Tikrit Journal of Pure Science Vol. 31 (1) 2026

DOI: https://doi.org/10.25130/tjps.v31i1.1890

IRAQI Academic Scientific Journals

Tikrit Journal of Pure Science

ISSN: 1813 – 1662 (Print) --- E-ISSN: 2415 – 1726 (Online)

Journal Homepage: https://tjpsj.org/

Assessment of the role of Adipsin and Hepassocin as biomarkers in males with untreated hypothyroidism and diabetes

Mustafa Najim Abdoun, Nagham Qasim Kadhim

Department of chemistry, College of science, University of Tikrit, Tikrit, Iraq

Received: 3 Feb. 2025 **Received in revised forum:** 7 Apr. 2025 **Accepted:** 24 Apr. 2025

Final Proofreading: 25 Jul. 2025 **Available online:** 25 Feb. 2026

ABSTRACT

Thyroid hormones are closely linked to metabolic and many physiological processes in the human body. Therefore, it is expected that hypothyroidism, which is a common disease in the world, is linked to many diseases such as diabetes, liver diseases, and everything related to metabolic processes. Therefore, we also expect a link between the difference in concentrations of biochemical variables such as heparin and adipsin in the bloodstream for patients with hypothyroidism and other diseases. All sixty men patients were suffering from hypothyroidism, their ages ranged from 30 to 61 years old. After collecting the samples, thyroid hormone concentrations in blood serum were measured using the Minividas technique, while heparin and adipsin were measured using kits from Sun Long Biotech (China). There was a highly significant increase (P≤0.001) in Thyroid-Stimulating Hormone (TSH), vasopressin, and adipsin levels in the men's patient group compared to healthy men in the control group. The results showed a highly significant decrease (P≤0.001) in T4 compared with the men's control group. Hepassocin and adipsin may be relatively independent good markers for the prognosis of an active thyroid gland “hypothyroidism”.

Keywords: Adipsin, Diabetes Hepassocin, Hypothyroidism

Name: Wafaa A. Abdulwahab **E-mail: mustafa.najim@st.tu.edu.iq**

Tikrit Journal of Pure Science Vol. 31 (1) 2026

DOI: *https://doi.org/10.25130/tjps.v31i1.1890*

دور الهيباسوسين والأديبسين في الرجال المرضى الذين يعانون من قصور الغدة الدرقية والسكري غير المعالجين

مصطفى نجم عبد عون، نغم قاسم كاظم

قسم الكيمياء، كلية العلوم، جامعة تكريت، تكريت، العراق

الملخص

ترتبط هرمونات الغدة الدرقية ارتباطًا وثيقًا بالعمليات الأيضية والعديد من العمليات الفسيولوجية في جسم الإنسان. لذلك، من المتوقع أن يرتبط قصور الغدة الدرقية، وهو مرض شائع في العالم، بالعديد من الأمراض مثل مرض السكري وأمراض الكبد وكل ما يتعلق بالعمليات الأيضية. لذلك، نتوقع أيضًا وجود ارتباط بين اختلاف تركيزات المتغيرات الكيميائية الحيوية مثل الهيباسوسين والأديبسين في مجرى الدم لدى مرضى قصور الغدة الدرقية وأمراض أخرى. تم أخذ جميع المرضى الستين من الرجال الذين يعانون من قصور الغدة الدرقية، وتراوحت أعمارهم بين 30 إلى 61 عامًا. بعد جمع العينات، تم قياس تركيز هرمونات الغدة الدرقية في مصل الدم بتقنية Minividas، بينما تم قياس تركيز هيباسوسين وأديبسين من Sun Long Biotech - Chinakit. كان هناك ارتفاع كبير معنوي ($P \geq 0.001$) في مستويات TSH والهيباسوسين والأديبسين لدى مجموعة مرضى الرجال عند مقارنتها بالرجال الأصحاء كمجموعة تحكم. أظهرت النتائج انخفاضًا كبيرًا ($P \geq 0.001$) في 4T مقارنة بمجموعة الرجال الضابطة. قد يكون كل من هيباسوسين وأديبسين علامات جيدة مستقلة نسبيًا لتشخيص قصور الغدة الدرقية النشط.

INTRODUCTION

Hypothyroidism, or an "inactive thyroid gland," is a significant endocrine disease worldwide. [1] , which is caused as a result of decreasing T3 and T4 production or a Malfunction in the activity associated with these hormones. The defects can be acquired "primary or secondary" or from birth, "congenital" or with a delayed result of hypothyroidism due to different congenital disabilities. It can have various or familial congenital causes.[2]. It is classified due to the function of the thyroid gland into primary and secondary hypothyroidism disorders. Primarily, the thyroid gland itself is defective, meaning the disorders are within the same gland. But secondary is characterized by a defect in the posterior pituitary gland, meaning a problem with the production and secretion of Thyroid Stimulating Hormone (TSH). This defect can alter thyroid function or impair the production of thyrotropin-releasing hormone (TRH), secreted by the hypothalamus. [3, 4].

Diabetes mellitus (DM) and hypothyroidism are two prevalent endocrine disorders that significantly impact global health. The link between Diabetes mellitus and hypothyroidism is multifaceted, with emerging evidence suggesting a bidirectional relationship between the two disorders[5]. Diabetes and thyroid dysfunction (prominently hypothyroidism) are two major endocrine defects that are diagnosed and present in clinical practice at various ages and in several populations that typically call for lifelong monitoring and therapy. Hypothyroidism has been reported to be associated with T2DM in several studies [6]. Many studies have inspected, the possible linkage between thyroid gland function and disorders with diabetes, for instance patients have diabetes (DM) are more likely in the early or far period to have hyperthyroidism than persons who do not have diabetes, those patients with type 2 diabetes who have overt hyperthyroidism “overproduction of thyroid hormone” make up a ratio 4.4% of the

DOI: https://doi.org/10.25130/tjps.v31i1.1890

population, while between 2% and 4% have subclinical hyperthyroidism in which high level of TSH and normal levels of T4 and T3 hormones [7].

Hepassocin is a protein called Fibrinogen-like protein 1, which is encoded by the "FGL1" gene in humans. FGL1 belongs to the family of fibrinogen-related proteins, hepatocyte-derived fibrinogen-related protein 1. It is a hepatokine that has been defined as a hepatocyte-stimulating factor and protects the liver from chemical injury. It is very important to note that hepatocyte nuclear factor 1 (HNF1) is essential and effective for the specific expression of hepatocin in the liver, and decreased HNF1 levels lead to reduced hepatocin expression in hepatocellular carcinoma. [8]. **Hepassocin** plays an important role in the pathogenesis of **metabolic** diseases. [9].

Adipokine is an adipokine that is synthesized and formed in adipose tissue and then secreted into the circulation and bloodstream. It can be scientifically defined as complement factor-D "CFD", and it acts as a rate-limiting factor in the alternative complement pathway and performs key functions and tasks in activating the complement system. CFD deficiency in humans is a very rare condition. However, increased and hyperactivity of the complement has been associated with the causes that lead to many disorders. [10].

In responding to physiological stimuli and metabolic stress, adipose tissue is essential for secreting bioactive molecules, including peptides, lipids, metabolites, and extracellular vesicles. These secretory factors control several adipose tissue processes via autocrine and paracrine mechanisms. The maintenance of equilibrium and proper function of the adipose tissue microenvironment depends on processes such as adipogenesis, glucose and lipid metabolism, inflammation, and adaptive thermogenesis. To control appetite, cognitive function, energy expenditure, insulin secretion and sensitivity, gluconeogenesis, cardiovascular remodeling, and exercise capacity, a subset of these adipose tissue-derived secretory factors can enter the bloodstream and target distant tissues. In this review, we emphasize how metabolic homeostasis is modulated by adipose-derived secretory factors and their signaling pathways. [11].

This study aimed to determine serum levels of hepassocin and adipsin, which may play a role as a biochemical marker of hypothyroidism and compare them with patients with hypothyroidism and diabetes, the investigation of hepassocin and adipsin in patients with hypothyroidism and diabetes is significant because it may uncover shared mechanisms between the two conditions (such as inflammation, insulin resistance, and lipid imbalance). Additionally, novel biomarkers can be used to identify the illness and assess how well a treatment is working.

METHODOLOGY: MATERIALS AND METHODS

The **collection of samples:**

This study includes 90 samples from people aged 30-61, collected at the specialized endocrinology center in Baghdad's Al-Nahda area, who live in different parts of the city. Blood samples were collected by withdrawing 7 ml from each man in the patient and control groups after obtaining their consent, and were divided into two parts. The first part (5 ml) was placed in a gel tube and then centrifuged at 3500xg for 5 minutes to obtain serum only. The serum was divided into three parts, placed in Ibn Daruf tubes, and stored at -30°C until used to obtain concentrations of biochemical variables. A second part (2 ml) was placed in tubes for glucose testing. Samples were obtained. During the period from 11/2023 to 5/2024, the samples were divided into five groups described below:

- Control as total: The 30 samples of healthy men.
- Patients as a total: The 60 samples of patients of all types as a total were compared with the 30 samples of healthy men as the total control.
- G1 is the first group, which included 30 samples of men with hypothyroidism.
- G2 is the second group, which included 15 samples of men with hypothyroidism and diabetes with treatment of thyroid disorder.

DOI: https://doi.org/10.25130/tjps.v31i1.1890

- G3 is the third group, which included 15 samples of men with hypothyroidism and diabetes without treatment of thyroid disorder.

Also, all groups above are divided into two groups (A1, A2) depending on age and (B1, B2) depending on BMI.

The determination of heparin and adipsin in the serum of healthy men and patients was performed using ELISA kits from SUNLONG (Biotech, China) and an automated ELISA Reader system (HUMAN, Germany). The determination of glucose by the "CBC" device provided by the Mandiri apparatus, a Chinese Company.

Statistical Analysis: "The XLSTAT statistical package software analyzed data". The probability thresholds are as follows: $P < 0.001$ indicates strong significance, $P < 0.05$ denotes significance, and $P > 0.05$ signifies non-significance; 95% confidence intervals.

RESULT AND DISCUSSION

TSH and T4

The result of this study showed that the average mean (±SD) of TSH µIU/ml of concentration in blood serum of healthy men and groups of patients, as total and groups (G1, G2, G3) according to age and BMI, are described in Table 1 and Figure 1, which is shown below.

- There was a highly significant increase ($P < 0.001$) in TSH level in the men patients' groups compared with the healthy men (G1) as a total.
- There was a highly significant increase in TSH ($P < 0.001$) between G1, G2, G3 men patients' groups comparing to each other.
- There was no significant difference ($P > 0.05$) in TSH levels in the BMI groups of men patients, the BMI men control groups, and the age men control and patient groups.
- There was significant increase (<0.05) between Age1 group patient compared to Age2 men patient's group.

Table 1: The Mean ± SD TSH µIU/ml for the studied Groups

TSH µIU/ml		Control G1 (n=30)	Patients (n=60)
Total		4.18±0.67	8.9±1.987
P value (T-TEST)		≤0.001	
G1 n=30)		14.29±2.94	
G2 n=15)		8.91±2.1	
G3 n=15)		3.69±0.92	
P value (ANOVA TEST)		≤0.001	
BMI (n=60)	BMI1(20-24.9)	3.90±0.87	8.63±1.27
(30 For Each group)	BMI2(25-29.9)	4.39±0.52	8.99+0.82
P value (T - TEST)		> 0.05	> 0.05
Age (year) (n=60)	Age1 (30-45)	4.34±0.88	9.62±1.33
(30 For Each group)	Age2 (46-61)	3.9±0.7	7.62±1.23
P value (T – TEST)		> 0.05	< 0.05

DOI: https://doi.org/10.25130/tjps.v31i1.1890

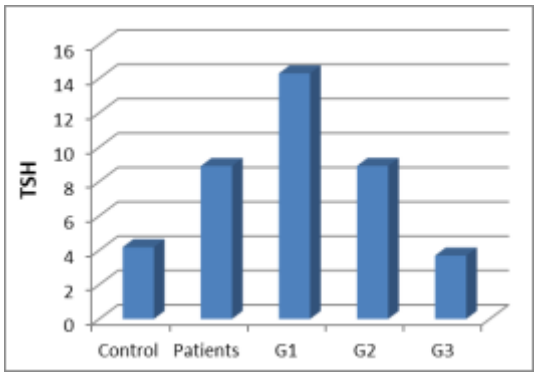

Fig. 1: The Mean ± SD TSH for the studied Groups

The result of this study describes that the mean (± SD) of **T4** ng/ml levels in blood serum of the control group "healthy men" and the group of patients, depending on age and BMI, are described in Table 2 and Fig 2, which are shown below:

- The results showed a highly significant decrease (P <0.001) in T4 level in the patient group compared to the healthy men control group.
- There was highly significant decrease in T4 (P < 0.001) between G1, G2, G3 men patients group compared to each other.
- Also, the results describe that there is no significant difference in T4 (P > 0.05) in T4 concentration, depending on the BMI groups of men patients, the BMI men control groups, and the age of men control and patient groups.
- There was significant increase (<0.05) between BM11 and BMI2 groups patient.

Table 2: The Mean ± SD of T4 ng/ml for the studied Groups

T4 ng/ml		**Control (n=30)**	**Patients (n=60)**
Total		8.97± 1.97	6.8±1.38
P value (T-TEST)		≤0.001	
G1(n=30)		5.86±1.42	
G2(n=15)		6.4 ±1.5	
G3(n=15)		8.18 ± 1.27	
P value (ANOVA TEST)		≤ 0 .001	
BMI (n=60)	**BMI1(20-24.9)**	8.9±1.70	7.61±1.27
(30 For Each group)	**BMI2(25-29.9)**	9.14±2.90	6.35±1.46
P value (T-TEST)		> 0.05	< 0.01
Age (year) (n=60)	**Age1 (30-45)**	8.67±2.67	6.84±1.38
(30 For Each group)	**Age2 (46-61)**	8.4±1.4	7.11±1.63
P value (T-TEST)		>0.05	>0.05

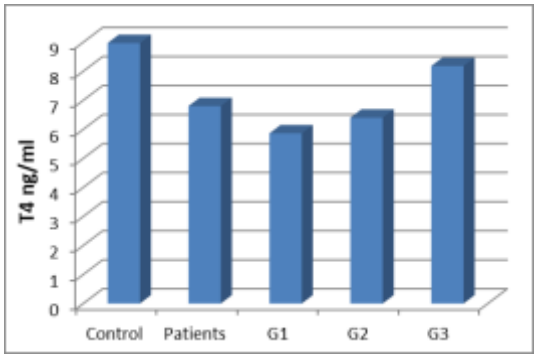

Fig. 2: The Mean ± SD T4 ng/ml for the studied Groups

An increase in TSH concentration and a decrease in T4 concentration can occur for several reasons, often indicating a problem with the thyroid gland or the body's metabolism.[12]. The thyroid gland synthesizes insufficient thyroid hormones (T3 and T4). This means the pituitary gland releases more TSH to stimulate and increase thyroid hormone production. Common causes may include primary hypothyroidism, as well as autoimmune conditions like Hashimoto's thyroiditis.[13], Iodine deficiency[14].

The results of high concentrations of TSH and low concentrations of T4 hormone are consistent with many research results related to hypothyroidism, for instance [15-20]. Also, the results agree with (21) that Hashimoto's thyroiditis and disorders linked to the

DOI: https://doi.org/10.25130/tjps.v31i1.1890

thyroid, such as chronic autoimmune serum-negative thyroiditis, require. In the [22], describe that Hypothyroidism can be overt due to thyroid gland disorders or subclinical hypothyroidism, which is a reduction in thyroid hormone production caused by a defect in the anterior pituitary or hypothalamus glands, and is a common disease among people.

Hepassocin

The results of this study indicate that the mean (±SD) concentration of hepassocin ng/ml in the serum of the control (healthy men) group and the men patient groups, depending on age and BMI, are shown in Table 3 and Fig 3 below. From the results obtained, a highly significant increase ($P < 0.001$) in heparin levels was observed in the patient groups compared to the healthy men control groups as a whole. There was a highly significant increase in heparin ($P < 0.001$) between the G1, G2, and G3 male patient groups. Also, there was a significant difference (< 0.05) between the BM11 and BMI2 patient groups.

Table 3: The Mean ± SD of Hepassocin for the studied Groups

Hepassocin ng/ml		Control (n=30)	Patients (n=60)
Total		74.75±10.82	152.2±16.243
P value (T – TEST)		≤ 0 .001	
G1(n=30)		153.3±15.71	
G2(n=15)		163.1±8.9	
G3(n=15)		140.61±24.12	
P value (ANOVA TEST)		≤0.001	
BMI (n=60)	**BMI1(20-24.9)**	76.82±11.19	148.52±13.04
(30 For Each group)	**BMI2(25-29.9)**	71.29±11.43	156.62±26.561
P value (T - TEST)		> 0 .05	> 0 .05
Age (year) (n=60)	**Age1 (30-45)**	75.68±11.35	138.98±10.98
(30 For Each group)	**Age2 (46-61)**	71.9±16.6	162.23±24.82
P value (T - TEST)		>0.05	≤0.01

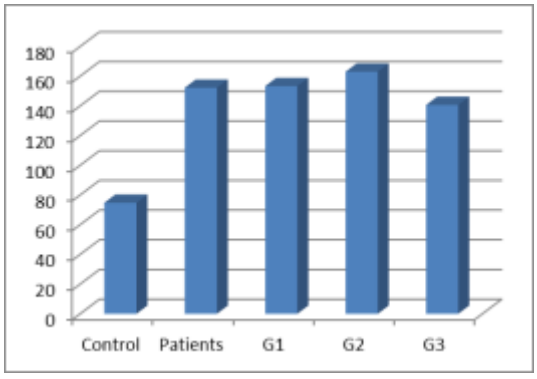

Fig. 3: The Mean ± SD of Hepassocin for the studied Groups

The relationship between hepassocin and hypothyroidism is still under investigation; early evidence suggests a potential link through their shared influence on metabolism, insulin sensitivity, and liver function. Since heparin is a protein derived from the liver that plays an important, fundamental role in liver metabolism and systemic metabolic regulation. The involvement of the liver in lipid and glucose metabolism is primarily due to signaling interactions between multiple organs mediated by hepatic hormones, cytokines, and hypokines. These are hormone-like proteins secreted by hepatocytes, and several hypokinases have been associated with extrahepatic metabolic regulation. Increasing evidence has revealed that their secretion patterns vary significantly in nonalcoholic fatty liver disease (NAFLD), the most obscure hepatic manifestation, which often overlooks other metabolic disorders, e.g., insulin resistance and type 2 diabetes [22, 23]. There is a relationship between free thyroxin (FT4) and plasma beta-2-HDL production in patients with type 2 diabetes mellitus (9), suggesting a link between increased heparan sulfate levels in hypothyroidism and diabetes [24]. A current result

DOI: https://doi.org/10.25130/tjps.v31i1.1890

disagrees with [9], who found an increase in hyperthyroidism.

Diabetes mellitus (DM) is characterized by elevated blood glucose levels, leading to disturbances in carbohydrate, protein, and lipid metabolism. DM is a defect in an important insulin metabolic pathway. The thyroid gland is a vital cog in the endocrine system. The thyroid gland plays a major role in regulating the body's metabolism by producing thyroid hormones. Therefore, research confirms that hypothyroidism is a disease condition in which the concentration of thyroid hormones is low due to various factors and is characterized by a state of metabolic inactivity. The relationship between insulin, which is involved in diabetes, and thyroid hormones is part of a complex abnormal process that regulates the body's metabolism. Research has found that both type 1 diabetes (T1DM) and type 2 diabetes (T2DM) are increasingly associated with hypothyroidism, especially in patients with risk factors such as female gender, hyperlipidemia (increased lipid in blood), overweight or obesity, and anemia. [25].

Through the above information, which was quoted from modern research sources, it confirms the existence of a strong relationship between hypothyroidism, diabetes of both types, and increased concentration of heparin in the men patients compared with healthy men.

Adipsin

The results of the study show that the mean (±SD) adipsin concentration (ng/mL) in the blood serum of the control group (healthy men) and the patient groups, by age and BMI, are shown in Table 4 and Fig 4 below.

- There was a great significant increase (P < 0 .001) in Adipsin level in the patient group compared to the healthy men control groups as a total [26, 27].
- There was a highly significant increase in Adipsin (P <0.001) between G1, G2, and G3 men patients' groups when we compared them with each other.
- There was a simple significant increase (<0.05) between BM11 and BMI2 patient groups.

Table 4: The Mean ± SD of Adipsin for the studied Groups

T4 ng/ml		Control (n=30)	Patients (n=60)
Total		212.64±41.09	488.4±62.647
P value (T-TEST)		≤0.001	
G1(n=30)		486.75±59.60	
G2(n=15)		547.6±75.2	
G3(n=15)		430.96±53.14	
P value (ANOVA TEST)		≤0.001	
BMI (n=60)	**BMI1(20-24.9)**	200.62±48.09	467.61±76.5
(30 For Each group)	**BMI2(25-29.9)**	236.12±39.22	510.8±97.43
P value (T - TEST)		> 0 .05	< 0 .05
Age (year) (n=60)	**Age1 (30-45)**	211.59±49.14	503.77±67.77
(30 For Each group)	**Age2 (46-61)**	218±18.7	500.95±61.06
P value (T - TEST)		> 0 .05	> 0 .05

DOI: https://doi.org/10.25130/tjps.v31i1.1890

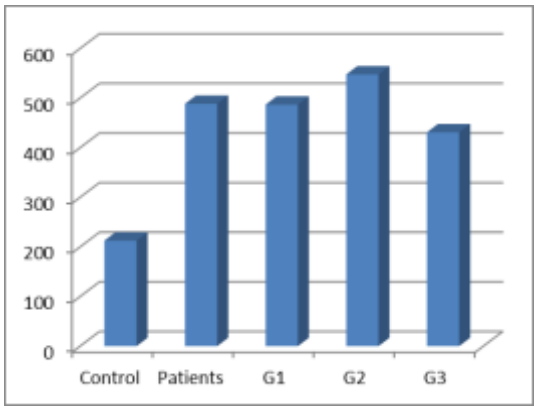

Fig 4: The Mean ± SD of Adipsin for the studied Groups

The research showed that adipsin acts as an adipokine with anti-inflammatory effects, and its concentration is elevated in obesity and type II DM. [28].

Because there is a relationship and connection between the liver, hypothyroidism and diabetes, and as studies show that in the case of diseases such as non - alcoholic liver disease, it leads to an increase in the amount of adipsin in the blood serum of patients, as a result, it is expected that the concentration of adipsin will increase in patients with hypothyroidism [29-31].

The results of our study support many studies with smaller conclusions and lower scores.[29-34] that adipsin blood serum concentration increases with body weight and BMI. The relationship between adipsin and body mass index has been reported to be associated with increased fat mass. Adipsin supports adipocyte production and affects adipose tissue rebuilding. Adipsin serum levels are linked to overweight, obesity, and age.[35].

CONCLUSION

Based on our study's findings, we can conclude that patients with overt and hypothyroidism had higher levels of hepasocin and adipsin overall than did the group of healthy men. In hypothyroidism and diabetes, compensatory metabolic reactions to insulin resistance, dyslipidemia, and chronic inflammation are reflected in elevated levels of hepasocin and adipsin. Adipsin elevation signifies adipose tissue dysfunction and complement system overactivation, whereas hepassocin rises to counteract metabolic stress. These indicators demonstrate the complex relationship between the development of metabolic diseases and endocrine dysfunction. Therefore, as a risk factor for hypothyroidism, these parameters may be used as a relatively independent marker for the diagnosis of metabolic problems or non-clinical to overt conditions in patients.

Conflict of interests: The authors declare that there is no conflict of interest with the interests of others.

Sources of funding: The **authors** of this research did not receive any grants from any public, commercial, or non-profit funding agencies.

Author contribution: I collected the samples and conducted the work, and Prof. Dr. Nagham helped me with the work plan, supervision, and statistics.

REFERENCE:

1. Otla AA, Saleh NA. Estimation of the level of homocysteine and vitamin B12 in the serum of patients with hypothyroidism. Tikrit J Pure Sci. 2019;2019:70-3.

2. Feldt-Rasmussen U, Effraimidis G, Bliddal S, Klose M. Consequences of undertreatment of hypothyroidism. Endocrine. 2024;84(2):301-8. https://doi.org/10.1007/s12020-023-03460-1

3. Hadeed WA, Alhially Y, Bashi A. Comparison of thyroid function tests between splenectomised and non-splenectomised β-thalassemia major patients. Tik J of Pure Sci. 2015;20:61-6.

4. Bereda G. Definition, causes, pathophysiology, and management of hypothyroidism. Mathews Journal of Pharmaceutical Science. 2023;7(1):1-5.

5. England ML, Gerrard JM. Hypothyroidism, diabetes, and cardiovascular disease. Cardiometabolic Diseases: Elsevier; 2025. p. 239-48. https://doi.org/10.1016/B978-0-323-95469-3.00004-8

6. Al-harbawi DJT, Al-obaidi WML. Determination Of Hepcidin Concentration And

DOI: https://doi.org/10.25130/tjps.v31i1.1890

Many Hematological And Biochemical Variations In Patients With Diabetes Type 2 Diabetes in Balad City. Tikrit Journal of Pure Science. 2017;22(3):1-6.

7. Kim HK, Song J. Hypothyroidism and diabetes-related dementia: Focused on neuronal dysfunction, insulin resistance, and dyslipidemia. International Journal of Molecular Sciences. 2022;23(6):2982.

https://doi.org/10.3390/ijms23062982

8. Chen J, Wu L, Li Y. FGL1 and FGL2: emerging regulators of liver health and disease. Biomarker Research. 2024.

https://doi.org/10.1186/s40364-024-00601-0.53:(1)12;

9. Wang C-C, Lin C-H, Chou H-W, Wang C-T, Liang Y-C, Wu H-T, et al. Compensatory Increase of Serum Hepassocin Protects Against Hyperthyroidism-Induced Hepatic Dysfunction. Biomedicines. 2023;11(7):1936.

https://doi.org/10.3390/biomedicines11071936

10. Milek M, Moulla Y, Kern M, Stroh C, Dietrich A, Schön MR, et al. Adipsin serum concentrations and adipose tissue expression in people with obesity and type 2 diabetes. International journal of molecular sciences. 2022;23(4):2222.

https://doi.org/10.3390/ijms23042222

11. Liu Y, Qian S-W, Tang Y, Tang Q-Q. The secretory function of adipose tissues in metabolic regulation. Life Metabolism. 2024;3(2):loae003.

https://doi.org/10.1093/lifemeta/loae003

12. Rasoulizadeh Z, Ordooei M, Akbarian E. Diagnostic options, physiopathology, risk factors and genetic causes of permanent congenital hypothyroidism: A narrative review. Caspian Journal of Internal Medicine. 2024;15(4):570.

https://doi.org/10.22088/cjim.15.4.570

13. Wrońska K, Hałasa M, Szczuko M. The role of the immune system in the course of Hashimoto's Thyroiditis: the current state of knowledge. International Journal of Molecular Sciences. 2024;25(13):6883.

https://doi.org/10.3390/ijms25136883

14 Grimmichova T, Verespejova L, Urbaniova Z, Chovanec M, Hill M, Bilek R. Acquired hypothyroidism, iodine status and hearing impairment in adults: A pilot study. PloS one. 2025;20(1):e0305787.

https://doi.org/10.1371/journal.pone.0305787

15. Ettleson MD, Bianco AC. Individualized therapy for hypothyroidism: Is T4 enough for everyone? The Journal of Clinical Endocrinology & Metabolism. 2020;105(9):e3090-e104.

doi:10.1210/clinem/dgaa430

16. Chaker L, Razvi S, Bensenor IM, Azizi F, Pearce EN, Peeters RP. Hypothyroidism (primer). Nature Reviews: Disease Primers. 2022;8(1).

doi:10.1210/clinem/dgaa430

17. Wilson SA, Stem LA, Bruehlman RD. Hypothyroidism: diagnosis and treatment. American family physician. 2021;103(10):605-13.

18. Salvatore D, Porcelli T, Ettleson MD, Bianco AC. The relevance of T3 in the management of hypothyroidism. The Lancet Diabetes & Endocrinology. 2022;10(5):366-72.

19. Croce L, De Martinis L, Pinto S, Coperchini F, Dito G, Bendotti G, et al. Compared with classic Hashimoto's thyroiditis, chronic autoimmune serum-negative thyroiditis requires a lower substitution dose of L-thyroxine to correct hypothyroidism. Journal of Endocrinological Investigation. 2020;43:1631-6.

https://doi.org/10.1007/s40618-020-01249-x

20. Liu H, Peng D. Update on dyslipidemia in hypothyroidism: the mechanism of dyslipidemia in hypothyroidism. Endocrine Connections. 2022;11(2.(DOI: https://doi.org/10.1530/EC-21-0002

21. Xue H, Xu R. The lymphocyte levels of Hashimoto thyroiditis patients were significantly lower than those of the healthy population. Frontiers in Endocrinology. 2025;16:1472856.

https://doi.org/10.3389/fendo.2025.1472856

22. Triolo M, Kwakernaak AJ, Perton FG, de Vries R, Dallinga-Thie GM, Dullaart RP. Low normal thyroid function enhances plasma cholesteryl ester transfer in Type 2 diabetes mellitus. Atherosclerosis. 2013;228(2):466-71. https://doi.org/10.1016/j.atherosclerosis.2013.03.009

23. Abdelmoemen G, Khodeir SA, Zaki AN, Kassab M, Abou-Saif S, Abd-Elsalam S. Overexpression of hepassocin in diabetic patients with nonalcoholic fatty liver disease may facilitate increased hepatic lipid accumulation. Endocrine, Metabolic & Immune Disorders-Drug Targets (Formerly Current Drug Targets-Immune, Endocrine & Metabolic Disorders .(.8−185:(2)19;2019

https://doi.org/10.2174/1871530318666180716100543

24. Vemula SL, Aramadaka S, Mannam R, Narayanan RS, Bansal A, Yanamaladoddi VR, et al. The impact of hypothyroidism on diabetes mellitus and its complications: a comprehensive review. Cureus. 2023;15(6.(DOI: 10.7759/cureus.40447

25. Kim TH, Hong D-G, Yang YM. Hepatokines and non-alcoholic fatty liver disease: linking liver pathophysiology to metabolism. Biomedicines. 2021;9(12):1903.

https://doi.org/10.3390/biomedicines9121903

26. Pan J, Ding Y, Sun Y, Li Q, Wei T, Gu Y, et al. Associations between adipokines and metabolic dysfunction-associated fatty liver disease using three different diagnostic criteria. Journal of Clinical Medicine. 2023;12(6):2126.

https://doi.org/10.3390/jcm12062126

27. Elshinshawy S, Elhaddad H, Alem SA, Shaker O, Salam R, Yosry A, et al. The interrelation between hypothyroidism and non-alcoholic fatty liver disease :a cross-sectional study. Journal of Clinical and Experimental Hepatology. 2023;13(4):638-48.

https://doi.org/10.1016/j.jceh.2023.03.004

28. Jiang M-Y, Man W-R, Zhang X-B, Zhang X-H, Duan Y, Lin J, et al. Adipsin inhibits Irak2 mitochondrial translocation and improves fatty acid β-oxidation to alleviate diabetic cardiomyopathy. Military Medical Research. 2023;10(1):63. https://doi.org/10.1186/s40779-023-00493-5

29. Flier JS, Cook KS, Usher P, Spiegelman BM. Severely impaired adipsin expression in genetic and acquired obesity. Science. 1987;237(4813):405-8.

https://doi.org/10.1126/science.3299706

30. Vasilenko M, Kirienkova E, Skuratovskaia D, Zatolokin P, Mironyuk N, Litvinova L, editors. The role of production of adipsin and leptin in the development of insulin resistance in patients with abdominal obesity. Doklady Biochemistry and Biophysics; 2017: Springer. https://doi.org/10.1134/S160767291704010X

31. Bansal A, Honnapurmath VK, Singh A. Serum adipsin levels as a new marker in type 2 diabetes mellitus: A meta-analysis. International Journal of Diabetes in Developing Countries. 2025:1-7.

https://doi.org/10.1007/s13410-025-01449-2

32. Gómez-Banoy N, Guseh JS, Li G, Rubio-Navarro A, Chen T, Poirier B, et al. Adipsin protects beta cells in diabetic mice and is associated with protection against type 2 diabetes in humans. Nature medicine. 2019;25(11):1739-47. https://doi.org/10.1038/s41591-019-0610-4

33. Park J-H, Nguyen TN, Shim HM, Yu GI, Ha EY, Cho H. Identification of Adipsin as a Biomarker of Beta Cell Function in Patients with Type 2 Diabetes. Journal of Clinical Medicine. 2024;13(23):7351.

https://doi.org/10.3390/jcm13237351

34. Emiral Ç, Buluş D, Yaşartekin Y, Akaydın S. Serum Adipsin Levels in Obese and Normal Weight Adolescents with Polycystic Ovary Syndrome. Journal of Gazi University Health Sciences Institute. 2024;6(3):107-16. https://doi.org/10.59124/guhes.1604306

35. Byeon HJ, Chae MK, Ko J, Lee EJ, Kikkawa DO, Jang SY, et al. The role of adipsin, complement factor D, in the pathogenesis of Graves' Orbitopathy. Investigative ophthalmology & visual science. 2023;64. https://doi.org/10.1167/iovs.64.11.13