

Micronutrient status in adolescents with autoimmune thyroiditis: a case-control study

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ABSTRACT

Objective: Autoimmune thyroiditis (AIT) is the most common thyroid disorder in adolescents, with genetic and environmental factors contributing to its pathogenesis. The role of micronutrients in AIT remains a topic of controversy. This study aims to evaluate the levels of iodine, selenium, vitamin A, vitamin E, magnesium, and vitamin B12 in adolescents diagnosed with AIT compared to healthy controls.

Methods: A case-control study was conducted from September 2022 to September 2023, including 37 adolescents with newly diagnosed AIT and 36 age- and sex-matched healthy controls. Serum levels of thyroid hormones, thyroid autoantibodies (anti-thyroid peroxidase [TPO] and anti-thyroglobulin [Tg]), and micronutrient levels were assessed. Statistical analyses were performed to compare the groups and to evaluate correlations between thyroid autoantibody levels and micronutrients.

Results: All patients had elevated thyroid autoantibody levels, with a median of 135.5 IU/mL for anti-Tg and 535 IU/mL for anti-TPO. No significant differences were observed in urinary iodine, selenium, magnesium, vitamin A, vitamin E, or vitamin B12 levels between the groups. Correlation analysis revealed no significant associations between thyroid autoantibodies and micronutrient levels ($p>0.05$).

Conclusion: This study suggests that iodine, selenium, magnesium, vitamin A, vitamin E, and vitamin B12 levels are not significantly altered in adolescents with AIT. These micronutrients alone may not serve as reliable biomarkers for the diagnosis or progression of AIT. Further research is needed to elucidate the potential role of micronutrient supplementation in the management of AIT.

Keywords: autoimmune thyroiditis, adolescents, micronutrients, selenium, iodine, vitamin B12, thyroid autoimmunity

INTRODUCTION

Autoimmune thyroiditis (AIT) is the most common thyroid disorder in the pediatric population in iodine-sufficient regions. Although AIT can manifest at any age, it is most frequently diagnosed during adolescence and exhibits a higher prevalence in females. The etiology of AIT is attributed to the presence of circulating autoantibodies against thyroid antigens, initiating a chronic autoimmune destructive process. This process involves the formation of immune complexes and complement activation in

the basement membrane of follicular cells, leading to lymphocytic infiltration, fibrosis, and a subsequent decline in the number of functional thyroid follicles necessary for hormone synthesis.¹

The diagnosis of AIT primarily relies on elevated serum titers of thyroid peroxidase antibodies (TPO-Ab) and thyroglobulin antibodies (Tg-Ab), along with diffuse hypoechogenicity on thyroid ultrasonography. AIT can present with a euthyroid state, hypothyroidism, or transient hyperthyroidism.² The exact pathogenesis of AIT



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remains incompletely understood; however, both genetic predisposition and environmental factors play crucial roles.³ Approximately 70% of disease susceptibility is attributed to the genetic background, with environmental triggers contributing significantly to disease onset. Family and twin studies further support the substantial genetic influence on AIT, yet the 55% concordance rate for overt hypothyroidism in monozygotic twins highlights the equally pivotal role of environmental factors.^{4,5} Potential environmental triggers for AIT include infections, medications, hormonal influences (such as estrogen), dietary factors, stress, and smoking.³ Among dietary factors, iodine excess or deficiency, selenium deficiency, and vitamin D deficiency have been associated with an increased risk of AIT.⁶

There is also limited evidence suggesting that vitamin A, zinc, and vitamin B12 may influence thyroid metabolism, although data on their direct relationship with AIT remain scarce.⁶ The objective of this study is to evaluate iodine, selenium, vitamins A, E, and B12, and magnesium levels in adolescents diagnosed with AIT compared to healthy adolescents, to further understand their potential role in thyroid autoimmunity.

MATERIALS AND METHODS

This case-control study was conducted over one year, from September 2022 to September 2023. During this timeframe, newly diagnosed adolescents aged 10–18 years with AIT were enrolled. Participants were included if they had been investigated for goiter and/or thyroid function abnormalities and subsequently diagnosed with AIT. The diagnosis of AIT was confirmed by elevated serum anti-thyroid peroxidase (anti-TPO) and/or anti-thyroglobulin (anti-Tg) antibodies, with positivity defined as levels exceeding 35 IU/mL for anti-TPO and 45 IU/mL for anti-Tg. Additionally, diffuse heterogeneity observed on thyroid ultrasonography was considered a supportive diagnostic criterion. Age- and sex-matched healthy adolescents were included as the control group. Pubertal status was assessed based on physical examination and the Tanner staging system. All participants were in Tanner stage II or higher, and pubertal status was similar between the two groups.

Exclusion criteria comprised individuals with a prior diagnosis of any chronic disease and those receiving multivitamin supplements or other medications that could influence thyroid function or metabolic parameters.

Thyroid function tests were performed using a chemiluminescent immunometric assay (Architect i4000,

Abbott Laboratories, Diagnostics Division, IL, USA). The reference ranges were as follows: thyroid-stimulating hormone (TSH), 0.35–4.94 mIU/L; free triiodothyronine (fT3), 2.43–4.47 pg/mL; and free thyroxine (fT4), 0.78–1.31 ng/dL. Anti-Tg antibodies (TG-Ab) were measured using the same assay, with values below 5.6 IU/mL considered normal. Similarly, anti-TPO antibodies (TPO-Ab) were quantified using the chemiluminescence immunometric method, with normal values defined as 0–4.1 IU/mL.

Serum glucose levels were measured using Abbott kits on an Abbott i-STAT 8000 analyzer. The hexokinase/glucose-6-phosphate dehydrogenase (G-6-PDH) method was used for measurement. Insulin levels were determined using the chemiluminescent microparticle immunoassay (CMIA) method with an Abbott i16000 analyzer and Abbott diagnostic kits. Vitamin A, vitamin E, and selenium levels were measured using inductively coupled plasma mass spectrometry (ICP-MS). Urinary iodine concentration was assessed using ammonium persulfate digestion followed by the Sandell-Kolthoff reaction, with a reference range of 100–199 µg/L. Vitamin B12 levels were determined using a chemiluminescent microparticle immunoassay (CMIA) method on an Abbott i2000 analyzer, with normal values ranging from 200 to 900 pg/mL.

This study has been approved by the Umraniye Training and Research Hospital Ethics Committee (approval date 25.08.2022, number 19661). Written informed consent was obtained from the parents of all enrolled participants.

Statistical analysis

Statistical analyses were performed using SPSS version 25.0 (IBM Corp, Armonk, NY, USA). The normality of distribution was assessed using the Kolmogorov-Smirnov test. Continuous variables were expressed as median and interquartile range (IQR) for non-normally distributed data and as mean ± standard deviation (SD) for normally distributed data. Categorical variables were presented as frequencies and percentages. The differences between the two groups were analyzed using the Mann-Whitney U test for non-normally distributed continuous variables and the independent samples t-test for normally distributed continuous variables. Categorical variables were compared using the Chi-square test or Fisher's exact test when appropriate. Correlation analyses were performed using Spearman's rank correlation coefficient. To determine whether micronutrient levels could serve as diagnostic markers for distinguishing patients with HT from controls,

we conducted an ROC analysis. A p-value of <0.05 was considered statistically significant.

RESULTS

A total of 73 adolescents (37 patients with autoimmune thyroiditis and 36 healthy controls) were included in the study. The median age was 14.5 years [IQR: 12-16] in the patient group and 14 years [IQR: 13-16] in the control group ($p=0.775$). The proportion of male participants was 27.0% (10 males, 27 females) in the patient group and 30.6% (11 males, 25 females) in the control group ($p=0.941$). All adolescents in both the patient and control groups were in the pubertal stage, as assessed by clinical evaluation.

The biochemical characteristics of the study groups are summarized in Table 1, which shows significant differences in Anti-TG, Anti-TPO, Glucose, LDL, Sex Hormone-Binding

Globulin (SHBG), fT3, and TSH levels, but no differences in terms of micronutrient levels.

To further explore the clinical relevance of micronutrient levels in Hashimoto's thyroiditis (HT), we assessed their correlation with thyroid autoantibodies (Anti-TG and Anti-TPO). No significant correlations were observed between thyroid autoantibodies and micronutrient levels (Table 2). Although not statistically significant, magnesium exhibited a weak negative correlation with Anti-TG ($r=-0.308$, $p=0.081$), and selenium demonstrated a weak negative correlation with Anti-TPO ($r=-0.296$, $p=0.094$).

Furthermore, the ROC analysis, conducted to ascertain whether micronutrient levels could serve as diagnostic markers for HT, demonstrated that none of the assessed micronutrients had adequate discriminative power, as their Area Under the Curve (AUC) values were close to 0.5 (Table 3).

Table 1. The biochemical parameters in patients with newly diagnosed Hashimoto thyroiditis and in the control group

Parameter	Patient Group (n=37)	Control Group (n=36)	p-value
Anti-TG (IU/ml)	135.5 [34-363]	0.885 [0.63-2.24]	<0.001*
Anti-TPO (IU/ml)	535 [181-1000]	0.5 [0.5-0.51]	<0.001*
fT3 (pg/mL)	3.11±1.06	3.54±0.51	0.001*
fT4 (ng/dL)	0.93±0.16	0.96±0.10	0.300
TSH (uIU/L)	3.19 [2.31-8.1]	2.06 [1.57-2.695]	0.001*
Urinary Iodine (ug/L)	112 [95-146]	107 [71-151]	0.321
Magnesium (mg/dL)	1.97 [1.65-2.10]	1.93 [1.71-1.51]	0.632
Selenium (ug/L)	67.9 [57.3-85.7]	69.25 [58.3-89.5]	0.556
Vitamin A (ug/dL)	37.9 [32.75-41.5]	39.2 [34.5-42.9]	0.846
Vitamin E (mg/dL)	0.85 [0.565-0.85]	0.84 [0.65-0.98]	0.960
Vitamin B12 (ng/L)	263.5 [207-337]	239 [194-400]	0.768

* $p < 0.05$. TSH: Thyroid-stimulating hormone, fT3: Free triiodothyronine, fT4: Free thyroxine, Anti-TPO: Anti-thyroid peroxidase antibody, Anti-TG: Anti-thyroglobulin antibody.

Table 2. Correlations between autoantibody and micronutrient levels

Parameter	Anti-TG (r)	Anti-TG (p)	Anti-TPO (r)	Anti-TPO (p)
Urinary Iodine	0.041	0.828	0.078	0.678
Magnesium	-0.308	0.081	0.194	0.278
Selenium	0.055	0.759	-0.296	0.094
Vitamin A	-0.23	0.222	0.027	0.889
Vitamin E	0.125	0.519	-0.194	0.313
Vitamin B12	0.092	0.618	-0.03	0.87

Statistical significance was defined as $p < 0.05$. Anti-TG: Anti-thyroglobulin antibody, Anti-TPO: Anti-thyroid peroxidase antibody.

Table 3. The results of the ROC Curve analysis for the micronutrient level

Test Variable	AUC	SE	p-value	95% CI
Urinary Iodine	0.569	0.079	0.384	0.415-0.724
Selenium	0.590	0.083	0.258	0.428-0.753
Magnesium	0.445	0.079	0.492	0.290-0.600
Vitamin A	0.493	0.08	0.931	0.335-0.651
Vitamin E	0.483	0.08	0.835	0.326-0.640
Vitamin B12	0.515	0.079	0.848	0.360-0.671

Statistical significance was defined as $p < 0.05$. AUC: Area under the curve, SE: Standard error, CI: Confidence interval.

DISCUSSION

In this study, we investigated the relationship between autoimmune thyroiditis (AIT) and micronutrient levels, including iodine, selenium, magnesium, vitamin A, vitamin E, and vitamin B12, in adolescents. Our findings indicated that while the thyroid autoantibody levels are significantly elevated in patients with AIT, no strong correlations were observed between these autoantibodies and micronutrient levels.

These results suggest that micronutrient status alone may not be a reliable distinguishing factor in adolescents with AIT.

Several studies have highlighted the role of micronutrients in thyroid function and autoimmunity. Iodine is an essential element for thyroid hormone synthesis, but both deficiency and excess have been implicated in the development of autoimmune thyroid disease.⁷ In our study, urinary iodine levels did not differ significantly between the AIT and control groups, suggesting that iodine status was not a major determinant of AIT in our population. However, considering regional variations in iodine intake, further studies with larger populations are needed to confirm this finding.

Selenium, an essential trace element with antioxidant properties, has been suggested to play a role in thyroid autoimmunity by modulating immune responses and reducing oxidative stress.⁸ Although previous research has demonstrated a potential protective effect of selenium supplementation in patients with AIT,⁹ our study did not find a significant difference in serum selenium levels between AIT patients and controls. Additionally, no strong correlation was observed between selenium levels and thyroid autoantibodies. These findings suggest that selenium's effects on AIT development and progression may be more complex and potentially influenced by both genetic and environmental factors.

Further systematic reviews and meta-analyses have provided additional insights into the role of selenium supplementation in AIT. A comprehensive meta-analysis by Huwiler et al. evaluated randomized controlled trials and found that selenium supplementation effectively reduced thyroid peroxidase antibodies (TPOAb) levels and thyrotropin (TSH) concentrations in patients with Hashimoto's thyroiditis.¹⁰ Wang et al. reported that selenium supplementation may reduce TPOAb and thyroglobulin antibody (TgAb) levels after 3 and 6 months, particularly in patients not receiving levothyroxine therapy.¹¹ These findings suggest that while selenium supplementation may have a beneficial effect on reducing thyroid autoantibody levels in AIT patients, the overall evidence remains inconclusive. Our results align with this uncertainty, reinforcing the need for further research on selenium's role in AIT management.

Magnesium plays a key role in enzymatic reactions, including those related to thyroid function. Emerging evidence suggests that its deficiency may heighten inflammatory responses in autoimmune diseases.⁶ While we observed a weak negative correlation between magnesium and anti-TG levels, this association was not statistically significant. Further research with larger sample sizes is needed to explore whether magnesium status influences thyroid autoimmunity.

The role of vitamins in thyroid health has been an area of growing interest. Vitamin A, through its effects on immune regulation, has been hypothesized to influence thyroid autoimmunity.⁶ Similarly, vitamin E has been investigated for its potential role in reducing oxidative stress in thyroid disorders.⁹ However, our study did not find significant differences in vitamin A or vitamin E levels between AIT patients and controls, nor were there any significant correlations with thyroid autoantibodies. These findings align with previous studies that have reported inconsistent results regarding the impact of these vitamins on AIT.¹²

Vitamin B12 deficiency has been frequently reported in patients with AIT and other autoimmune disorders.⁶ However, our study found no significant difference in vitamin B12 levels between AIT patients and controls. The lack of a significant association may be attributed to differences in dietary intake, absorption efficiency, or genetic predisposition in our study population.

There are several limitations to consider. First, the relatively small sample size may have limited our ability to detect weak associations. Second, we did not assess dietary intake, which could have provided additional insights into the role of nutritional factors in AIT.

In conclusion, our study suggests that while thyroid autoantibodies are significantly elevated in adolescents with AIT, their levels do not strongly correlate with iodine, selenium, magnesium, vitamin A, vitamin E, or vitamin B12 levels.

These findings suggest that micronutrient status alone may not be a distinguishing factor for AIT in adolescents. Further research involving larger and more diverse populations is warranted to better understand the relationship between micronutrients and thyroid autoimmunity.

Ethical approval

This study has been approved by the Umraniye Training and Research Hospital Ethics Committee (approval date 25.08.2022, number 19661). Written informed consent was obtained from the participants.

Author contribution

The authors declare contribution to the paper as follows: Study conception and design: GS; data collection: GS; analysis and interpretation of results: GS, HK; draft manuscript preparation: GS, HK. All authors reviewed the results and approved the final version of the article.

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Conflict of interest

The authors declare that there is no conflict of interest.

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