ISSN: 0067-2904

Evaluation of Neudesin Level in A sample of Iraqi Patients with Hypothyroidism

Ashgan Slman Dawood[1], Baydaa Ahmed Abed[2], Layla Othman Farhan[*1], Isam N. Salman[2]

[1]*Department of Chemistry, College of Science for Women, University of Baghdad, Baghdad, Iraq*
[2]*National Diabetes Center, Mustansiriyah University, Baghdad, Iraq*

Received: 2/4/2023 Accepted: 16/9/2023 Published: 30/11/2024

Abstract

Hypothyroidism, a condition where the thyroid gland does not produce enough thyroid hormone to maintain health, is most often caused by iodine deficiency in areas where iodine levels are low. However, in regions with adequate iodine, Hashimoto's disease is the leading cause of hypothyroidism and thyroid failure. Neudesin in neuropeptide hormone, which is released by the brain and fat tissue, has both metabolic effects and neural. The study included ninety participants divided in two groups: in this study, the initial group comprised 30 female and 30 male individuals diagnosed with hypothyroidism, while the second group consisted of 15 female and 15 male participants who were healthy controls. The age range for both groups spanned from 30 to 60 years. The findings indicated that the hypothyroidism group exhibited significantly elevated levels of WHR, BMI, TC, TG, LDL, VLDL, TSH, and Neudesin compared to the control group. Particularly noteworthy, Neudesin displayed remarkable proficiency in distinguishing hypothyroidism patients from the control group, achieving an outstanding AUC 0.965. Using the findings, we deduced that the evaluation. Neudesin indicators may be beneficial for the diagnosis and response to therapy. The most sensitive and specific marker for hypothyroidism individuals is neudesin.

Keyword: *Neudesin, Hypothyroidism, Thyroid Hormone, Thyroxin*

تقييم مستوى هرمون نيوديسين في عينة من المرضى العراقيين المصابين بقصور الغدة الدرقية

اشكان سلمان داود[1], بيداء احمد عبد[2] , ليلى عثمان فرحان[*1] , عصام نوري سلمان[2]

[1]قسم الكيمياء , كلية العلوم للبنات , جامعة بغداد ,بغداد , العراق

[2]المركز الوطني لعلاج وبحوث السكري ,الجامعة المستنصرية ,بغداد , العراق.

الخلاصة:

قصور الغدة الدرقية، وهي حالة لا تنتج فيها الغدة الدرقية ما يكفي من هرمون الغدة الدرقية للحفاظ على الصحة، غالبًا ما يكون سببها نقص اليود في المناطق التي تكون فيها مستويات اليود منخفضة. ومع ذلك، في المناطق التي تتوفر فيها كمية كافية من اليود، يعتبر مرض هاشيموتو هو السبب الرئيسي لقصور الغدة الدرقية وفشل الغدة الدرقية. Neudesin هو هرمون الببتيد العصبي، الذي يفرزه الدماغ والأنسجة الدهنية، له تأثيرات ايضية وعصبية. شملت الدراسة تسعين مشاركاً تم تقسيمهم إلى مجموعتين: في هذه الدراسة ضمت

[*]Email: laylaof_chem@csw.uobaghdad.edu.iq

المجموعة الأولى (30 أنثى و 30 ذكراً) مصابين بقصور الغدة الدرقية، بينما تكونت المجموعة الثانية من (15 أنثى و 15 ذكراً) من الاشخاص الأصحاء . شملت الفئة العمرية لكلتا المجموعتين من 30 إلى 60 سنة. أشارت النتائج إلى أن مجموعة قصور الغدة الدرقية أظهرت لديهم مستويات عالية في (WHR، BMI، TC، TG، LDL، VLDL، TSH، وNeudesin) مقارنة مجموعة الاشخاص الأصحاء. ومن الجدير وبالشكل الخاص اظهر Neudesin كفاءة ملحوظة في التمييز بين مرضى قصور الغدة الدرقية من المجموعة الاشخاص الأصحاء ، حيث حقق (AUC 0.96). وباستخدام النتائج، استنتجنا أنه قد تكون مؤشرات Neudesin مفيدة للتشخيص والاستجابة للعلاج. حيث يعتبر Neudesin الأكثر حساسية وتشخيصية في مرض قصور الغدة الدرقية .

الكلمات المفتاحية : نيوديسين ، قصور الغدة الدرقية ، هرمون الغدة الدرقية ، ثيروكسين

1.Introduction

Thyroid hormone plays a pivotal role in human physiology, influencing essential aspects such as metabolism, growth, brain development, and differentiation [1]. Among the prevalent endocrine disorders affecting a significant portion of the population, thyroid dysfunction stands out. Thyroid-stimulating hormone (TSH) levels serve as the most accurate indicators of thyroid health and are primarily employed in biochemical assessments to diagnose thyroid irregularities [2]. Hypothyroidism, characterized by insufficient levels of thyroid hormones, specifically thyroxine (T4) and triiodothyronine (T3), is a notable manifestation of thyroid dysfunction. TSH is secreted to regulate the synthesis and production of T3 and T4 [3]. The frequency of hypothyroidism in the general population is expected to range from (0.3% to 3.7%) in the USA and from (0.2% to 5.3%) in Europe [4,5]. In 1930, it was discovered that dyslipidemia and thyroid problems were related. Since then, it has gradually come to light that hypothyroidism may result in lipid metabolism issues[6,7]. Lethargy, tiredness, sensitivity to the cold, dry skin, and a bad quality of life are all symptoms of hypothyroidism, which is a slowing of systemic activity [8 ,9]. Neudesin is a recently identified protein that is primarily released from the brain and the adipose tissue, but also observable in the liver, lungs, and heart. Its potential role as negative regulator of the energy consumption is currently being investigated[10,11]. Neudesin is a multifunctional secreted protein that is hypothesized to play important regulatory roles in various physiological processes like glucose metabolism, appetite control, neurotrophic effects, and energy homeostasis [12 ,13]. Structurally, neudesin is comprised of 171 amino acids. At the cellular level, neudesin is involved in neural cell differentiation, growth, and cancer progression through activation of signaling pathways including phosphoinositide 3-kinase and mitogen-activated protein kinase [14–16]. Overall, existing research suggests neudesin has diverse functions related to metabolism, neural function, cell growth, and activation of key intracellular signaling cascades [15,17]. The fact that neudesin inhibits adipogenesis during the initial stages of adipocyte development raises the prospect that neudesin may be crucial role to adipogenesis[18, 19]. This study aims to evaluate the levels of neudesin hormone and other biochemical markers in a group of Iraqi patients with hypothyroidism. It will also investigate the impact of thyroxine treatment on these biochemical markers.

2. Subjects and Methods

2.1. Studied groups

This case-control study included two groups: 1) 60 hypothyroidism patients (30 females, 30 males) aged 30-60 years and 2) 30 healthy controls (15 females, 15 males) in the same age range. Data was collected from September 2022 to December 2022. The hypothyroidism patients were receiving daily thyroxine therapy, with 28 participants taking 50 µg daily and 32 participants taking 100 µg daily. The goal of the study was to compare various health

parameters between hypothyroidism patients on thyroxine therapy and healthy matched controls.

2.2. Inclusion and Exclusion Criteria

Inclusion Criteria

The study participants were individuals aged 30-65 years with hypothyroidism disease. The participants recruited for this study were adults between the ages of 30 and 65 who had been diagnosed with hypothyroidism by their healthcare provider.

Exclusion Criteria

The individuals with Hyperthyroidism, those diagnosed with thyroid cancer, expectant mothers, and those who have undergone prior thyroid gland removal (thyroidectomy).

2.3. Blood Sample

Following an overnight fast lasting 8 to 12 hours, blood samples were collected between 8:30 AM and 11:30 AM using sterile 10 cc syringes. The collected blood was then transferred into gel tubes and allowed to clot at room temperature. Subsequently, the blood underwent centrifugation at 3000 rotations per minute for 15 minutes. From this process, 1 mL of serum was utilized for the establishment of the lipid profile, which included measurements for total cholesterol (TC), low-density lipoprotein (LDL), triglycerides (TG), very low-density lipoprotein (VLDL), and fasting blood glucose levels. Additionally, 1.5 mL of serum was dedicated to further thyroid function testing, encompassing Thyroid-stimulating hormone (TSH), Triiodothyronine (T3), and Thyroxine (T4). The remained were put in an eppendorf tube and placed in a deep freezer (-20oC) to be used for further research on the neudesin hormone.

2.4. Experimental methods

In the Cobas c111 device, all biochemistry factors (FBG, TG ,TC, LDL, and HDL) were measured. The Thyroid Hormone were assayed with Vidas Tools and a Biomerieux reagent (T3, TSH and T4). The ELISA kit for neudesin hormone was assay by (Al-Shkairate-Jordan)**.**Weight (kg)/Height(m)2 is the formula for calculating the body mass index (BMI) Anthropometric readings are obtained at BMI measurements of fat [20].

2.5. Statistical analysis

The gathered data underwent analysis employing SPSS version 24.0 software. To evaluate the data's normality, tests including Kolmogorov-Smirnov and Shapiro-Wilk were executed. As the continuous variables displayed non-normal distribution patterns, they were summarized using the median and interquartile range. Differences in continuous variables between the two study groups were assessed using the Mann-Whitney U test. A value of ($P \leq 0.05$) was used as the significance level. MedClac (19.7.4 soft wear) was used to estimate the Neudesin cutoff value using receiver operating characteristic curve (ROC) analysis.

3. Result

Table 1 shows a comparison of various biomarkers between the hypothyroidism patient group and healthy control group. Waist-hip ratio (WHR), body mass index (BMI), total cholesterol (TC), triglycerides (TG), low-density lipoprotein (LDL), very low-density lipoprotein (VLDL), and thyroid-stimulating hormone (TSH) levels were significantly higher in patients with hypothyroidism compared to controls. In contrast, high-density lipoprotein (HDL), thyroxine (T3), and triiodothyronine (T4) levels were significantly lower in hypothyroidism patients versus controls. Additionally, Neudesin levels exhibited a highly

significant elevation in hypothyroidism patients relative to healthy individuals, as visualized in Figure 1 and depicted numerically in Table 1. In summary, the results indicate several biomarkers can differentiate between hypothyroidism patients and normal controls, with Neudesin showing especially strong associations with hypothyroidism.

Table 1: Biochemical parameters (Age, WHR ,BMI ,FBG ,TC,TG, HDL, LDL,VLDL,T3,T4,TSH,and Neudesin) in the study group.

Variables	Hypothyroidism Median (range)	Control Median (range)	*P* value
Age (year)	53.50 (60.00 -45.00)	50.50(42.00-57.00)	0.450
WHR	0.98 (1.02 -0.93)	0.82(0.79-0.84)	0.001
BMI Kg/m2	34.21(36.54-29.43)	24.32(23.49-25.05)	0.001
TC(mg/dl)	229.50(274.50-200.00)	135.50(113.00-147.75)	0.001
TG(mg/dl)	235.50 (339.00-180.00)	83.00(76.75-90.00)	0.001
HDL(mg/dl)	38.00 (40.00 -32.00)	47.00(45.00-49.00)	0.001
LDL (mg/dl)	147.50(175.00-118.00)	71.50(49.00-84.75)	0.001
VLDL(mg/dl)	47.00(67.50-36.00)	17.00(15.50-18.00)	0.001
T3(ng/ml)	0.67(0.91-0.50)	1.50(1.20-1.90)	0.001
T4(ng/ml)	58.50(60.00-51.00)	87.00(79.00-89.00)	0.001
TSH(ulU/mL)	10.00(15.50-8.25)	1.40(1.00-1.80)	0.001
Neudesin(ng/ml)	3.42(3.61-2.84)	1.88(2.01-1.39)	0.001
The median ($25^{th}$and 75^{th} percentiles)were used the (Mann Whitny test)at the 0.05 level to assess whether there was a significant variation between three independent means.			

Table (2), show significantly higher (WHR,TG, LDL, and VLDL) in patient with Hypothyroidism take thyroxine (100µg) when compared to patient with Hypothyroidism take thyroxine (50µg), whereas, it is significantly lower in (BMI, and HDL) in patient with Hypothyroidism take thyroxine (100µg) when compared to patient with Hypothyroidism take thyroxine (50µg).

Table 2: Anthropometric and biochemical parameters (Age, WHR, BMI, FBG,TC,TG,HDL, LDL,VLDL,T3,T4,TSH,and Neudesin) in Hypothyroidism group(50,and 100) thyroxin concentration treatment .

Variables	Hypothyroidism		*P* value
	[50] ,n=28	[100], n=32	
Age (year)	51.00	56.00	0.063
WHR	0.95	0.98	0.046*
BMI Kg/m2	35.55	33.33	0.016*
TC(mg/dl)	220.00	264.00	0.129
TG(mg/dl)	210.00	330.00	0.016*
HDL(mg/dl)	40.00	32.00	0.015*
LDL(mg/dl)	126.00	165.00	0.010*
VLDL(mg/dl)	42.00	66.00	0.018*
T3(ng/ml)	0.75	0.63	0.552
T4(ng/ml)	58.50	57.50	0.311
TSH(ulU/mL)	10.40	9.65	0.558
Neudesin(ng/ml)	3.53	3.39	0.182

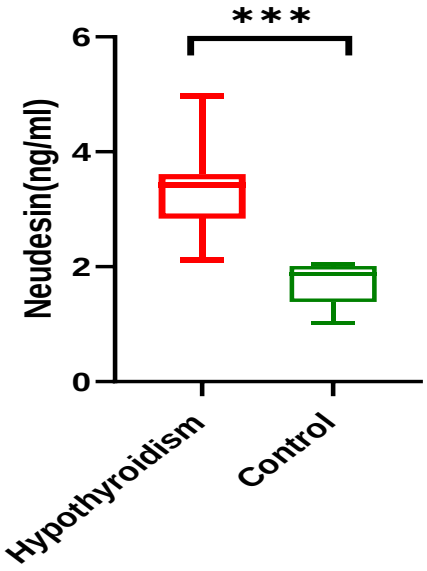

Figure 1: The serum Neudesin in Hypothyroidism and control groups

Table 3: The Neudesin (AUC and validity) in distinguishing between Hypothyroidism against Control

Variable	AUC	*P*-Value	Cut off value	Sensitivity	Specificity	Accuracy	PPV	NPV
Neudesin	0.965	0.001	2	90	100	0.900	100	83.3

Area under the curve (AUC). Positive predictive value (PPV), negative predictive value (NPV)

Neudesin showed an excellent ability (since AUC between 0.9 – 0.99) to identify hypothyroidism patient against control as illustrated in Table (3), and Figure (2) respectively.

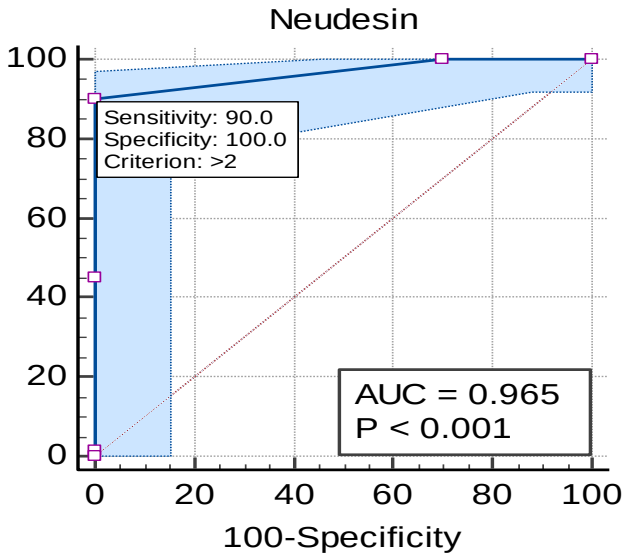

Figure 2: ROC curve analysis of serum Neudesin concentrations in Hypothyroidism against Control.

4. Discussion

The studies revealed a significant association between human food composition and thyroid disorders [21].Age makes thyroid problems worse, especially in women. Total cholesterol and LDL tend to increase as thyroid function declines. Because the thyroid hormone controls lipid metabolism, production, digestion, and catabolism in a variety of ways. The thyroid hormone causes the liver to produce more cholesterol [22 , 23].Thyroid hormone (T3)can increase adipocytes' sensitivity to adrenaline's lipolytic activity, which increases fatty acid transfer to the liver and indirectly increases hepatic triacylglycerol synthesis [24]. Result of the present study were close with Alsamghan AS*et al* [25,26], who found increased in TC,TG and LDL levels in hypothyroidism patients. The inhibition of the (lipoprotein lipase (LPL)) activity, a the triglyceride hydrolysing enzyme found in the capillary walls in the adipose tissue, may be the cause of the rise in triglyceride levels in hypothyroid individuals.

Accurately differentiating between obesity-related hormonal changes and those caused by underlying endocrine conditions is crucial for properly treating obese patients. Obese individuals often have elevated thyroid stimulating hormone (TSH) levels combined with low free thyroxine (FT) levels, indicating potential hypothyroidism [27]. This can contribute to weight gain beyond what is caused by excess body fat. L-thyroxine, the main thyroid hormone replacement medication, has a long half-life and is auto-converted to the active form triiodothyronine (T3). This conversion increases at low T4 levels and decreases at high levels, providing regulatory feedback. For optimal absorption, L-thyroxine should be taken on an empty stomach [28]. Thyroid hormones influence lipid biosynthesis. Numerous studies have found that as TSH levels rise, fat levels also rise. Some research shows individuals with hypothyroidism tend to have higher levels of LDL cholesterol. Proper diagnosis and treatment of any underlying endocrine conditions is important for managing weight and health in obese patients [17].

The results of the present study agreed with Efstathiadou Z et al, [29,30], who showed a significant decreased in HDL in patients with L-thyroxine therapy.
Recently, novel regulatory peptides implicated in the control of carbohydrate metabolism have been identified by researchers. Numerous investigations into various medical disciplines are still showing novel properties. A comprehensive knowledge of these peptides' processes and the variables that affect their release may open up new avenues for the detection and management of metabolic diseases, including thyroid disease.

Neudesin is a recently discovered element that plays a role in the intricate regulation of energy balance [31].The family of four proteins known as the membrane-associated progesterone receptors, which includes neudesin, all share a heme/steroid binding region that is similar to that of cytochrome 5 [32]. It can affect how the hypothalamus regulates hunger in addition to having neurotrophic benefits [33]. Neudesin hormone level was found to be elevated and to be associated with insulin resistance (IR) scores in individuals with recently diagnosed type 2 diabetes. As a result, it was found that increased neudesin amounts may be related to insulin resistance[34]. Increased energy utilization, brown adipose tissue heat generation, white adipose tissue lipolysis, and a protection from IR associated with a high-fat diet were all observed in response to neudesin[11]. And, Bozkaya G*etal* [13] ,found the Neudesin levels was significantly lower in patient with Polycystic ovary syndrome(PCOS) when compared to the controls groups.

While research on neudesin remains limited to a handful of studies, experts concur that it holds promise for potential applications in the treatment of obesity and related disorders [35]. Due to the novelty of these markers and the scarcity of references and investigations, deciphering their exact role in the pathophysiology of thyroid dysfunction presents a significant challenge. This is because the real mechanism by which neudesin affect patients with thyroid dysfunction (hypothyroidism) is difficult to explain properly, and some information may be missed as a result.

Conclusion

In hypothyroidism patients, levels of BMI, total cholesterol, triglycerides, LDL, VLDL, TSH and neudesin were elevated compared to controls. Meanwhile, levels of T3 and T4 thyroid hormones were decreased in the hypothyroidism patients. These findings suggest neudesin and other indicators may be useful for diagnosis and therapeutic monitoring in hypothyroidism. Of all the biomarkers assessed, neudesin appeared to be the most sensitive and specific marker for hypothyroidism. The elevated neudesin levels alongside changes in BMI, cholesterol, triglycerides, TSH and thyroid hormones reflect the metabolic disturbances and hormonal imbalances associated with hypothyroidism. Further research on neudesin levels may establish its clinical utility as a diagnostic and prognostic marker in patients with deficient thyroid hormone.

Ethical Clearance

The Research Ethical Committee at scientific research by ethical approval of both environmental, health, higher education, and scientific research ministries in Iraq.

Conflict of interest:

The authors have no conflicts of interest regarding this investigation

Reference

[1] S. P. Fitzgerald and H. Falhammar, "Redefinition of Successful Treatment of Patients With Hypothyroidism. Is TSH the Best Biomarker of Euthyroidism?" , *Frontiers in Endocrinology,* vol. 13, pp. 1-12, 2022.

[2] E. Solmunde *et al.*, "Breast cancer, breast cancer-directed radiation therapy and risk of hypothyroidism: A systematic review and meta-analysis", *The Breast,* vol. 68,pp. 216–224.2023.

[3] H. I. Jansen, A. Boelen, A. C. Heijboer, E. Bruinstroop, and E. Fliers, "Hypothyroidism: The difficulty in attributing symptoms to their underlying cause", *Frontiers in Endocrinology,* vol. 14, p. 251, 2023.

[4] H. Liu and D. Peng, "Update on dyslipidemia in hypothyroidism: the mechanism of dyslipidemia in hypothyroidism", *Endocrine Connections,* vol. 11, no. 2,p.1-14, 2022.

[5] S. A. Ibrahim, H. M. Jasim, and J. A. Zainulabdeen, "Association of Arginase I Gene Polymorphism with the Risk of Atherosclerosis in a Sample of Iraqi Patients ", *Indian Journal of Public Health Research & Development,* vol. 10, no. 6,pp. 1389-1396, 2019.

[6] I. Strikić Đula *et al.*, "Epidemiology of hypothyroidism, hyperthyroidism and positive thyroid antibodies in the Croatian population" , *Biology,* vol. 11, no. 3, pp.1-10,2022.

[7] L. O. Farhan, E. M. Taha, and A. M. Farhan, "A Case control study to determine Macrophage migration inhibitor, and N-telopeptides of type I bone collagen Levels in the sera of osteoporosis patients", *Baghdad Science Journal,* vol. 19, no. 4,pp. 848-854, 2022.

[8] Y. Wang and H. Wang, "Effects of hypothyroidism and subclinical hypothyroidism on sexual function: a meta-analysis of studies using the female sexual function index", *Sexual Medicine,* vol. 8, no. 2, pp. 156–167, 2020.

[9] A. Ibrahim Suhad, A. Zainulabdeen Jwan, and M. Jasim Hameed, "Levels of Arginase Isoenzymes in Sera of Iraqi Patients with Atherosclerosis and Type 2 Diabetes Mellitus", *Research Journal of Biotechnology,* vol. 14, pp. 201–207, 2019.

[10] E. Vergani, C. Bruno, C. Gavotti, A. Oliva, D. Currò, and A. Mancini, "Increased levels of plasma neudesin in adult growth hormone deficiency and their relationship with plasma liver-expressed antimicrobial peptide-2 levels: a cross-sectional study", *Journal of Endocrinological Investigation*, pp. 1–9, 2022.

[11] E. Vergani, C. Bruno, C. Cipolla, D. Currò, and A. Mancini, "Plasma Levels of Neudesin and Glucose Metabolism in Obese and Overweight Children", *Frontiers in Endocrinology*, vol. 13,pp.1-7, 2022.

[12] E. Ç. Eren, S. Kaya, and D. Argun, "The assessment of maternal and umbilical cord neudesin levels in pregnancies with gestational diabetes mellitus", *Journal of Obstetrics and Gynaecology*, vol. 42, no. 7, pp. 2941–2945, 2022.

[13] G. Bozkaya, O. Fenercioglu, İ. Demir, A. Guler, B. Aslanipour, and M. Calan, "Neudesin: a neuropeptide hormone decreased in subjects with polycystic ovary syndrome", *Gynecological Endocrinology*, vol. 36, no. 10, pp. 849–853, 2020.

[14] X. Su, Y. Wang, A. Li, L. Zan, and H. Wang, "Neudesin neurotrophic factor promotes bovine preadipocyte differentiation and inhibits myoblast Myogenesis", *Animals*, vol. 9, no. 12, p. 1109, 2019.

[15] G. J. Kashtl, B. A. Abed, L. O. Farhan, I. Noori, and A. S. D. Salman, "A Comparative Study to Determine LDH Enzyme Levels in Serum Samples of Women with Breast Cancer and Women with Breast Cancer and Type 2 Diabetes Mellitus"vol.6,no 4,pp.883-890,2023.

[16] N. U. G. Mohammed, F. M. Khaleel, and F. I. Gorial, "Cystatin D as a new diagnostic marker in rheumatoid arthritis", *Gene Reports*, vol. 23, p. 101027, 2021.

[17] S. Kumar, T. Masood, N. Bhaskar, A. K. Shah, and P. Tangri, "Study of association of serum lipid profile, IL-6, & ADMA levels with subclinical hypothyroidism", *Journal of Pharmaceutical Negative Results*, pp. 1430–1434, 2023.

[18] A. Li, X. Su, Y. Wang, G. Cheng, L. Zan, and H. Wang, "Effect of neudesin neurotrophic factor on differentiation of bovine preadipocytes and myoblasts in a co-culture system", *Animals*, vol. 11, no. 1, p. 34, 2020.

[19] E. M. Taha, M. Mohialdeen Taha, S. K. Al-Obaidy, B. Faris Hasan, and S. M. Rahim, "Association between Atherogenic Index and Cholesterol to HDL Ratio in COVID-19 Patients During the Initial Phase of Infection", *Archives of Razi Institute*, vol. 77, no. 3, pp. 1303–1310, 2022.

[20] E. Anuurad *et al.*, "The new BMI criteria for asians by the regional office for the western pacific region of WHO are suitable for screening of overweight to prevent metabolic syndrome in elder Japanese workers", *Journal of occupational health*, vol. 45, no. 6, pp. 335–343, 2003.

[21] Y. Luo, F. Wu, Z. Huang, Y. Gong, and Y. Zheng, "Assessment of the relationship between subclinical hypothyroidism and blood lipid profile: reliable or not? ", *Lipids in Health and Disease*, vol. 21, no. 1, pp. 1–11, 2022.

[22] A. M. Hashim, S. J. Al-Harbi, M. M. Burhan, Y. H. Al-Mawlah, and A. M. Hadi, "Histological and physiological determinants of hypothyroidism in patients and its relationship with lipid profile", *J Adv Biotechnol Exp Ther*, vol. 6, pp. 9–16, 2023.

[23] F. M. Khaleel, N. N-Oda, and B. A Abed, "Disturbance of Arginase Activity and Nitric Oxide Levels in Iraqi Type 2 Diabetes Mellitus", *Baghdad Science Journal*, vol. 15, no. 2, pp. 189–191, 2018.

[24] M. P. Czech, "Mechanisms of insulin resistance related to white, beige, and brown adipocytes", *Molecular metabolism*, vol. 34, pp. 27–42, 2020.

[25] A. S. Alsamghan, S. A. Alsaleem, M. A. S. Alzahrani, A. Patel, A. K. Mallick, and S. A. Sheweita", Effect of hypovitaminosis D on lipid profile in hypothyroid patients in Saudi Arabia," *Oxidative Medicine and Cellular Longevity*, vol. 2020,pp.1-8, 2020.

[26] R. J. Abd Al-Ghanny, M. M. B. Al-Moosawi, and B. A. Abd, "Effects of Vitamin D Deficiency in Polycystic Ovarian Syndrome", *Iraqi Journal of Science*, pp. 33–42, 2022.

[27] A. Bouazza, R. Favier, E. Fontaine, X. Leverve, and E.-A. Koceir, "Potential Applications of Thyroid Hormone Derivatives in Obesity and Type 2 Diabetes: Focus on 3, 5-Diiodothyronine (3, 5-T2) in Psammomys obesus (Fat Sand Rat) Model", *Nutrients*, vol. 14, no. 15, p. 3044, 2022.

[28] N. A. Zakaria and M. A. Shahar, "Comparison Between Weekly vs Daily Dosing L-thyroxine for the Treatment of Hypothyroidism in Ramadan–A Pilot Randomized Controlled Trial", vol.

18(SUPP19) pp.49-54,2021.

[29] Z. Efstathiadou *et al.*, "Lipid profile in subclinical hypothyroidism: is L-thyroxine substitution beneficial? ", *European Journal of Endocrinology*, vol. 145, no. 6, pp. 705–710, 2001.

[30] B. A. Abed and G. S. Hamid, "Evaluation of Lipocalin-2 and Vaspin Levels in In Iraqi Women with Type 2 Diabetes Mellitus", *Iraqi Journal of Science*, pp. 4650–4658, 2022.

[31] O. Karatas *et al.*, "The level of the neudesin in Type-2 Diabetic patients and the relationship between the metabolic parameters and carotid intima-media thickness", *Minerva Endocrinologica*, 2021.

[32] H. Kratochvilova *et al.*, "Neudesin in obesity and type 2 diabetes mellitus: the effect of acute fasting and weight reducing interventions", *Diabetes, metabolic syndrome and obesity: targets and therapy*, pp. 423–430, 2019.

[33] H. Hasegawa, M. Kondo, K. Nakayama, T. Okuno, N. Itoh, and M. Konishi, "Testicular Hypoplasia with Normal Fertility in Neudesin-Knockout Mice", *Biological and Pharmaceutical Bulletin*, vol. 45, no. 12, pp. 1791–1797, 2022.

[34] H. A. L. Jouad and S. A. W. AL-Shammaree, "Neudesin Levels in Patients with Thyroidism", *The Egyptian Journal of Hospital Medicine*, vol. 89, no. 2, pp. 7809–7813, 2022.

[35] A. Çelikkol, Ç. Binay, Ö. Ayçiçek, and S. Güzel, "Serum neudesin levels in obese adolescents", *Journal of clinical research in pediatric endocrinology*, vol. 14, no. 1, pp. 69–75, 2021.