Journal of Cardiovascular Disease Research

ISSN: 0975-3583, 0976-2833 VOL15, ISSUE 6, 2024

Afamin, Vimentin levels and number of biochemical variables in female patients with thyroid disorders in Samarra city

Shelan Weli Hasan Faris[1], Aseel Mokdad Hatam AbdulWahed[1]

[1]University of Samarra- college of applied sciences/Iraq

Email: [1]usach23011@uosamarra.edu.iq, [1]aseel.mh@uosamarra.edu.iq

Abstract

Background: Function of thyroid gland is regulated by the axis hypothalamic- pituitary-thyroid through these hormones: Thyrotrophin releasing hormone(TRH), thyroid stimulating hormone (TSH), tetraiodothyronine hormone(T4) and triiodothyronine hormone(T3). Thyroid disorders(hyperthyroidism or hypothyroidism) are common around the world and are common diseases in Iraq. Thyroid disorders are states that initially affect on amount of hormones that produced by the thyroid, and affects on all physiological systems including central nervous system , cardiovascular system, blood, and others. Afamin(AFM) is an 87 Kilodalton (kDa) glycoprotein that shares 55% of the amino acid sequence of albumin and contains 15% of carbohydrates. Vimentin (VIM) is a protein among 70 types of intermediate filaments, including Vimentin, Keratin, Desmin and Lamin. Vimentin is a cytoskeleton is an intermediate filament protein that makes up the nucleus and muscle cells.

Aimes of study: We aimed to evaluate levels of Afamin, Vimentin and number of biochemical variables(TRH,TSH,T3 and T4) with Body mass index(BMI) in females patients with thyroid disorders .

Methods: The study groups include 30 women with hyperthyroidism, 30 women with hypothyroidism and a control group of 30 healthy women with ages between(18-45) years, From September 2023 until March 2024. Protein assays include Afamin, Vimentin levels and number of biochemical variables(TRH,TSH,T3 and T4) in females patients with thyroid disorders .

Results: The results of current study showed a significant increase at($P \leq 0.05$) in AFM(227.67 ± 32.31) , VIM(40.00 ± 4.39) levels with TRH(225.04± 57.08), TSH(11.71 ± 2.77) and BMI(29.70 ± 2.86) in patients with hypothyroidism group compared to (hyperthyroidism and healthy) groups. Levels of T3(0.76 ± 0.14) and T4(3.33 ± 0.79) showed a significant decrease at($P \leq 0.05$) in hypothyroidism group compared to hyperthyroidism and healthy groups, While TSH(0.25 ± 0.08) levels showed a significant decrease at($P \leq 0.05$) in hyperthyroidism group compared to hypothyroidism group and healthy group. Concentrations of T4(13.42 ± 1.36) with T3(2.16 ± 0.42) showed a significant increase at($P \leq 0.05$) in hyperthyroidism group compared to hypothyroidism and healthy groups.

Conclusions: We conclude from results of current study that high levels of AFM and VIM are associated with high levels of TRH,TSH and BMI in hypothyroidism group . Serum levels of AFM and VIM may be a new biomarkers for detecting and monitoring thyroid disorders, and may be an important useful clinical tools for detecting and monitoring thyroid disturbances.

ISSN: 0975-3583, 0976-2833 VOL15, ISSUE 6, 2024

Key words: AFM, VIM, , TRH, TSH, T3, T4, thyroid disorder, hyperthyroidism, hypothyroidism.

Introduction

Thyroid hormones T4 and T3 have a metabolic effect on many tissues and systems in the organism, so in the event of a deficiency or excess of these two hormones, it will lead to the occurrence of some disorders[1]. Thyroid hormones are necessary for development, normal growth and metabolic processes, and an imbalance of its hormones leads to either hyperthyroidism or hypothyroidism[2]. Hypothyroidism state is a disease caused by low secretion of thyroid hormones. Hypothyroidism leads to low heart rate, fatigue, facial puffiness, weight gain, dry skin, and neck swelling[3,4]. It is believed that women with hypothyroidism are more susceptible to changes in thyroid function than men[5,6]. Hyperthyroidism is a disease caused by excessive secretion of thyroid hormone, which accelerates metabolism[3,4]. Afamin(AFM) is a glycoprotein was discovered as a fourth member of human albumin family gene that includes albumin, vitamin D binding protein and alpha-fetoprotein[7]. Afamin is a vitamin E-binding protein, most of it is produced from liver and then released into the circulatory system, it is a new metabolic marker for gestational diabetes mellitus (GDM), metabolic syndrome (MetS) and cancer[8]. Vimentin (VIM) is a protein among 70 types of intermediate filaments, including Vimentin, Keratin, Desmin, and Lamin[9]. Vimentin is built in a highly dynamic manner as networks specific to the cell type in the cytoplasm[10]. Vimentin is associated with a number of cancers, including papillary thyroid carcinoma[11].

Aimes of study: We aimed to evaluate levels of Afamin, Vimentin and number of biochemical variables(TRH,TSH,T3 and T4) with Body mass index(BMI) in females patients with thyroid disorders .

Materials and Methods

Samples:

Study samples consist of 30 women with hyperthyroidism, and 30 women with hypothyroidism, compared with 30 healthy women control group, all samples collection patients from hospital, out clinic and laboratories in Samarra city.

Equipments and tools used: Enzyme linked immunosorbent assay(ELISA), Human reader(HS), Centrifuge, Incubator, Deep freezer, Gel tubes, Test tubes, Plain tubes, Eppendrof tubes, Pipette tips, Micropipette, and Disposable syringes.

Blood collection:

Samples was collected from the vein and left at room temperature for 15 minutes. then centrifuged at 5000 rpm for 10 minutes. Serum blood put in test tubes.

ISSN: 0975-3583, 0976-2833 VOL15, ISSUE 6, 2024

others.

Hormonal analysis:

Concentrations of AFM,VIM and thyroid hormones(T3 andT4), TSH and TRH measured by enzyme linked immune sorbent assay(ELIZA) by procedures in kits catalogs.

ELIZA kit: Abbexa LTD, UK for VIM,AFM and TRH and Monobind Inc- USA for

Statistical analysis:

All values of parameters expressed as mean± S.D. Data analyzed using Statistical Analysis System(SAS) software 9.4M8 version.

Results of study:

The results of current study in table(1) showed a significant increase at($P \leq 0.05$)

Parameters	Control group	Hypothyroidism patients	Hyperthyroidism patients
TRH	**19.54 ± 6.82 b**	**225.04± 57.08 a**	**12.81 ± 4.10 b**
TSH	**3.57 ± 1.29 b**	**11.71 ± 2.77 a**	**0.25 ± 0.08 c**
T4	**6.52 ± 1.53 b**	**3.33 ± 0.79 c**	**13.42 ± 1.36 a**
T3	**1.90 ± 0.26 b**	**0.76 ± 0.14 c**	**2.16 ± 0.42 a**
AFM	**24.76 ± 6.89 c**	**227.67 ± 32.31 a**	**89.86 ± 17.38 b**
VIM	**21.50 ± 5.43 b**	**40.00 ± 4.39 a**	**21.00 ± 5.91 b**
BMI	**20.17 ± 3.14 b**	**29.70 ± 2.86 a**	**20. 02± 1.61 b**

ISSN: 0975-3583, 0976-2833 VOL15, ISSUE 6, 2024

in AFM(227.67 ± 32.31) , VIM(40.00 ± 4.39) levels with TRH(225.04± 57.08), TSH(11.71 ±2.77) and BMI(29.70 ± 2.86) in patients with hypothyroidism group compared to (hyperthyroidism and healthy) groups. Levels of T3(0.76 ± 0.14) and T4(3.33 ± 0.79) showed a significant decrease at(P≤0.05) in hypothyroidism group compared to hyperthyroidism and healthy groups, While TSH(0.25 ± 0.08) levels showed a significant decrease at(P≤ 0.05) in hyperthyroidism group compared to hypothyroidism group and healthy group. Concentrations of T4(13.42 ± 1.36) with T3(2.16 ± 0.42) showed a significant increase at(P≤ 0.05) in hyperthyroidism group compared to hypothyroidism and healthy groups.

Table(1): Hormonal parameters between studied groups.

*** All values of parameters expressed as mean± S.D.**

***Different letter refer to significant differences.**

Discussion: Regulating activity of thyroid gland and the secretion of its hormones depends on the negative feedback mechanism, which includes the pituitary gland, which secretes TSH hormone, and the main hormone from the hypothalamus, Thyrotrophin releasing hormone (TRH)[12]. Results of our current study are showed an increase in concentration for TRH in hypothyroidism group with high TSH, while in hyperthyroidism group, we observed a decrease in levels of both hormones(TRH and TSH). This may be due to the fact that when it is released from the neurons of paraventricular nucleus(PVN) of hypothalamus to portal blood, and stimulates synthesis and release of TSH hormone, which reaches thyroid gland and stimulates to synthesis and release of thyroid hormones into bloodstream. It is known that metabolic rate, energy balance, and thermogenesis are under the control of TRH, considering as a neurohormone[13]. TSH is the most important chemical marker in thyroid disorders, as a low level of it is due to hyperthyroidism, while a high level of it is hallmark of hypothyroidism[14]. Pituitary gland secretes TSH as a result of the negative feedback mechanism. High concentrations of Free T4 (FT4) hormone and Free T3(FT3) hormone negatively affect on anterior pituitary gland, which reduces secretion of TSH, due to the abnormally high production and secretion of thyroid hormones[15]. In our study Decreased levels of T3 and T4 in hypothyroidism patients, lack of production of thyroid hormones may be due to the inhibition of thyroid peroxidase enzyme and a decrease in the concentration of iodine in the thyroid. Low concentrations of T3 and T4 stimulate TSH secretion from pituitary gland through a negative feedback mechanism, and when this cause is removed, the hormones will return to their normal level[16]. It is known that the secretion of thyroid hormones happen through negative feedback mechanism, when concentration

ISSN: 0975-3583, 0976-2833 VOL15, ISSUE 6, 2024

of T4 and T3 hormones decreases, the concentration of TSH increases, as in state of hypothyroidism, and when concentration of T4 and T3 hormones increases, concentration of TSH decreases, as in state of hyperthyroidism[17]. Another reason for the disturbance in levels of T4 and T3 hormones in females may be due to disturbances in the sex hormones, such as a decrease in estrogen, which stimulates the production of TBG(Thyroxin binding globulin), or due to diseases that may affect the thyroid, causing it to lose its effectiveness, and as a result of the deficiency in thyroid hormones, TRH hormone is secreted from the hypothalamus, in turn, stimulates increased secretion of TSH from thyrotrophes cells in pituitary gland, and this explain elevated TSH in our study compared to T4 and T3 in state of hypothyroidism, and opposite of this is true for hyperthyroidism[18]. The low levels of afamin in our study with a group of hyperthyroidism patients may be due to a weakness in liver synthesis, as a liver is main source of circulating afamin in the blood[19]. Excessive accumulation of hepatic lipid is connected with non-alcoholic fatty liver disease, Hepatitis, insulin resistance and increase risk of development diabetes mellitus type 2[20]. In our study showed high BMI levels in hypothyroidism group may be due to the fact that hypothyroidism is associated with a lower metabolic rate and decreased thermogenesis. It also appears to be associated with a higher body mass index and a higher prevalence of obesity, with some clinical evidence indicating that even disorders Mild hypothyroidism in subclinical hypothyroidism is associated with marked changes in body weight and indicates a risk factor for overweight and obesity[21], While in the group of hyperthyroidism , lower body mass index levels were observed, as it is known that hyperthyroidism is associated with weight loss[22]. Afamin can serve as a sign of an increase hepatic lipid content, that closely related to development of metabolic diseases[23,24]. Afamin reflects to some extent functional ability of the liver (reserve), as the liver plays an essential role in pathophysiology of glucose metabolism, and hepatic glucose production, hepatic glucose is almost exclusive source of circulating glucose in fasting state[25]. Afamin serve as an excellent clinical sign for metabolic diseases in general population, and plasma concentrations of afamin are strongly connected with prevalence and progression metabolic syndrome[26].

Our current study showed that the levels of AFM and BMI are elevated in hypothyroidism group and in a study it was shown that overexpression of afamin led to an increase in body weight, concentrations of cholesterol, triglycerides and glucose in blood[26], It was reported that metabolic syndrome and BMI are directly related to afamin levels in serum[8,27], It was concluded through the results of a study that afamin may play a role in the development of early abnormal levels of carbohydrates, lipids, and oxidative stress in obese patients[28]. which indicates afamin role in glucose metabolism and systemic energy. Our study showed that levels of vimentin and body mass index increased in hypothyroidism group. A study

ISSN: 0975-3583, 0976-2833 VOL15, ISSUE 6, 2024

showed that VIM deficiency prevent obesity and insulin resistance in mice fed a high- fat diet and suggest VIM is a central mediator connect between obesity and diabetes mellitus type 2[29]. Vimentin is only intermediate filament protein expressed in adipocytes, and as a result, it has been suggested vimentin play role in lipogenesis[30]. It is important for mobilization of cholesterol from lipid droplets in cytoplasm to mitochondria. In order to form steroids and to maintain the balance of lipid droplets in general, results of a study showed that vimentin participates in movement of cholesterol from its storage in lipid droplets for steroidogenesis[31]. Vimentin shows that it reacts with hormone sensitive lipase in a hormone-dependent manner and facilitate lipolysis[32]. A study has found that extracellular vimentin increases energy absorption and storage as Triglyceride (TG), Extracellular vimentin causes an anabolic effect in adipocytes, adipose tissue acts as an endocrine organ that regulate energy balance[33]. It was concluded through a study that Vimentin is required for the normal distribution of lipid in the body[34]. Vimentin has also been shown to be an interacting partner of stimulating β3-adrenergic receptors, which is important for activating extracellular signal-regulated kinase (ERK) and stimulating lipolysis[35].

Conclusion: We conclude from results of current study that high levels of AFM and VIM are associated with high levels of TRH,TSH and BMI in hypothyroidism group. Serum levels of AFM and VIM may be a new biomarkers for detecting and monitoring thyroid disorders, and may be an important useful clinical tools for detecting and monitoring thyroid disturbances.

References

1. **GELEN,** Volkan; ŞENGÜL, Emin; KÜKÜRT, Abdulsamed. Thyroid Hormones (T3 and T4) and Their Effects on the Cardiovascular System. In: Hyperthyroidism-Recent Updates. IntechOpen, 2023.
2. **ANANDKUMAR,** S., et al. Thyroid disorder: An overview. Research Journal of Pharmacology and Pharmacodynamics, 2020, 12.1: 1-4.
3. **SIEGEL,** Rebecca; DESANTIS, Carol; JEMAL, Ahmedin. Colorectal cancer statistics, 2014. CA: a cancer journal for clinicians, 2014, 64.2: 104-117.
4. **SONUÇ,** Emrullah, et al. Thyroid disease classification using machine learning algorithms. In: Journal of Physics: Conference Series. IOP Publishing, 2021. p. 012140.
5. **VANDERPUMP,** Mark PJ. Epidemiology of thyroid disorders. In: The thyroid and its diseases: A comprehensive guide for the clinician. Cham: Springer International Publishing, 2019. p. 75-85.
6. **ALQAHTANI,** Saif Aboud M. Prevalence and characteristics of thyroid abnormalities and its association with anemia in ASIR region of Saudi Arabia: a cross-

ISSN: 0975-3583, 0976-2833 VOL15, ISSUE 6, 2024

sectional study. Clinics and practice, 2021, 11.3: 494-504.

7. **LICHENSTEIN,** Henri S., et al. Afamin is a new member of the albumin, alpha-fetoprotein, and vitamin D-binding protein gene family. Journal of Biological Chemistry, 1994, 269.27: 18149-18154.
8. **ABED,** Baydaa Ahmed; FARHAN, Layla Othman; SALMAN, Isam Noori. A Review of Afamin as Metabolic Novel Marker of Many Diseases. Wasit Journal for Pure Sciences, 2023, 2.4.
9. **DUTOUR-PROVENZANO,** Gaëlle; ETIENNE-MANNEVILLE, Sandrine. Intermediate filaments. Current Biology, 2021, 31.10: R522-R529.
10. **HASHEMI KAROII,** Danial; AZIZI, Hossein. A review of protein-protein interaction and signaling pathway of Vimentin in cell regulation, morphology and cell differentiation in normal cells. Journal of Receptors and Signal Transduction, 2022, 42.5: 512-520.
11. **LIN,** Tsungnan, et al. Learning long-term dependencies in NARX recurrent neural networks. IEEE transactions on neural networks, 1996, 7.6: 1329-1338.
12. **BATISTUZZO,** Alice, et al. Sustained pituitary T3 production explains the T4-mediated TSH feedback mechanism. Endocrinology, 2023, 164.12: bqad155.
13. **NILLNI,** Eduardo A.; SEVARINO, Kevin A. The biology of pro-thyrotropin-releasing hormone-derived peptides. Endocrine reviews, 1999, 20.5: 599-648.
14. **PANDEY,** Arti Sharma. Case reports of metabolic disorders from Nepal. Molecular Genetics and Metabolism Reports, 2019, 21: 100542.
15. **IBRAHIM,** Sarah, et al. Characteristics of thyrotoxicosis among thyroid patients and their quality of life in a teaching hospital in Jordan: A cross-sectional study. Pharmacy Practice, 2022, 20.1: 1-7.
16. **CHANDRA,** Amar K., et al. Goitrogenic content of Indian cyanogenic plant food & their in vitro anti-thyroidal activity. Indian Journal of Medical Research, 2004, 119: 180-185.
17. **NESS,** Gene C., et al. Stimulation of hepatic β-hydroxy-β-methylglutaryl coenzyme A reductase activity in hypophysectomized rats by L-triiodothyronine. Proceedings of the National Academy of Sciences, 1973, 70.12: 3839-3842.
18. **KUMAR,** P. and Clark , M. Clinical medicine . W. B. Saunders

ISSN: 0975-3583, 0976-2833 VOL15, ISSUE 6, 2024

comp. UK, 2004, 5th ed. P. 1001-1039 .

19. **JERKOVIC,** Lidija, et al. Afamin is a novel human vitamin E-binding glycoprotein characterization and in vitro expression. Journal of proteome research, 2005, 4.3: 889-899.
20. **PRYSTUPA,** Andrzej, et al. Afamin and adropin in patients with alcohol-induced liver cirrhosis. Annals of Agricultural and Environmental Medicine, 2018, 25.3: 527-531.
21. **ABDULRAZAQ,** Haider Y., et al. Obesity And Graves' Disease, Possible Association. Journal of Pharmaceutical Negative Results, 2022, 226-229.
22. **AMOUZEGAR,** Atieh, et al. Association between thyroid function and development of different obesity phenotypes in euthyroid adults: a nine-year follow-up. Thyroid, 2018, 28.4: 458-464.
23. **MAŁECKI,** Paweł, et al. Serum proteome assessment in nonalcoholic fatty liver disease in children: a preliminary study. Expert Review of Proteomics, 2020, 17.7-8: 623-632.
24. **MILLER,** Michael H., et al. The serum proteome of nonalcoholic fatty liver disease: a multimodal approach to discovery of biomarkers of nonalcoholic steatohepatitis. Journal of gastroenterology and hepatology, 2014, 29.10: 1839-1847.
25. **CHOUKEM,** S.-P.; GAUTIER, J.-F. How to measure hepatic insulin resistance?. Diabetes & metabolism, 2008, 34.6: 664-673.
26. **KRONENBERG,** Florian, et al. Plasma concentrations of afamin are associated with the prevalence and development of metabolic syndrome. Circulation: cardiovascular genetics, 2014, 7.6: 822-829.
27. **CHEN,** Shenghui, et al. Association between serum afamin levels with nonalcoholic associated fatty liver disease. Canadian Journal of Gastroenterology and Hepatology, 2022, 2022.
28. **JUHÁSZ,** Imre, et al. Afamin levels and their correlation with oxidative and lipid parameters in non-diabetic, obese patients. Biomolecules, 2022, 12.1: 116.
29. **KIM,** SeoYeon, et al. Vimentin deficiency prevents high-fat diet-induced obesity and insulin resistance in mice. Diabetes & Metabolism Journal, 2021, 45.1: 97.
30. **FRANKE,** Werner W.; HERGT, Michaela; GRUND, Christine. Rearrangement of the vimentin cytoskeleton during adipose conversion: formation of an intermediate filament cage

ISSN: 0975-3583, 0976-2833 VOL15, ISSUE 6, 2024

around lipid globules. Cell, 1987, 49.1: 131-141.

31. **SHEN,** Wen-Jun, et al. Ablation of vimentin results in defective steroidogenesis. Endocrinology, 2012, 153.7: 3249-3257.
32. **SHEN,** Wen-Jun, et al. Vimentin is a functional partner of hormone sensitive lipase and facilitates lipolysis. Journal of proteome research, 2010, 9.4: 1786-1794.
33. **PARK,** Ji-Hae; KWON, Soyeon; PARK, Young Mi. Extracellular Vimentin Alters Energy Metabolism And Induces Adipocyte Hypertrophy. Diabetes & Metabolism Journal, 2023.
34. **WILHELMSSON,** Ulrika, et al. Vimentin is required for normal accumulation of body fat. Biological chemistry, 2019, 400.9: 1157-1162.
35. **KUMAR,** Naresh, et al. Requirement of vimentin filament assembly for β3-adrenergic receptor activation of ERK MAP kinase and lipolysis. Journal of biological chemistry, 2007, 282.12: 9244-9250.