

The thyroid gland is very important for controlling and keeping an eye on a person's growth and metabolism. Thyroid hormones are constantly put into the bloodstream in reaction to the body's needs. They help to control a number of complex biological processes [1]. One of the most widespread endocrine problems is thyroid disease. Patients may experience major health effects, and they frequently need ongoing therapy and supervision [2].

Appetite and calorie intake are regulated by thyroid hormones. T3 controls metabolic and energy balance, which has an impact on body weight, thermogenesis, and lipid metabolism.

TSH receptors on preadipocytes cause them to develop into adipocytes, resulting in an increase in adipose tissue. Hyperthyroidism and hypothyroidism are the two most common thyroid disorders [3].

As enhanced T4 to T3 conversion keeps T3 blood levels within the normal range until hypothyroidism becomes severe, T3 levels are insufficient for the diagnosis of hypothyroidism [4]. The following are some of the benefits of using T3 testing along with FT4 interpretation to identify and track hyperthyroidism [5]: Graves' illness is indicated by a high total T3/total T4 (TT3/TT4) ratio (> 20); When nonthyroidal disease is present and TSH is suppressed (0.01 mIU/L), critical patients with high or curiously normal T3 levels may be hyperthyroid; Amiodarone-induced hyperthyroidism may be indicated by high or abnormally normal T3 levels; High T3 levels are common in people with pituitary tumors that make TSH and people with resistance to TH syndrome who don't have signs of

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hyperthyroidism; T3 levels are helpful for tracking GD patients' acute thyrotoxicosis therapy response; Elevated T3 is a typical early indicator of GDs recurrence, and T3 can identify a thyrotoxicosis relapse quickly following a break in anti-thyroid medication therapy.

Neudesin, also known as neuron-derived neurotropic released protein (NENF), is a membrane-bound progesterone receptor that is involved in energy metabolism and the growth of tumors [6]. Neudesin is found in adipose and brain tissue. Because it controls how much energy was used, it was presumed that the thyroid gland's pathology may affect how much was produced at any one time. Neudesin turns on two different ways for cells to send signals: phosphoinositide 3-kinase and mitogen-activated protein kinase (MAPK). Neudesin encourages the growth of nerve cells and is found in the brain and spinal cord. Another study that shows a link between neudesin levels and polycystic ovary syndrome found that neudesin levels have gone down a lot, even though progesterone levels were the same in both groups and there was a strong link between progesterone and neudesin levels [7]. Additionally, there is a study that supports the function of neudesin regulators in insulin sensitivity and glucose metabolism [8]. previous study indicated, when serum neudesin levels in children with type 1 diabetes were tested, it was discovered that these children's serum neudesin levels were considerably greater than those of the control group. In light of these findings, the scientists hypothesized that neudesin could serve as a new biomarker for the future prediction of metabolic illnesses as a possible regulator protein of glucose metabolism [9]. Thyroid dysfunction has a big effect on lipids and a number of other risk factors for heart disease. Thyroid function is essential for the regulation of several metabolic processes. Thyroid function has a significant effect on various CVD risk factors and lipoprotein metabolism [10,11], and hence on the overall CVD risk. Even within the normal range of thyroid-stimulating hormone (TSH) concentrations, there has been evidence of a linear rise in TC, LDL-C, and TG and a linear decline in HDL-C with increasing TSH. Lipid abnormalities are a common consequence of hypothyroidism. Substitution therapy improves the lipid profiles of patients with overt hypothyroidism. However, hyperthyroidism may cause abnormally low cholesterol

levels or an improvement in lipid profile for no apparent reason [12]. Many Iraqi studies have examined the relationship between inflammatory variables and various diseases [13,14], but this study is the first to study the relationship of neudesin to thyroid dysfunction.

This study aims to compare serum neudesin levels and lipid profiles between people with and without thyroid dysfunction.

2. MATERIALS AND METHODS

Present study included 56 females with TDs patients (28 hypothyroidism and 28 hyperthyroidism). Their age ranged from 20-60 years, a study was conducted in more than one medical laboratory from October 2022 to December 2022, moreover. Control group included 28 healthy females who apparently don't have any disease and without a history of thyroid problems; they were selected randomly and their ages from 20 to 60 years. They were considered as a control group. To determine the concentrations of neudesin in the subjects, we used ELISA kits (BT LAB Inc. China), while TGs, T.Chol, and HDL-C were measured using enzymatic colorimetric techniques.

Exclusion criteria: The study excluded patients with any chronic or immune diseases like diabetic disease, infection, and inflammation, and patients suffering from cancer and kidney diseases.

Statistical Analysis

We used Graph Pad Prism version 7 to look at the data. As basic measures, the standard deviation (SD) and mean numbers were used to show the data. When analyzing quantitative data with more than two means, the analysis of variance (ANOVA) test was employed to draw conclusions about the importance of the data. When the P value was 0.05 or below, statistical significance was taken into account. To determine the relationship between two numerical variables, Pearson correlation was used. The ROC analysis (Receiver Operator Curve) was also implemented. How successfully a parameter separates three groups, one of which is a control group, may be determined by calculating the area under the ROC curve. A cut-off value was calculated for each variable, well as sensitivity (sen%), specificity (spec%) and likelihood ratio (LHR).

3. RESULTS AND DISCUSSION

Table 1, demonstrates the common experimental characteristics of the participants mentioned, with a mean age of 37.75 years among HCs, 39.3 years in hypothyroidism patients, and 38.54 years in hyperthyroidism patients (P=0.8662). Results demonstrated that TD patients had importantly lower serum neudesin levels (ng/mL) compared to HCs (p<0.0001), also showed that the levels of T3 significantly higher in hyperthyroidism than hypothyroidism and HCs (p<0.0001), the current study also shown that hyperthyroidism had considerably greater T4 levels than hypothyroidism and HCs (p<0.0001), however TSH was significant higher in hypothyroidism than hyperthyroidism and HCs (p<0.0001), there were significant difference in total cholesterol (T.Cho.) in hypo-hyperthyroidism patients than HCs p-value of T.Cho (p<0.0001), but showed that the levels of TGs (mg/dL) significantly higher in hypothyroidism and HCs compared to hyperthyroidism p-value of TG (p<0.0001), however HDL was lower in hypo-hyperthyroidism patients than HCs (p=0.0765). also this study showed the levels of LDL were significant higher in hypothyroidism with non-significantly in hyperthyroidism with HCs (p<0.0001), but there were significant difference in VLDL in hypothyroidism and HCs cases than in hyperthyroidism with (p<0.0001).

T4 nmol/L	93.71	4.129	68.81	15.72	175.4	29.54	<0.0001
TSH mIU/mL	1.912	0.629	5.205	1.699	1.384	0.465	<0.0001
T. Cho. mg/mL	145.6	16.88	182.0	22.60	160.0	23.07	<0.0001
TGs mg/mL	132.2	15.07	176.1	28.33	121.6	19.70	<0.0001
HDL mg/mL	44.46	3.666	41.96	4.359	43.39	4.166	0.0765
LDL mg/mL	74.56	16.36	106.1	26.71	92.25	19.76	<0.0001
VLDL mg/mL	26.44	3.013	35.24	5.773	24.32	3.940	<0.0001

Table 1: Distribution of Studied Parameters in HCs and in (Hyper & Hypothyroidism) Patients Groups.

Parameter	Controls		Hypothyroidism		Hyperthyroidism		p-value
	Mean	SD	Mean	SD	Mean	SD	
Age years	37.75	11.21	39.30	10.28	38.54	9.375	0.8662
Neudesin ng/mL	7.235	1.698	5.666	2.162	4.683	1.336	<0.0001
T3 nmol/L	1.690	0.296	1.175	0.369	3.671	1.048	<0.0001

Important negative correlation was detected between neudesin with TSH (r=-0.229, p=0.090), there was also a bad link between neudesin and TGs (r=-0.248, p=0.065), HDL (r=-0.026, p=0.840) and VLDL (r=-0.239, p=0.079) in hypothyroidism patients, while showed were positive relationship between neudesin with T3 (r=0.321, p=0.016), T4 (r=0.4171, p=0.001), T. Cho. (r=0.016, p=0.909) and LDL (r=0.052, p=0.706) in hypothyroidism patients, were shown as in **table 2**. Neudesin was shown to have a significant inverse connection with T3 in the current investigation (r=-0.621, p<0.0001) and T4(r=-0.566, p<0.0001) in hyperthyroidism patients, also, there is a bad link between neudesin and T.Cho. (r=-0.327, p=0.014), HDL (r=-0.075, p=0.583) and LDL (r=-0.368, p=0.005), while were detected positive relationship between neudesin with TSH (r=0.252, p=0.060), TGs (r=0.195, p=0.149) and VLDL (r=0.195, r=0.149) in hyperthyroidism patients, were shown as in **table 3**.

Table 2: Association of Neudesin with Studied Parameters in Hypothyroidism

Parameter Hyperthyroidism	r (Neudesin ng/mL)	p-value
T3 nmol/L	-0.621	<0.0001

T4 nmol/L	-0.566	<0.0001
TSH mIU/ml	0.252	0.060
T. Cho. mg/mL	-0.327	0.014
TGs mg/mL	0.195	0.149
HDL mg/mL	-0.075	0.583
LDL mg/mL	-0.368	0.005
VLDL mg/mL	0.195	0.149

Table 3: Association of Neudesin with Studied Parameters in Hyperthyroidism

Parameter Hypothyroidism	r (Neudesin ng/mL)	p-value
T3 nmol/L	0.321	0.016
T4 nmol/L	0.4171	0.001
TSH mIU/mL	-0.229	0.090
T. Cho. mg/mL	0.016	0.909
TGs mg/mL	-0.248	0.065
HDL mg/mL	-0.026	0.840
LDL mg/mL	0.052	0.706
VLDL mg/mL	-0.239	0.079

Receiver operating characteristic (ROC) curve checking offered that the best biomarkers were fit to distinguish patients with hypothyroidism patients from HCs T4, T3, and TSH [AUC= 0.9872; P<0.0001; Cut-off value: < 87.2; Sen%: 92.86; Spec%: 92.86 and LHR: 13], [AUC=0.8578;p<0.0001; Cut-off value: <1.425; Sen%: 71.43; Spec%: 75 and LHR: 2.857], [AUC=0.9847; P <0.0001; Cut-off value: > 2.685; Sen%: 96.43; Spec%: 96.43 and LHR: 27], respectively, as shown in **table 4**, also neudesin was established to be a better predictor for hypothyroidism [AUC =0.8017; P = <0.0001; Cut-off value: < 6.008; Sen%: 78.57; Spec%: 78.57 and LHR: 3.667] as shown in **table 4**, while (TGs, LDL, VLDL, and T. Cho.) exhibited excellent ability to distinguish between healthy people and sick [AUC=0.9445; p<0.0001; Cut-off value: >148; Sen%: 82.14; Spec%: 75 and LHR: 3.286], [AUC=0.8724; P<0.0001; Cut-off value: > 86.1; Sen%: 78.57; Spec%: 78.57 and LHR: 3.667], [AUC=0.9425;p<0.0001; Cut-off value: >29.6; Sen%: 81.48; Spec%: 75 and LHR: 3.259], and [AUC=0.9094; P<0.0001; Cut-off value: > 164.5; Sen%: 82.14; Spec%: 82.14 and LHR: 4.6], respectively. While HDL showed a low discriminatory efficacy between healthy individuals, patients [AUC=0.6773; P=0.0227; Cut-off value: < 42.5; Sen%: 60.71; Spec%: 64.29 and LHR: 1.7].

Table 4. Area under curve for all analyzed Parameters in hypothyroidism

Hypothyroidism						
Parameter	Positive if cut-off value	AUC	Sensitivity %	Specificity %	Likelihood Ratio	P-value
Neudesin ng/mL	< 6.008	0.8017	78.57	78.57	3.667	0.0001
T3 nmol/L	< 1.425	0.8578	71.43	75	2.857	<0.0001
T4 nmol/L	< 87.2	0.9872	92.86	92.86	13	<0.0001
TSH mIU/ml	> 2.685	0.9847	96.43	96.43	27	<0.0001
T. Cho. mg/mL	> 164.5	0.9094	82.14	82.14	4.6	<0.0001
TGs mg/mL	> 148	0.9445	82.14	75	3.286	<0.0001
HDL mg/mL	< 42.5	0.6773	60.71	64.29	1.7	0.0227
LDL mg/mL	> 86.1	0.8724	78.57	78.57	3.667	<0.0001
VLDL mg/mL	> 29.6	0.9425	81.48	75	3.259	<0.0001

Table 5. Area under curve for all analyzed Parameters in hyperthyroidism

Hyperthyroidism						
Parameter	Positive if cut-off value	AUC	Sen%	Spec%	LHR	P-value
Neudesin ng/mL	< 5.87	0.9043	82.14	82.14	4.6	<0.0001

	T3 nmol/L	T4 nmol/L	TSH mIU/mL	T. Cho. mg/mL	TGs mg/mL	HDL mg/mL	LDL mg/mL	VLDL mg/mL
	> 2.22	> 106.9	< 1.675	> 148.5	< 130.5	< 44.5	> 79.4	< 26.1
	1	1	0.757	0.6645	0.669	0.5708	0.7526	0.669
	100	100	71.43	60.71	64.29	64.29	67.86	64.29
	100	100	71.43	67.86	60.71	50	67.86	60.71
	<0.0001	<0.0001	0.0010	0.0345	0.0299	0.3631	0.0012	0.0299

In table 5, ROC curve checking offered that the best biomarkers were fit to distinguish patients with hyperthyroidism patients from HCs T3 and T4 [AUS= 1; P<0.0001; Cut-off value: (> 2.22, > 106.9) ; Sen%: 100 and Spec%: 100] respectively, also neudesin was established to be a better predictor for hyperthyroidism [AUC =0.9043; P = <0.0001; Cut-off value: < 5.87; Sen%: 82.14; Spec%: 82.14 and LHR: 4.6], while (T. Cho., TGs, HDL, VLDL,) showed low validity in predicting validity [AUC=0.6645; P= 0.0345; Cut-off value: > 148.5; Sen%: 60.71; Spec%: 67.86 and LHR: 1.889], [AUC=0.669; P=0.0299; Cut-off value: < 130.5; Sen%: 64.29; Spec%: 60.71 and LHR: 1.636], [AUC; 0.5708; p=0.3631; Cut-off value: < 44.5; Sen%: 64.29; Spec%: 50 and LHR: 1.286], [AUC=0.669; P=0.0299; Cut-off value: < 26.1; Sen%: 64.29; Spec%: 60.71 and LHR: 1.636], respectively, while LDL and TSH revealed strong discriminatory effectiveness between sick and healthy people. [AUC=0.7526; P=0.0012; Cut-off value: > 79.4; Sen%: 67.86; Spec%: 67.86 and LHR: 2.111], and [AUC=0.757;p=0.0010; Cut-off value: < 1.675;

Sen%: 71.43; Spec%: 71.43 and Likelihood Ratio: 2.5], respectively.

Thyroid dysfunction can manifest as low hyperthyroidism or high hypothyroidism, respectively, with raised or lowered serum TSH levels that affect the synthesis of the thyroid hormones T3 and/or T4, respectively. The most frequent causes of thyroid dysfunction in places with abundant iodine are autoimmune diseases like Graves' disease and Hashimoto's thyroiditis. Both sexes are susceptible to thyroid dysfunction, however women over 40 are more likely than males to have it, with a frequency of 5–15% in areas where iodine is abundant [15]. Since neudesin has been shown to have a role in metabolism, it is essential for proper thyroid operation. Neudesin is a neuroprotective agent that also alters anxiety-like behavior regulation and hypothalamic appetite regulation [16]. Although neudesin has only been investigated in a few trials, current agreement is that, due to its capacity to suppress hunger and encourage weight reduction, it may have the potential to treat obesity and problems associated with obesity [6].

In the present study, the levels of neudesin in those with TDs were considerably lower than those in the control group. Previous research found that people with hyperthyroidism had much higher amounts of neudesin than those with hypothyroidism or in the control group. However, the new study shows that the opposite is true [17]. Neudesin levels in the blood of adults with a recent diagnosis of type 2 diabetes were greater than those of controls of the same age and body mass index [18]. In contrast to the majority of the earlier publications, in which neudesin serum concentrations are around 30 times greater than in our study [16, 7], We found that the amount of neudesin in the blood of fat teens was much lower than that of normal-weight teens [19].

Thyroid-stimulating hormone and free T4 (FT4) were often used to measure thyroid activity and keep track of treatment for hyper- and hypothyroidism. Little intra-individual variation exists in FT4, which is not sensitive to variations in the expression of TH transporters. Current results show a significant increase in T3 level in hyperthyroidism compared with hypothyroidism and control patients, However, T4 level showed a significant increase in hyperthyroidism

compared to control, while it showed a decrease in the hypothyroidism group. But a study showed a significant increase in TSH levels in hypothyroidism compared to hyperthyroidism and control. The results from this study also showed that the HDL levels of hypo- and hyperthyroidism patients when compared with control, while T. Cho., LDL and were increased in hypo- and hyperthyroidism patients compared with control. but the show was level of TGs, and VLDL showed a significant increase in hypothyroidism and control than hyperthyroidism, A prior investigation, however, has confirmed that TC, HDL-C, and LDL-C are elevated in untreated hypothyroidism, a finding that is in stark contrast to the results described in our work. However, TGs levels were comparable to controls when compared to the control group patients' results. While TC, HDL-C, and LDL-C values in individuals with hyperthyroidism were comparable to those in control patients [20].

Our study suffers from a number of limitations. First, a very small number of participants are Iraqi females with thyroid dysfunction patients. Additionally, one of the drawbacks of this study might be attributed to the analyses being performed in private laboratories. Second, elderly respondents had greater exposure to significant risk factors such as smoking, hypertension, and diabetes. Therefore, these findings need be confirmed by prospective study using larger samples, and more ethnic collections are required to look into the biological effects of serum neudesin levels in TDs instances.

Conclusion

In conclusion; Neudesin, because of the role it plays in metabolism, plays an essential role in thyroidism. To verify these findings, we need to conduct additional research. Because of these properties, neudesin has the potential to be the focus of additional research regarding the treatment and prevention of thyroidism.

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دراسة مصل النيوديسين لدى مرضى الغدة الدرقية في العراق

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قسم الكيمياء ، كلية التربية للعلوم الصرفة ، جامعة الانبار ، العراق

الخلاصة:

تعتبر اضطرابات الغدة الدرقية (TDs) أكثر أمراض الغدد الصماء شيوعاً ، خاصة عند النساء. تشير عبارة "قصور الغدة الدرقية" إلى مجموعة متنوعة من الأمراض التي تصيب الغدة الدرقية وهرموناتها. تهدف هذه الدراسة إلى مقارنة مستويات مصل النيوديسين وخصائص الدهون لدى الأشخاص الذين يعانون من اختلال وظيفي في الغدة الدرقية والذين لا يعانون منها. اشتملت الدراسة على 56 مريضاً من مرضى TDs من مختبر طبي و 28 من المجموعة الضابطة الممثلة بالأصحاء (HCs). تم تقييم تركيز نيوديسين في مصل الدم باستخدام اختبار الامتصاص المناعي المرتبط بالإنزيم (ELISA) ، بينما تم قياس الدهون الثلاثية (TGs) والكوليسترول الكلي (T. Cho) وكوليسترول البروتين الدهني عالي الكثافة (HDL-C) ومستويات الكوليسترول الكلي باستخدام طرق لونية انزيمية. كان مستوى النيوديسين في مصل الدم منخفضاً لدى مرضى قصور الغدة الدرقية بالمقارنة مع المجموعة الضابطة ($P < 0.0001$) ، يتسم النيوديسين بعلاقة سلبية مهمة مع HDL ، TGs ، والبروتين الدهني منخفض الكثافة (VLDL) ($P < 0.000$ لتر) ، بينما أظهر ارتباطاً إيجابياً مع البروتين الدهني منخفض الكثافة (LDL) (مجم / ديسيلتر) ($P < 0.0001$). أظهرت المتغيرات المدروسة في المنحنى المميز لأداء المستقبل (AUROC) قصور الغدة الدرقية وفرط نشاط الغدة الدرقية ، على التوالي: Neudesin (0.8017 و 0.9043 نانوغرام / مل) ، HDL (0.677 و 0.5708 مجم / ديسيلتر) ، ثلاثي يودوثيرونين (T3) (0.8578 و 1 نانومول / L) ، هرمون الغدة الدرقية (T4) (0.9872 و 1 نانومول / لتر) ، هرمون محفز للغدة الدرقية (0.9847) (TSH و 0.757 ميكرو مول / مل) ، (0.909) T. Cho. و 0.6645 مجم / ديسيلتر) و TGs (0.944 و 0.669 مجم / ديسيلتر) و VLDL (0.942 و 0.669 مجم / ديسيلتر) و LDL (0.872 و 0.7526 مجم / ديسيلتر). وجدت الدراسة الحالية أن مستويات مصل النيوديسين أظهرت ارتباطاً سلبياً مع T. Cho و LDL في مرضى فرط نشاط الغدة الدرقية بينما أظهرت ارتباطاً سلبياً مع الدهون الثلاثية و VLDL في مرضى قصور الغدة الدرقية.

الكلمات المفتاحية: فرط نشاط الغدة الدرقية ، قصور الغدة الدرقية ، هرمون الغدة الدرقية ، كوليسترول البروتين الدهني عالي الكثافة ، الدهون الثلاثية