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Serum Asprosin Levels in Patients with Hashimoto's Thyroiditis

Hashimoto Tiroiditi Olan Hastalarda Serum Asprosin Düzeylerinin araştırılması

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Abstract: Asprosin is an orexigenic hormone secreted by adipose tissue, known to stimulate appetite. This study aimed to explore the relationship between appetite reduction, a commonly observed symptom in hypothyroidism, and serum asprosin levels, while also investigating potential metabolic implications beyond appetite regulation.We compared serum asprosin levels in 28 patients with hypothyroidism secondary to newly diagnosed Hashimoto's thyroiditis and 16 healthy controls. Additionally, serum asprosin levels were reassessed after patients achieved a euthyroid state following levothyroxine treatment, to evaluate any potential changes in relation to thyroid hormone normalization.There was no significant difference in serum asprosin levels between hypothyroid patients and healthy controls. No statistically significant difference was found between serum asprosin levels and thyroid function status. The serum asprosin levels were 4.8 ± 1.2 ng/mL in the hypothyroid group and 4.9 ± 1.1 ng/mL in the euthyroid group (p = 0.89). Furthermore, no significant change in asprosin levels was observed following levothyroxine treatment, compared to pre-treatment levels, suggesting that asprosin levels are not directly influenced by thyroid function.Ghrelin, an orexigenic hormone, is typically low in hypothyroid patients, contributing to reduced appetite. However, our study did not observe a similar decrease in asprosin levels in these patients. This suggests that, unlike ghrelin, asprosin may not be significantly affected by hypothyroidism or its treatment. Additionally, the lack of change in asprosin levels after treatment raises questions about its role in broader metabolic processes, beyond appetite regulation.The findings suggest no significant relationship between hypothyroidism and serum asprosin levels, indicating that asprosin may not play a central role in appetite reduction in hypothyroid patients.
Keywords: Hashimoto, Hypothyroidism, Adipose tissue, Asprosin

Özet: Asprosin, yağ dokusu tarafından salgılanan, iştahı uyaran bir hormondur. Bu çalışmanın amacı, hipotiroidizmde yaygın olarak gözlemlenen iştah azalması semptomu ile serum asprosin düzeyleri arasındaki ilişkiyi incelemek ve ayrıca iştah düzenlemesinin ötesinde metabolik etkilerini araştırmaktır.
Hipotiroidizm tanısı almış 28 Hashimoto tiroiditi hastası ile 16 sağlıklı kontrol grubunun serum asprosin düzeyleri karşılaştırıldı. Ayrıca, hastaların levotiroksin tedavisi sonrası ötiroid duruma ulaşmalarının ardından serum asprosin düzeyleri yeniden değerlendirilerek, tiroid hormonlarının normale dönmesiyle ilişkili herhangi bir değişiklik olup olmadığı incelendi.Hipotiroidizm hastaları ile sağlıklı kontrol grubunun serum asprosin düzeyleri arasında anlamlı bir fark gözlemlenmedi. Hipotiroid grup serum asprosin düzeyleri 4.8 ± 1.2 ng/mL, ötroid grup serum asprosin düzeyleri ise 4.9 ± 1.1 ng/mL olarak saptanmıştır (p = 0.89). Ayrıca, levotiroksin tedavisi sonrası serum asprosin düzeylerinde, tedavi öncesi seviyelere kıyasla belirgin bir değişiklik görülmedi. Bu durum, asprosin düzeylerinin doğrudan tiroid fonksiyonlarından etkilenmediğini göstermektedir.Hipotiroid hastalarında iştahı azaltan bir oreksijenik hormon olan ghrelin genellikle düşüktür. Ancak, bu çalışmamızda asprosin düzeylerinde benzer bir azalma gözlemlenmemiştir. Bu durum, asprosin'in ghrelin'den farklı olarak hipotiroidizm veya tedavisinden önemli ölçüde etkilenmediğini düşündürmektedir. Ayrıca, tedavi sonrası asprosin düzeylerinde herhangi bir değişiklik gözlenmemesi, bu hormonun iştah düzenlemesinin ötesinde daha geniş metabolik süreçlerdeki rolü hakkında soru işaretleri oluşturmuştur.Elde edilen bulgular, hipotiroidizm ile serum asprosin düzeyleri arasında anlamlı bir ilişki bulunmadığını ve asprosin'in hipotiroid hastalarında iştah azalmasında merkezi bir rol oynamadığını göstermektedir.
Anahtar Kelimeler: Hashimoto Tiroiditi, Hipotiroidizm, Yağ Dokusu, Asprosin

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1. Introduction

Thyroid hormones regulate the functions of many organs and tissues, such as the heart, liver, brain, skeletal muscle, and adipose tissue. Triiodothyronine (sT3) increases lipid turnover in adipocytes and appetite in the hypothalamus. TSH and thyroid hormones control adipocyte differentiation and proliferation. When excess calories are consumed, leptin is released from the white adipose tissue. Leptin increases the synthesis of TSH and thyroid hormones, suppresses appetite, and increases thermogenesis and lipolysis[1]. Leptin has been associated with obesity, insulin resistance, and dyslipidemia. Leptin increases obesity, insulin resistance, and dyslipidemia. As TSH levels increase in patients with hypothyroidism, the risk of weight gain and metabolic syndrome increases[2]. Hypothyroidism may be complicated by obesity, hyperlipidemia, and hypertension. Leptin levels and insulin resistance are typically high, while adiponectin levels are low in hypothyroid patients[3].

In patients with hypothyroidism, appetite decreases because their sense of taste and smell is impaired. The disorder in the sense of taste and smell improves with thyroid hormone treatment[4]. It has been shown that serum ghrelin, an orexigenic (appetite-increasing) hormone released from adipose tissue in patients with hypothyroidism, is low, but normalizes after thyroid hormone replacement[5]. Apolipoprotein A4, another hormone secreted by adipose tissue, plays a role in appetite and satiety. This hormone is elevated in patients with hyperthyroidism but decreases following treatment, and its levels are low in hypothyroid patients[6].

Asprosin is a protein hormone released from white adipose tissue after fasting and increases glycogenolysis and gluconeogenesis in the liver[7]. It crosses the blood-brain barrier and exerts an orexigenic effect. In animal studies, eating and weight gain were reduced in obese mice administered anti-asprosin antibodies[8]. Asprosin increases inflammation in skeletal muscles, leading to insulin resistance. It also reduces cAMP-dependent insulin secretion in the pancreas. It increases in the blood of patients with diabetes and may be a target for treatment[9]. It has been shown that asprosin levels in blood and saliva increase in obese individuals in parallel with body mass index, while decreasing in lean individuals[10].

In this study, we aimed to investigate the relationship between the decrease in appetite observed in patients with hypothyroidism and asprosin levels. Therefore, we compared the serum asprosin levels of patients with hypothyroidism secondary to Hashimoto's thyroiditis at the time of diagnosis and after they became euthyroid after treatment. We also compared the serum asprosin levels between the hypothyroid and healthy control groups.

2. Materials and methods

Blood samples were collected from 28 patients who underwent Kayseri City Hospital Internal Medicine Polyclinic between April 1, 2022, and April 1, 2024, and were diagnosed with hypothyroidism due to Hashimoto's thyroiditis, during diagnosis and after they became euthyroid after treatment. In addition, blood samples were collected from 16 volunteers who did not have any disease and had normal thyroid hormone levels as healthy controls.

Inclusion criteria were: (1) patients aged between 18 and 65 years, (2) diagnosis of hypothyroidism confirmed by clinical and laboratory findings, (3) patients who had not been treated with thyroid hormone replacement therapy for at least 3 months prior to the study.

Exclusion criteria were: (1) patients with other endocrine disorders, (2) patients on medications affecting thyroid function, (3) patients with a history of obesity-related metabolic diseases.

Power Analysis and Sample Size Calculation

An a priori power analysis was performed using G*Power software to determine the required sample size for comparing two independent means via a t-test. The analysis was conducted under the following parameters:

The results of the power analysis indicated that for a significant effect size (d = 0.8), a desired power level of 0.80, and an alpha of 0.10, the required sample sizes were 11 participants for Group 1 and 23 participants for Group 2. Therefore, the total sample size for the study was determined to be 34 participants. Based on these findings, the minimum sample size was set at 23 for the patient group and 11 for the control group.

The noncentrality parameter (δ) was calculated to be 2.18, with a critical t-value of 1.31 and 32 degrees of freedom (df). The actual power of the test was estimated at approximately 0.81, which meets the target power threshold.

The study was approved by the ethics committee of Kayseri City Hospital (10.03.2022/600).

This was a case-control study. PS version 3.0 package program was used to determine the number of samples.

Before obtaining a blood sample, the volunteers were informed, volunteer consent forms were filled out, and their consent was obtained. Blood samples were taken during morning fasting, as tsh and asprosin levels may be affected by satisfaction and diurnal rhythm. Blood samples were delivered to the Kayseri City Hospital Medical Biochemistry laboratory, centrifuged, and stored at -80 °C. When the target number of patients and healthy volunteers was reached, the stored blood samples were removed from the refrigerator and analyzed, and the results were recorded. Serum asprosin levels were measured using a commercially available ELISA kit (Catalog number: 201-12-7193, Company Name: Sunredbio).

The results were entered into the SPSS software. As a statistical method, Shapiro-Wilk test was used to determine normal distribution, Independent Samples T-Test was used for parametric comparisons, and Mann-Whitney U test was used for non-parametric comparisons. In case control comparisons, the paired samples t-test was used for parametric data, and the Wilcoxon signed-rank test was used for non-parametric data. Spearman's correlation analysis was used for correlation analysis.

3. Results

A total of 44 patients, including 28 diagnosed with hypothyroidism secondary to newly diagnosed Hashimoto's thyroiditis and 16 volunteers in the healthy control group, were included in the study. The duration of euthyroid status after treatment was 187 ± 25 days. No significant difference was detected between the hypothyroid and healthy control groups in terms of age, sex, glucose, Creatinine, ALT, AST, GGT, cholesterol, and asprosin levels. The body mass index of patients with hypothyroidism was significantly higher than that of the healthy control group (Table 1).

Table 1. Comparison of hypothyroidism and healthy control groups

		Hypothyroidism n (28)	**Healty control n (16)**	**P value**
Age,mean±SD		39.89±10.94	36.63±9.38	0.322
Gender	**Female**	22 (%78.6)	10 (%62.5)	0.303
	Male	6 (%21.4)	6 (%37.5)	
BMI,kg/m^2,mean±SD		29.34±7.64	24.04±2.25	**0.004**
Glucose,mg/dL,mean±SD		87.4±11.41	87.8±5.77	0.908
Creatinine,mg/dL,mean±SD		0.76±0.16	0.77±0.15	0.932
AST,U/L,median(min-max)		18 (10-35)	15 (11-28)	0.041
ALT,U/L,median(min-max)		15 (5-38)	15 (8-39)	0.940
GGT,U/L,median(min-max)		14 (6-61)	16 (6-33)	0.922
TSH,mU/L,median(min-max)		14.25 (5.06-245.8)	1.45 (0.41-3.87)	**<0.001**
Free T4,ng/L,median(min-max)		8.45 (1.2-12.1)	12.6 (9.6-14.8)	**<0.001**
Cholesterol,mg/Dl,median(min-max)		177 (140-288)	189 (114-224)	0.831
LDL,mg/dL,median(min-max)		119 (72-205)	123 (47-153)	0.800
TG,mg/dL,median(min-max)		120 (43-345)	87 (42-238)	0.087
Asprosin,ng/mL,median(min-max)		50.78 (41.47-202.68)	56.17 (18.87-115.43)	0.380

After levothyroxine treatment given to patients with hypothyroidism and after the patients became euthyroid, no significant difference was detected in asprosin levels when compared with before treatment. Total cholesterol and LDL levels were significantly lower after treatment than before treatment (Table 2).

Table 2. Comparison of biochemical parameters and asprosin level before and after treatment

	Before treatment	After treatment	P value
Glucose,mg/dL,median(min-max)	90 (52-107)	92 (75-192)	0.432
Creatinine,mg/dL,mean±SD	0.76±0.16	0.72±0.17	0.285
AST, U/L,mean±SD	18.9±5.63	17.5±4.53	0.091
ALT,U/L,median(min-max)	15 (5-38)	14 (6-54)	0.659
GGT,U/L,median(min-max)	14 (5.61)	14 (9-23)	0.324
TSH,mU/L,median(min-max)	14.25 (5.06-245.8)	2.72 (0.46-27.4)	**<0.001**
Free T4,ng/L,median(min-max)	8.45 (1.2-12.1)	13.5 (21.3)	**<0.001**
Cholesterol,mg/dLmedian(min-max)	177 (140-288)	174 (126-304)	**0.024**
LDL,mg/dL,median(min-max)	119 (72-205)	108 (59-237)	**0.046**
TG,mg/dL,median(min-max)	120 (43-345)	120 (73-367)	0.510
Asprosin,ng/mL,median(min-max)	50.8 (41.5-202.7)	56.4 (44.8-119.4)	0.142

When a correlation analysis was performed, no relationship was detected between asprosin, TSH, and free T4 levels. While there was a positive relationship between TSH and AST levels, a negative relationship was found between free t4 and AST levels (Table 3).

Table 3. Correlation analysis results between asprosin and other parameters

		BMI	Glucose	Cre	AST	ALT	GGT	T.Col	LDL	TG	TSH	fT4
Asprosin	**Correlation Coefficient**	0.029	-0.041	-0.143	0.087	0.238	0.173	-0.058	-0.106	0.135	0.028	0.002
	Sig. (2-tailed)	0.861	0.796	0.360	0.577	0.125	0.285	0.719	0.511	0.400	0.857	0.992
TSH	**Correlation Coefficient**	0.215	-0.001	0.094	0.490	0.111	-0.033	-0.026	-0.048	0.259	1	-0.879
	Sig. (2-tailed)	0.189	0.994	0.550	**0.001**	0.478	0.838	0.870	0.764	0.103	-	**<0.001**
Free t4 (fT4)	**Correlation Coefficient**	-0.336	-0.097	-0.079	-0.373	-0.002	-0.033	-0.102	-0.075	-0.345*	-0.879	1
	Sig. (2-tailed)	**0.036**	0.534	0.617	**0.014**	0.991	0.838	0.525	0.642	**0.027**	**<0.001**	-

4. Discussion

Serum ghrelin, an orexigenic hormone released from adipose tissue, is typically found to be low in patients with hypothyroidism but returns to normal following thyroid hormone replacement therapy[5,11]. In contrast, asprosin, another orexigenic hormone also secreted by adipose tissue, did not show a reduction in levels in our study. Although reduced appetite in hypothyroidism is likely mediated by changes in ghrelin, our findings suggest that asprosin may not play a significant role in appetite regulation in this condition. Additionally, no significant changes in asprosin levels were observed after thyroid hormone replacement, further supporting the idea that asprosin may not be directly involved in appetite suppression in hypothyroid patients.

Asprosin, known for its appetite-stimulating effects, may interact with other metabolic factors in complex ways. Despite its potential role in appetite regulation, our results indicate that it does not significantly influence the appetite suppression seen in hypothyroidism. In this context, the orexigenic effects of asprosin might be overshadowed by other mechanisms, such as changes in ghrelin levels, which are known to be more influential in appetite control in hypothyroid individuals.

Previous animal studies suggested that hypothyroidism could lead to lower asprosin

levels[12]. However, this was not replicated in our human study, where we found no significant correlation between thyroid hormone levels and asprosin concentrations. This discrepancy could be due to the differing physiological mechanisms of asprosin in humans and animals, which may not have been fully captured in the current research.

The lack of a relationship between asprosin and glucose levels in our study may be explained by the exclusion of diabetic patients from the cohort. Similarly, no significant correlations were found between asprosin levels and cholesterol or liver enzymes in the hypothyroid group.

Additionally, the duration of time it took for the patients to reach euthyroid status after treatment was 187 ± 25 days. This information is important as it could potentially influence the serum asprosin levels, which may vary according to thyroid function status. However, we did not observe a significant correlation between the thyroid function normalization and asprosin levels in this study.

In line with some earlier studies, such as that by Hussein et al. (2024), which investigated asprosin levels in patients with double diabetes and hypothyroidism, our findings also highlight the complexity of the relationship between asprosin and thyroid function. Hussein et al. reported elevated asprosin levels in patients with both double diabetes and hypothyroidism, suggesting that asprosin might play a role in insulin resistance and glucose metabolism alterations. However, unlike their findings, we observed no significant difference in asprosin levels between hypothyroid and euthyroid patients. This discrepancy could be due to differences in study design, sample size, or the specific patient populations involved. Hussein et al.'s study emphasized the importance of insulin resistance as a factor influencing asprosin levels, which might explain the higher levels observed in their cohort. Our study, however, did not explore insulin resistance markers as extensively, which may be a factor contributing to the lack of significant findings in relation to asprosin levels[13].

Our study did not find a statistically significant difference between serum asprosin levels in hypothyroid and euthyroid patients, which may seem surprising given the potential association of thyroid dysfunction with altered appetite regulation. However, this study contributes valuable insights into the complex interplay between thyroid hormones and asprosin, a hormone involved in appetite regulation. While some previous studies have suggested a link between thyroid dysfunction and altered asprosin levels, our findings add to the growing body of literature by highlighting that the relationship between thyroid function and asprosin may not be as straightforward as initially thought.

It is important to acknowledge that our study provides an early glimpse into this area, and the results should be interpreted in the context of several limitations, including the small sample size. Despite these limitations, our findings lay the groundwork for future studies that may explore this relationship more comprehensively, possibly incorporating larger, more diverse patient populations and longitudinal designs.

Furthermore, while the study did not reveal a clear relationship between thyroid function and serum asprosin levels, it highlights the need for further research to investigate the potential role of asprosin in appetite regulation and its interaction with thyroid function. Asprosin's complex role in metabolism and energy homeostasis suggests that it may influence other factors beyond thyroid hormone levels, and understanding these mechanisms could have important clinical implications in the management of thyroid-related disorders.

5. Conclusion

No significant relationship was found between hypothyroidism and serum asprosin levels, suggesting that asprosin may not be involved in the appetite reduction commonly observed in hypothyroid patients. Further research is needed to fully understand asprosin’s orexigenic effects and its role in metabolic disorders, particularly in relation to thyroid function and appetite regulation.

6. Limitations

The overweight status of the patient group could have influenced the results of this study. The appetite levels of overweight individuals may differ, potentially affecting asprosin levels. In the initial power analysis of this study, an alpha value of 0.10 was used. This could lead to an increased false positive rate, and the smaller sample size (28 patients in the study group) may limit the robustness of the findings. The small sample size limits the generalizability of the findings. Larger studies with broader sample sizes would provide more robust results. This study did not assess the appetite levels of the patients or controls. A more objective evaluation of appetite could have strengthened the

study's conclusions and provided clearer insight into the relationship between asprosin levels and appetite.

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