Asprosin Levels as New Metabolic Marker for the Early Detection and Diagnosis of Hypothyroidism Complications

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Abstract

Introduction: Hypothyroidism is a term used to describe any condition that causes a thyroid hormone shortage, such as hypothalamus or pituitary disease, widespread tissue resistance to thyroid hormones, and thyroid gland diseases. Asprosin is a newly discovered peptide hormone produced by white adipose tissue. It's worth noting that high asprosin levels are linked to insulin resistance. The goal of this study was to determine the levels of asprosin in patients' serum for early hypothyroidism and to see if there was a link between insulin resistance and asprosin in this group of patients.

Materials and methods: A case-control study design involved 120 Iraqi subjects, 60 of whom had hypothyroidism (42 females and 18 males) and were compared with 60 healthy adults (45 females and 15 males) whose ages were close to the group of patients ranging from (20 – 60) years. All subjects' serum levels of Asprosin, as well as metabolic indices such as BMI, WHR, (TT3, TT4, TSH), FSG, HOMA-IR, Insulin, QUICKI, (T-CHO, TG, HDL-C, VLDL-C, LDL-C,and zinc, were measured. The findings were subjected to statistical analysis in order to analyze the differences between the groups tested and to determine the relationship between parameters.

Results: There was no statistically significant difference in mean age between the patients and the control groups, according to the statistical analysis. In the hypothyroidism patient group, however, mean values of HOMA-IR, T-CHO, TG, LDL-C, VLDL-C, and asprosin were significantly higher than in the control group. TT3, TT4, QUICKI, and HDL-C levels in the blood were considerably lower than in the control group. Asporsin levels in patients had a substantial positive connection with W/H, TT3, and TT4 levels.

Conclusions: Hypothyroidism patients had significantly greater levels of Asprosin than the control group, according to the current study. W/H and HOMA-IR have a strong positive association with asprosin levels, while TT3, TT4, and QUICKI have a significant negative correlation. These findings imply that lowering asprosin levels in hypothyroidism patients could be a useful method for treating insulin resistance and T2DM.

Key Words: Hypothyroidism, Asprosin, HOMA-IR, QUICKI, and Zinc.

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Introduction

Hypothyroidism is defined as any condition that causes a thyroid hormone shortage, including hypothalamus or pituitary disease, widespread tissue resistance to thyroid hormones, and thyroid gland problems (Woeber KA et al., 2000). Thyroid dysfunction causes alterations in lipoprotein composition and transport (Duntas LH et al., 2002).

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Thyroid hormones, in particular, HMG-CoA reductase, the primary enzyme in cholesterol biosynthesis, is activated to promote hepatic de novo cholesterol production (Ness G C et al., 1973). Low-density lipoprotein (LDL) receptors are also activated by thyroid hormones; the promoter of the LDL receptor gene has a thyroid hormone responsive region, allowing T3 to up-regulate LDL receptor gene expression, resulting in accelerated LDL particle catabolism. (Bakker O et al., 1998).

Thyroid hormones play a function in glucose metabolism and the development of insulin resistance. The evidence suggests that in hypothyroidism, insulin resistance of peripheral tissues predominates. A direct regulation of thyroid responsive genes at the target organ, as well as an indirect regulation of thyroid responsive genes at the target organ, has been described, (Gabriela B et al., 2011) an indirect impact involving hypothalamic mechanisms that regulate glucose metabolism via sympathetic nervous system regulation was discovered.

Fasting-induced glucogenic adipokine Asprosin, a 140-amino-acid C-terminal profibrillin, is encoded by two exons (exons 65 and 66) of the Fibrillin1 gene (FBN1) (Romere C et al., 2016). This was first discovered in newborns with progeroid syndrome. It is mostly produced by white adipose tissue and triggers the G protein-cAMP-PKA pathway, which encourages the liver to create glucose. Through PKC-activated endoplasmic reticulum stress and TLR4/JNK-mediated inflammatory pathways, it also impairs insulin sensitivity and secretion (Jung T W et al., 2019). Asprosin can also penetrate the blood-brain barrier, activating orexigenic AgRP+ neurons and inhibiting downstream anorexigenic proopiomelanocortin (POMC)-positive neurons, resulting in appetite stimulation. Importantly, the amount of asprosin is pathologically elevated in humans and mice with insulin resistance or type 2 diabetes (T2D), as well as in obese humans and mice (Duerrschmid C et al., 2017) and (Zhang L et al., 2019).

Material and Methods

Subjects and Study Design

All of the investigations were carried out with the agreement of the University of Kufa's Faculty of Science's regional ethics committee. Before starting the study, each participant signed an informed consent form. This study was planned as a case control study, with 120 people divided into two groups: 60 hypothyroidism patients (42 females and 18 men) ranging in age from 20 to 60 years old. Between January 2020 and September 2021, patients were registered in the "Diwaniya Teaching Hospital" in Al-Qadisiyah, Iraq. A control group of 60 healthy adults was used to compare the results. Their ages were similar to the patients', ranging from 20 to 60 years (45 females and 15 males).

Exclusion Criteria

Subjects suffered from diseases (diabetes mellitus, smokers, Liver disease and systemic sickness, Subjects getting treatment with diuretics, ß blockers, or cholesterol lowering medications, or any other medications that may affect lipid characteristics in the blood and thyroid function, a history of heart surgery or other cardiovascular interventions, a pregnancy a chronic kidney disease, and smokers were excluded in this study.

Collection of Samples

Five milliliters of venous blood were taken from hypothyroidism patients and a healthy group between 8:30 and 10:00 a.m. using antecubital venipuncture using G 23 needles after an 8-12 hour fast. At room temperature, 5ml of blood was allowed to coagulate in a plain test tube. After centrifugation at (3000 X g) for 15 minutes, the serum was separated into four tubes and kept at -20°C until analysis.

Anthropometric Evaluation

Age, weight (kg), height (cm), waist circumference (cm), and hip circumference (cm) are all anthropometric measurements (cm). Furthermore, the Body Mass Index was calculated by dividing an individual's weight in kilograms by their square meter length: BMI = (weight in kg) / (height in meters2) (McDougall K E et al. , 2018).

Biochemical Evaluation

Thyroid-stimulating hormone (TSH), total triiodothyronine (TT3), and total thyroxine (TT4) levels in the blood were determined using an ELISA microplate washer and reader, which is a compact immunoassay system based on the Enzyme Linked Immunosorbent Assay (ELISA) principles, and a commercial kit from CORTEZ (USA). Using a commercial kit from LiNEAR, the concentrations of fasting serum glucose, total cholesterol, high

density lipoprotein cholesterol (HDL-C), and triglyceride were analyzed using a colorimetric approach for quantitative in vitro diagnostic testing (SPAIN). Fried Ewald's formula was used to calculate the levels of low-density lipoprotein cholesterol (LDL-C) (Freidewald W T et al., 1972). A commercial kit from LTA was used to assess serum zinc content using an atomic absorption spectropotometer advice at (578 nm) (Italia). Fasting insulin levels were determined using a commercial Monobind Inc. immunoenzymometric assay (TYPE 3) and a commercial kit (USA). Insulin resistance was computed using the homeostasis model assessment (HOMA-IR) score, which applies the formula, and serum asprosin was tested using enzyme-linked immunosorbent assay kits (MELSIN, China): fasting insulin concentration (µIU/L) glucose (mmoL/L)/22.5. Insulin resistance was defined as having a HOMA-IR of greater than 2.7. Insulin resistance was defined as having a HOMA-IR of greater than 2.7 (Matthews D R et al., 1985). QUICKI values (quantitative insulin sensitivity check index) was estimated by equation: QUICKI= 1/log(I0) + log(G0), where I0 is the fasting insulin (µIU/ml), and G0 is the fasting glucose (mg/dL), according to (Grzesiuk W et al., 2008) and (Szurkowska M et al., 2005).

Bio-statistical Analysis

The statistical analysis was carried out using Microsoft Excel 2010 and SPSS-24 (statistical package for social science-version 24) software. The data was statistically examined, and the t-test was employed to look for differences between the groups studied. The correlation between parameters was determined using Pearson's correlation coefficient.

Results

Comparison between Clinical Laboratory Characteristics of the Study Population

In table (1) demonstrated the mean of age has no significant difference between patients group compared with control group. But found the mean of BMI, W/H, TSH, FSG, insulin, HOMA-IR, T-CHO, TG, LDL-C, VLDL-C and asprosin levels showed a significant increase in hypothyroidism when compared with control group. Decreased serum levels of zinic, TT3, TT4, QUICKI, HDL-C in hypothyroidism compared with control group.

Table 1. Demographic and clinical characteristics for hypothyroidism patients and control groups

Parameters	Groups		P-Value
	Control Mean ±SD (n=60)	Hypothyroidism Mean ±SD (n=60)	
Age (year)	36.03±9.17	40.1±17.3	0.586
SBP		130.13±18.05	
DBP		78.70±11.38	
BMI (Kg/m^2)	24.3±2.0	32.7 ±4.7	0.000
W/H	0.82±0.19	2.11±0.74	0.000
TT3 (ng/mL)	1.92±0.33	0.51±0.10	0.000
TT4 (ng/mL)	73.3±12.5	44.3±12.9	0.000
TSH (µIU/mL)	2.30±0.81	20.1±8.30	0.000
FSG (mg/dL)	82.5±6.38	139.3±54.5	0.000
Insulin (µU/mL)	3.92±1.34	15.6±2.51	0.000
HOMA-IR	0.80±0.28	5.43±2.48	0.000
QUICKI	0.41±0.04	0.30±0.01	0.000
T-CHO (mg/dL)	112.0±30.3	149.0±46.8	0.001
TG (mg/dL)	94.1±12.7	160.9±34.3	0.000
HDL-C (mg/dL)	43.9±8.92	20.7±7.55	0.000
VLDL-C(mg/dL)	20.4±7.94	32.8±7.61	0.000
LDL-C (mg/dL)	59.2±18.5	121.5±50.2	0.000
Zinc (µg/dL)	115.4±8.55	107.2±24.7	0.339
Asprosin (ng/mL)	1.35±0.50	1.99±0.41	0.000

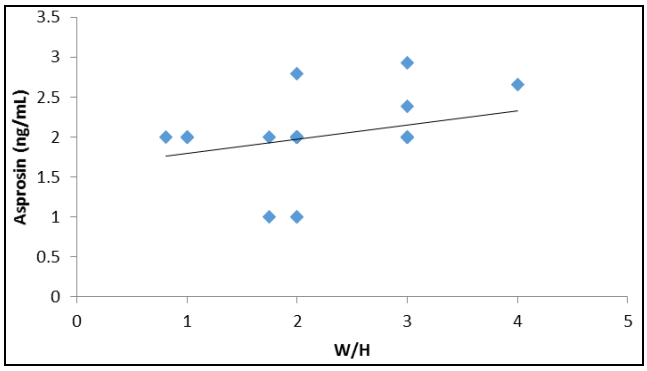
A p-value of ≤.05 was considered significant, Data represented as Mean ±SD, SD: Stander deviation, n: Number of subjects, BMI: Body mass index, W/H: The waist to hip ratio, SBP: Systolic blood pressure, DBP: Diastolic blood pressure, TT3: Total Thyroxine, TT3: Total Triiodothyronine, TSH: Thyroid-stimulating hormone, FSG: fasting serum glucose, HOMA-IR: Homeostatic Model Assessment for Insulin Resistance, QUICKI: quantitative insulin sensitivity check index, T-CHO: total cholesterol, TG: triglyceride, HDL-C: high density lipoprotein-cholesterol, LDL-C: low density lipoprotein - cholesterol, VLDL-C: Very low density lipoprotein-cholesterol.

The linear regression analysis shown in table (2) shown the relationships between Asprosin and other biochemical studied of hypothyroidism patients group. The results of Asprosin levels given asignificant positive correlation with W/H, TT3 and TT4 as shown in figure (1a, b, c, d, e).

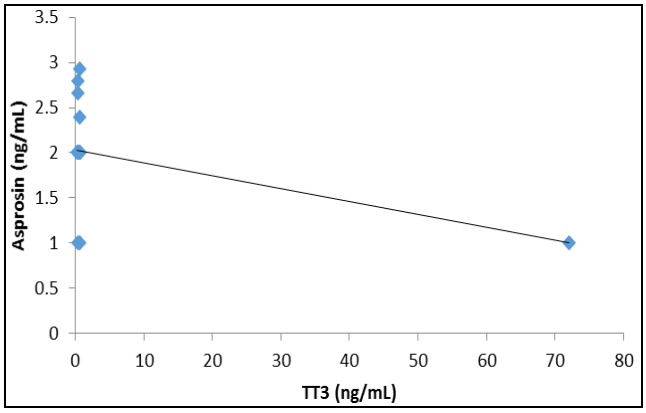
Table 2. Correlation between levels of serum asprosin and others biochemical studied in hypothyroidism patients group

Parameters	Asprosin (ng/mL)	
Age (year)	r	-0.286
	P-value	0.12
BMI (kg/m²)	r	0.127
	P-value	0.505
W/H	r	0.321
	P-value	0.05
TT3 (ng/mL)	r	-0.449
	P-value	0.03
TT4 (ng/mL)	r	-0.374
	P-value	0.04
TSH (µIU/mL)	r	0.076
	P-value	0.69
FSG (mg/dL)	r	0.069
	P-value	0.717
Insulin (µU/mL)	r	0.279
	P-value	0.054
HOMA-IR	r	0.323
	P-value	0.018
QUICKI	r	-0.203
	P-value	0.08
T-CHO (mg/dL)	r	0.029
	P-value	0.88
TG (mg/dL)	r	0.137
	P-value	0.470
HDL-C (mg/dL)	r	-0.300
	P-value	0.108
VLDL-C(mg/dL)	r	0.197
	P-value	0.29
LDL-C(mg/dL)	r	0.169
	P-value	0.371
Zinc (µg/dL)	r	-0.133
	P-value	0.48

A p-value of ≤.05 was considered significant, r: Person s correlation, BMI: Body mass index, W/H: The waist to hip ratio, TT3: Total Thyroxine, TT3: Total Triiodothyronine, TSH: Thyroid-stimulating hormone. FSG: fasting serum glucose, HOMA-IR: Homeostatic Model Assessment for Insulin Resistance, QUICKI: quantitative insulin sensitivity check index, T-CHO: Total cholesterol, TG: Triglyceride, HDL-c: High density lipoprotein-cholesterol, LDL: Low density lipoprotein, VLDL.C: Very low density lipoprotein- cholesterol.



(a)



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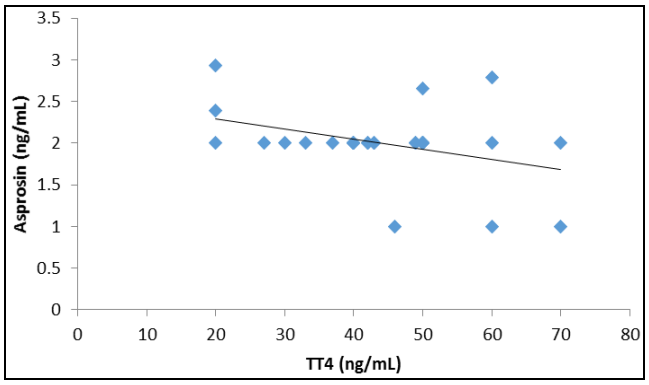
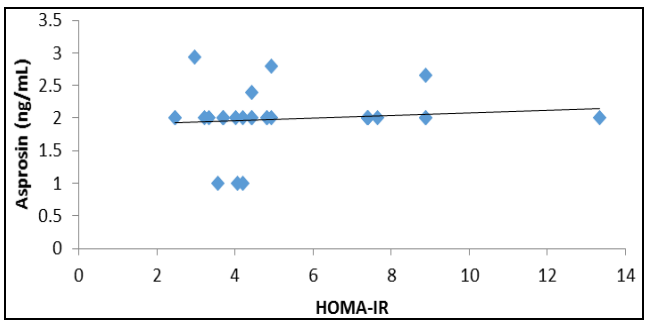


(c)



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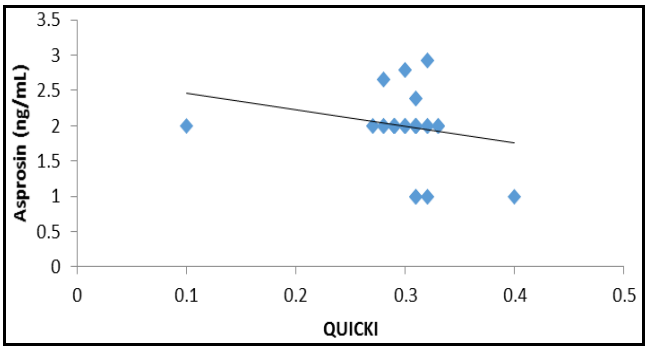

(e)

Figure 1. Correlation between Serum Asprosin and (a): W/H, (b): TT3, (c): TT4, (d): HOMA-IR and (e): QUICKI in hypothyroidism patients group

Discussion

Thyroid hormones are involved in the regulation of body metabolism. Their effects include increased energy expenditure, regulation of catecholamine response, and stimulation of resting metabolic rate and energy homeostasis, all of which influence in adipose tissue, body weight, thermogenesis, and lipolysis all play a role. Previous studies shown thermogenesis in adipose tissue. It has been proven that adipose tissue is a gland that secretes many chemicals with multiple metabolic activities (Krotkiewski M et al., 2002) (Lopez M et al., 2010). Adipocytokines are biologically active molecules produced by adipocytes that serve a variety of physiological purposes. These chemicals have a wide range of impacts on a variety of tissues, affecting intermediate and energy metabolism. As a result, the possibility of a link between adipocytokines and thyroid function has recently gotten a lot of attention, as well as thyroid issues. When thyroid function is interrupted, changes in body weight, muscle mass, and fat tissue occur. Thyroid-stimulating hormone (TSH) receptors have been found in adipose tissues, suggesting that they are involved in the control of adipocytokines, which regulate energy balance (Endo T et al., 1995).

The present study shown increased level of the novel adipocytokines (Asprosin) and HOMA-IR in hypothyroidism. A prior study indicated that impaired glucose regulation (IGR) and newly diagnosed type 2 diabetes mellitus (nT2DM) were the two groups that were studied had higher plasma asprosin than the normal glucose regulation (NGR) group, particularly in IGR participants. The homeostasis model assessment for IR was positively related with asprosin (HOMA-IR), While circulating asprosin concentrations are positively connected to waist circumference and lipid levels, (Wang Y et al., 2018) found that they are inversely associated to the homeostasis model assessment for -cell function (HOMA-) (TG). When comparing persons with T2DM to controls, Zhang et al discovered greater serum asprosin concentrations, as well as an independent association between fasting glucose and serum asprosin in T2DM (Zhang L et al., 2019). The exact mechanism through which asprosin impacts obesity has yet to be discovered. Plasma asprosin levels and appetite were lower in NPS patients and animals with an NPS-related mutation and extreme leanness by (Romere C et al., 2016). This suggested that asprosin may have a role in obesity by influencing hunger.

Serum asprosin was found to be able to cross the blood-brain barrier and activate AgRP neurons via a cAMP-dependent pathway, which could contribute to excessive energy absorption and obesity (Duerrschmid C. et al., 2017). Recent studies reported that the level of asprosin has a key and contradictory role in obesity. Obesity has been linked to higher asprosin levels in human and animals in a previous studies. Obese adults have been found to have pathologically increased serum asprosin levels, Asprosin stimulates hepatic gluconeogenesis under fasting conditions. However, the roles of asprosin in inflammation, endoplasmic reticulum (ER) stress, and insulin resistance in skeletal muscle has not been studied. In the recent studies, elevated levels of asprosin expression were observed in adipocytes under hyperlipidemic conditions, whereas used asprosin-specific antibody to observe lower body weight and food intake in obese mice (Wang C. et al., 2019) (Wang M. et al., 2019). Blood asprosin concentrations in obese 6- to 14-year-old children were considerably lower than in healthy normal-weight youngsters in another cross-sectional study. When age and gender were taken into account, asprosin was found to be negatively associated with BMI, contradicting prior findings; this indicates the complex role of asprosin in obesity by (Long W. et al. 2019).

In addition, another study discovered that human salivary glands can synthesize asprosin. As respondents' body mass index (BMI) increased, so did their levels of low-density lipoprotein cholesterol (LDL-C) and asprosin in saliva and blood (Ugur K et al., 2019).

Groener et colleagues discovered that serum asprosin levels were diminished or muted in type 1 diabetes mellitus (T1DM) and type 2 diabetes mellitus (T2DM) patients in response to blood

glucose changes (Groener J et al., 2019). According to a recent study, the levels of serum asprosin in pregnant women with GDM and their newborns' umbilical cords are higher than in controls (Baykus Y et al., 2019).

T1DM mice have increased amounts of hepatic asprosin. As a result, serum asprosin, which might be used as a biomarker, could help detect diabetes early (Ko J. et al., 2019).

Chang C et al discovered that PCOS patients' metabolic characteristics differed significantly from diabetes individuals'. The findings demonstrated that irisin levels in PCOS patients were aberrant, but no direct links between plasma asprosin levels and metabolic symptoms in PCOS patients were discovered. Asprosin is a biomarker that can be used to predict and diagnose PCOS (Chang C. et al., 2019).

Acara AC et al claimed that asprosin could be a suitable marker for unstable angina pectoris (UAP) and that the severity of acute coronary syndrome (ACS) with UAP could be predicted in a prior study where changes in asprosin levels were found to be positively linked with the Syntax score (Acara AC et al., 2018). The current findings contradicted those of a recent study (Rasim M et al., 2020),

Asprosin has been linked to a reduction in the risk of cardiovascular disease. An in vitro study on MCMs found that asprosin can prevent cardiomyocyte death under high glucose conditions by reducing MDA and ROS production, which was used to investigate the link between blood asprosin levels and diabetic cardiomyopathy (DCM) (Feng J et al., 2018).

Conclusions

Hypothyroidism patients had significantly greater levels of Asprosin than the control group, according to the current study. Level of asprosin has asignificant positive association with W/H, HOMA-IR and a significant negative correlation with TT3, TT4, and QUICKI. These findings imply that measuring asprosin levels in hypothyroidism patients could be a useful technique for managing insulin resistance and T2DM in those individuals, as well as a predictor of hypothyroidism complications.

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Conflict of Interest

There are no conflicts of interest declared by the authors.

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References

Woeber KA, Update on the Management of hyperthyroidism and hypothyroidism., *Arch Fam Med*., 2000, 9: 743-747.

Duntas LH, Thyroid disease and lipids, *Thyroid.*, 2002, 12: 287-293.

Ness GC, Dugan RE, Lakshmanan MR, Nepokroeff CM and Porter JW, Stimulation of hepatic hydroxy-methyl-glutaryl coenzyme A reductase in hypophysectomized rats by L-triiodothyronine, *Proc Natl Acad Sci* USA., 1973, 70: 3839-3842.

Bakker O, Hudig F, Meijssen S and Wiersinga W M, Effects of triiodothyronine and amiodarone on the promoter of the human LDL receptor gene, *Biochem Biophys Res Commun*., 1998, 240: 517-521.

Gabriela B, Why Can Insulin Resistance Be a Natural Consequence of Thyroid Dysfunction?. *Journal of Thyroid Research*, 2011, 2011, 9: 152-161.

Romere C, Duerrschmid C, Bournat J, Constable P, Jain M, Xia F and et al., Asprosin, a fasting-induced glucogenic protein hormone, *Cell*., 2016, 165: 79–566.

Jung TW, Kim HC, Kim HU, et al., Asprosin attenuates insulin signaling pathway through PKCδ-activated ER stress and inflammation in skeletal muscle, *Journal of Cellular Physiology*, 2019, 234: 20888–20899.

Duerrschmid, C. et al., Asprosin is a centrally acting orexigenic hormone, *Nat Med*., 2017, 23: 1444–1453.

Zhang L, Chen C, Zhou N, Fu Y and Cheng X, Circulating asprosin concentrations are increased in type 2 diabetes mellitus and independently associated with fasting glucose and triglyceride, *Clin Chim Acta*, 2019, 489: 8–183.

McDougall KE, Stewart AJ, Comparison of three methods for measuring height in rehabilitation inpatients and the impact on body mass index classification: An open prospective study, *Nutrition & Dietetics*, 2018, 75: 123–128.

Freidewald WT, Levy RI, Fredickson DS, Estimation of the concentration of low-density lipoprotein cholesterol in plasma, without use of the preparative ultracentrifuge. *Clin. Chem*., 1972, 18: 499–502

Matthews DR, Hosker JP, Rudenski AS, Naylor BA, Treacher DF, Turner RC, Homeostasis model assessment: insulin resistance and b-cell function from fasting plasma glucose and insulin concentrations in man, *Diabetologia*, 1985, 28: 29-41

Grzesiuk W, Szydlarska D, Jóźwik K, Insulinooporność w endokrynopataich, *Endokrynol Otył Zab Przem Mat*., 2008, 5: 38–44.

Szurkowska M, Szafraniec K, Gilis-Janiuszewska A et al., Wskaźniki insulinooporności w badaniu populacyjnym i ich wartość predykcyjna w określeniu zespołu metabolicznego, *Przegląd Epidemiologiczny*, 2005, 59: 743–751.

Krotkiewski M, Thyroid hormones in the pathogenesis and treatment of obesity, *European Journal of Pharmacology*, 2002, 44: 85–98.

Lopez M, Varela L, Vazquez MJ, Rodriguez S, Gonzalez CR, Velag apudi V R, Mogan D A, Schoenmakers E, Agassand an K, Lage R et al., Hypothalamic AMPK and fatty acid metabolism mediate thyroid regulation of energy balance, *Nature Medicine*, 2010, 16: 1001–1008.

Endo T, Ohta K, Haraguchi K, Onaya T, Cloning and functional expression of a thyrotropin receptor cDNA from rat fat cells, *Journal of Biological Chemistry*, 1995, 270: 10833–10837.

Wang Y, Qu H, Xiong X, Qiu Y, Liao Y, Chen Y, et al., Plasma asprosin concentrations are increased in individuals with glucose dysregulation and correlated with insulin resistance and first-phase insulin secretion, Med Inflam., 2018, 2018: 947-1583.

Wang CY, Lin TA, Liu K H, Liao C H, Liu YY, Wu VC, et al., Serum asprosin levels and bariatric surgery outcomes in obese adults, *Int J Obesity*., 2019, 43: 25–1019.

Wang M, Yin C, Wang L, Liu Y, Li H, Li M, et al., Serum asprosin concentrations are increased and associated with insulin resistance in children with obesity, *Ann Nutr Metab*., 2019, 75: 12–205.

Long W, Xie X, Du C, Zhao Y, Zhang C, Zhan D, et al., Decreased circulating levels of asprosin in obese children. *Horm Res Paediatr*, 2019, 91: 7–271.

Ugur K, Aydin S, Saliva and blood asprosin hormone concentration associated with obesity. *Int J Endocrinol*., 2019, 2019: 252-1096.

Groener JB, Valkanou A, Kender Z, Pfeiffenberger J, Kihm L, Fleming T, et al., Asprosin response in hypoglycemia is not related to hypoglycemia unawareness but rather to insulin resistance in type 1 diabetes, *PLoS ONE*, 2019, 14: 222-771.

Baykus Y, Yavuzkir S, Ustebay S, Ugur K, Deniz R, Aydin S, Asprosin in umbilical cord of newborns and maternal blood of gestational diabetes, preeclampsia, severe preeclampsia, intrauterine growth retardation and macrosemic fetus, *Peptides.*, 2019, 120: 170-132.

Ko JR, Seo DY, Kim TN, Park SH, Kwak HB, Ko KS, et al., Aerobic exercise training decreases hepatic asprosin in diabetic rats. *J Clin Med*., 2019, 8: 666-673.

Chang CL, Huang SY, Hsu YC, Chin TH, Soong YK, The serum level of irisin, but not asprosin, is abnormal in polycystic ovary syndrome patients, *Sci Rep*., 2019, 9: 1-9.

Acara AC, Bolatkale M, Kiziloglu I, Ibisoglu E, Can C, A novel biochemical marker for predicting the severity of ACS with unstable angina pectoris: asprosin, *Am J Emerg Med.*, 2018, 36: 5–1504.

Rasim M, Dervis D , Saltuk BB, Abdulkerim KB, Abdullah S, The effect of thyroid dysfunction and treatment on adropin, asprosin and preptin levels in rats, *Horm Mol Biol Clin Investig*., 2020, 42: 37-42.

Feng J, Yang Y, Yang Y, Pei H, The protective role of Asprosin against diabetes in cardiomyocytes*. J Am Colle Cardiol.*, 2018, 72: 1-8.