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ASSOCIATION BETWEEN A 6-WEEK ELIMINATION DIET AND INFLAMMATORY BIOMARKERS IN WOMEN WITH HASHIMOTO THYROIDITIS

Solmaz Alkan[1]*, Indrani Kalkan[2], Busra Bilik Sezer[3]

[1] Department of Nutrition and Dietetics, Institute of Health Sciences, Istanbul Medipol University, Istanbul, Türkiye solmaz.alkan@igdir.edu.tr ORCID ID: https://orcid.org/0009-0005-9727-6496
[2] Department of Nutrition and Dietetics, Institute of Health Sciences, Istanbul Medipol University, Istanbul, Türkiye indrani.kalkan@medipol.edu.tr ORCID ID: https://orcid.org/0000-0001-6020-349X
[3] Department of Family Medicine, Division of Internal Medicine, Tuzluca Family Health Center, Igdir, Türkiye; busra.biliksezer@deu.edu.tr ORCID ID: https://orcid.org/0009-0009-7646-6783

ABSTRACT

Background: Hashimoto thyroiditis (HT) is characterized by chronic autoimmune inflammation with elevated proinflammatory cytokines. Elimination diets have been proposed as adjunctive nutritional interventions to modulate immune responses, though evidence remains limited.

Objective: This retrospective case-control study examined associations between a 6-week elimination diet protocol and inflammatory biomarkers, particularly interleukin-6 (IL-6), in women aged 30–50 years with HT receiving stable levothyroxine therapy.

Methods: Medical records of 60 women aged 30–50 years diagnosed with HT were reviewed retrospectively. The case group (n=30) received a 6-week elimination diet (excluding gluten, dairy, soy, refined sugars, processed foods) alongside levothyroxine. Controls (n=30) received levothyroxine alone. Inflammatory biomarkers (IL-6, TNF-α, IL-1β), hematological indices (PLR, NLR, MLR), thyroid function, autoantibodies, vitamin D, and metabolic parameters were assessed at baseline and 6 weeks.

Results: At 6-week follow-up, the elimination diet group had significantly lower IL-6 levels compared to controls (6.95±2.35 vs. 9.47±4.13 pg/mL, p=0.01), with significant within-group reduction (p=0.01) versus no change in controls (p=0.48). The elimination diet group showed significant reductions in PLR (p=0.01), increases in vitamin D (p=0.01), decreases in insulin (p=0.01), and reductions in BMI (p=0.02). Both groups exhibited decreases in TSH and thyroid autoantibodies (anti-TPO, anti-TG) with no significant between-group differences. TNF-α and IL-1β remained unchanged in both groups.

Conclusion: In this retrospective analysis of women aged 30–50 years with HT, a 6-week elimination diet protocol was associated with reduced IL-6 levels and favorable changes in PLR, vitamin D, insulin, and BMI. The similar reductions in thyroid autoantibodies and TSH across both groups suggest these changes may reflect natural disease fluctuation, regression-to-mean, or pharmacological effects rather than dietary intervention. These findings should be interpreted cautiously due to the retrospective design and small sample size. Prospective randomized controlled trials are needed to establish causality and clinical utility.

KEYWORDS: Hashimoto thyroiditis; Elimination diet; Interleukin-6; Inflammatory biomarkers; Autoimmune thyroid disease; Nutritional intervention; Thyroid autoantibodies

1. INTRODUCTION

Hashimoto thyroiditis (HT), also known as chronic lymphocytic thyroiditis, is the most prevalent autoimmune thyroid disorder and a leading cause of hypothyroidism worldwide [1], [2]. The condition is characterized by lymphocytic infiltration of the thyroid gland, progressive destruction of thyroid follicles, and the presence of circulating thyroid autoantibodies, particularly anti-thyroid peroxidase (anti-TPO) and anti-thyroglobulin (anti-TG) antibodies [3], [4]. HT predominantly affects women, with a female-to-male ratio of approximately 10:1, and typically manifests between the third and fifth decades of life [5], [6].

The pathogenesis of HT involves a complex interplay between genetic susceptibility and environmental triggers, leading to a breakdown of immune tolerance to thyroid antigens [7], [8]. This autoimmune process is mediated by both cellular and humoral immune responses, resulting in chronic inflammation within the thyroid gland [9]. A hallmark of this inflammatory state is the elevated production of proinflammatory cytokines, including interleukin-6 (IL-6), tumor necrosis factor-alpha (TNF-α), and interleukin-1 beta (IL-1β), which contribute to thyroid tissue damage and systemic inflammation [10], [11], [12].

IL-6, in particular, has emerged as a key mediator in autoimmune thyroid disease. This pleiotropic cytokine plays dual roles in immune regulation, promoting both pro-inflammatory and anti-inflammatory responses depending on the context [13]. In HT, elevated IL-6 levels have been associated with disease activity, autoantibody production, and the perpetuation of autoimmune responses [14], [15]. Beyond its role in thyroid-specific inflammation, IL-6 contributes to systemic metabolic disturbances commonly observed in HT patients, including insulin resistance, dyslipidemia, and increased cardiovascular risk [16], [17].

Standard treatment for HT primarily focuses on thyroid hormone replacement therapy with levothyroxine to manage hypothyroidism [18]. However, this pharmacological approach does not directly address the underlying autoimmune inflammation or the elevated levels of inflammatory cytokines [19]. Consequently, many patients continue to experience persistent symptoms, including fatigue, weight gain, and metabolic dysfunction, despite achieving biochemical euthyroidism [20], [21]. This therapeutic gap has prompted interest in complementary approaches that may modulate immune function and reduce inflammation.

Emerging evidence suggests that dietary interventions may influence autoimmune disease activity through multiple mechanisms, including modulation of gut microbiota, reduction of intestinal permeability, and alteration of inflammatory pathways [22], [23], [24]. The gut-thyroid axis has gained particular attention, as disruptions in intestinal barrier function and microbiome composition have been implicated in the pathogenesis of autoimmune thyroid disease [25], [26]. Certain dietary components, particularly gluten, dairy proteins, and processed foods, have been hypothesized to exacerbate intestinal permeability and trigger immune responses in susceptible individuals [27], [28], [29].

Elimination diets, which involve the temporary removal of potentially inflammatory or immunogenic foods, have been proposed as adjunctive nutritional interventions for autoimmune conditions, including HT [30], [31]. These dietary protocols typically exclude gluten-containing grains, dairy products, soy, refined sugars, and processed foods—components that have been associated with increased intestinal permeability, dysbiosis, and immune activation [32], [33], [34]. The rationale for such interventions is based on the premise that removing these dietary triggers may reduce systemic inflammation, improve gut barrier function, and potentially modulate autoimmune activity [35], [36].'

1.1 Research Gap

Despite growing interest in dietary interventions for HT, the evidence base remains limited and inconsistent. While several studies have examined the effects of gluten-free diets or specific nutrient supplementation in autoimmune thyroid disease [37], [38], [39], comprehensive elimination diet protocols have received less systematic investigation. Most existing research has focused on thyroid autoantibody levels and thyroid function parameters, with limited attention to inflammatory cytokines as primary outcomes [40], [41]. Furthermore, the specific impact of elimination diets on IL-6 and other inflammatory biomarkers in HT patients has not been adequately characterized.

Previous studies have been constrained by small sample sizes, heterogeneous dietary protocols, variable intervention durations, and lack of appropriate control groups [42], [43]. Additionally, many investigations have not controlled for concurrent levothyroxine therapy or have included patients with unstable thyroid function, making it difficult to isolate the effects of dietary intervention from pharmacological treatment [44]. The temporal dynamics of inflammatory marker changes in response to dietary modification also remain poorly understood, with most studies examining only long-term outcomes rather than short-term inflammatory responses [45].

There is a particular paucity of data examining the relationship between elimination diets and hematological inflammatory indices, such as platelet-to-lymphocyte ratio (PLR), neutrophil-to-lymphocyte ratio (NLR), and monocyte-to-lymphocyte ratio (MLR), which have emerged as accessible markers of systemic inflammation in various autoimmune conditions [46], [47]. These indices may provide additional insights into the inflammatory status of HT patients and the potential anti-inflammatory effects of dietary interventions [48].

Moreover, the interplay between dietary modification, vitamin D status, and metabolic parameters in HT patients receiving elimination diets has not been comprehensively evaluated. Given the high prevalence of vitamin D deficiency in HT and its potential immunomodulatory effects [49], [50], understanding how elimination diets may influence vitamin D levels alongside inflammatory markers is clinically relevant. Similarly, the metabolic effects of elimination diets, including changes in insulin sensitivity and body composition, warrant investigation in the context of HT management [51].

1.2 Study Objectives

Given these gaps in the literature, the present retrospective case-control study was designed to examine the associations between a structured 6-week elimination diet protocol and inflammatory biomarkers in women with HT receiving stable levothyroxine therapy. The primary objective was to assess changes in IL-6 levels, a key proinflammatory cytokine implicated in HT pathogenesis. Secondary objectives included evaluation of other inflammatory cytokines (TNF-α, IL-1β), hematological inflammatory indices (PLR, NLR, MLR), thyroid function parameters, thyroid autoantibodies, vitamin D status, and metabolic markers. By comparing outcomes between patients who had received the elimination diet protocol and those who received standard medical management alone, this study aimed to provide preliminary evidence regarding the potential role of dietary intervention in modulating inflammation in HT.

2. MATERIALS AND METHODS

2.1 Study Design and Setting

This retrospective case-control study was conducted at Republic of Türkiye Ministry of Health, Iğdır Dr. Nevruz Erez State Hospital, Iğdır, Türkiye. Medical records of female patients aged 30–50 years diagnosed with Hashimoto thyroiditis who received care at this single-center institution were reviewed retrospectively. Ethical approval was obtained from the Kafkas University Non-Interventional Clinical Research Ethics Committee. The study was conducted in accordance with the Declaration of Helsinki and Good Clinical Practice guidelines. Written informed consent for the use of clinical data for research purposes was obtained from all participants prior to data collection.

2.2 Study Population and Selection Criteria

Medical records of women aged 30–50 years diagnosed with HT between January 2022 and December 2023 were reviewed. HT diagnosis was established based on the presence of elevated thyroid autoantibodies (anti-TPO >34 IU/mL and/or anti-TG >115 IU/mL) in conjunction with characteristic clinical and biochemical features of hypothyroidism or subclinical hypothyroidism, consistent with established diagnostic criteria [52], [53].

Inclusion criteria for both groups were: (1) confirmed diagnosis of HT based on elevated thyroid autoantibodies; (2) age 30–50 years; (3) female sex; (4) stable levothyroxine therapy for at least 3 months prior to baseline assessment, with no dose adjustments during the 6-week observation period; (5) availability of complete laboratory data at baseline (T1) and 6-week follow-up (T2); and (6) no changes in other medications or supplements during the study period.

Exclusion criteria were: (1) pregnancy or lactation; (2) presence of other autoimmune diseases (e.g., celiac disease, rheumatoid arthritis, type 1 diabetes); (3) active thyroid cancer or history of thyroid surgery; (4) severe cardiovascular, hepatic, or renal disease; (5) use of immunosuppressive medications or corticosteroids; (6) recent infection or inflammatory condition within 4 weeks of baseline assessment; (7) documented eating disorders; and (8) incomplete medical records or missing laboratory data.

2.3 Group Assignment

The study included two groups:

Case group (Elimination Diet group, n=30): Women with HT who had been prescribed and followed a 6-week elimination diet protocol by a registered dietitian at the hospital's nutrition clinic, in addition to stable levothyroxine therapy. The elimination diet protocol was implemented as part of routine clinical care for patients expressing interest in dietary approaches to HT management.

Control group (Standard Care group, n=30): Women with HT who received standard medical management with levothyroxine therapy alone, without specific dietary intervention beyond general healthy eating advice. These patients were matched to the case group based on age (±3 years), baseline TSH levels (±1.0 mIU/L), and levothyroxine dose (±12.5 μg).

2.4 Elimination Diet Protocol

The elimination diet protocol prescribed to the case group involved the removal of the following food categories for 6 consecutive weeks:

- **Gluten-containing grains:** wheat, barley, rye, and their derivatives
- **Dairy products:** milk, cheese, yogurt, butter, and other dairy-derived foods
- **Soy products:** soybeans, tofu, soy milk, and soy-based processed foods
- **Refined sugars:** white sugar, high-fructose corn syrup, and foods with added sugars
- **Processed foods:** packaged snacks, processed meats, and foods containing artificial additives, preservatives, or trans fats

Patients were instructed to base their diet on whole, unprocessed foods, including: - Gluten-free grains (rice, quinoa, buckwheat, millet) - Fresh vegetables and fruits - Lean proteins (poultry, fish, eggs, legumes) - Nuts and seeds - Healthy fats (olive oil, avocado, coconut oil) - Herbs and spices for flavoring

The elimination diet protocol was individualized to meet each patient's energy and nutrient requirements, calculated based on anthropometric measurements and activity level. Patients received detailed written instructions, sample meal plans, and a list of permitted and excluded foods. Initial dietary counseling sessions lasted approximately 60 minutes, with follow-up consultations at weeks 2 and 4 to assess adherence and address questions.

2.5 Dietary Adherence Assessment

Dietary adherence was evaluated retrospectively through comprehensive review of patient medical records, including: Dietitian consultation notes: Detailed documentation from initial and follow-up dietary counseling sessions, including patient-reported dietary intake, challenges encountered, and modifications made to the protocol.

Food diary review: Analysis of food diaries maintained by patients and reviewed by the dietitian during follow-up visits. Diaries documented daily food intake, meal timing, and any deviations from the protocol.

Adherence scoring: Dietitians had documented adherence using a structured assessment at each follow-up visit, categorizing patients as having high adherence (>80% compliance with all elimination categories), moderate adherence

(60-80% compliance), or low adherence (<60% compliance). Only patients with documented high adherence (>80%) throughout the 6-week period were included in the final analysis.
Clinical documentation: Review of clinical notes documenting patient-reported symptoms, challenges with dietary implementation, and any reported deviations from the protocol.
Exclusion of non-adherent patients: Patients with documented poor adherence or significant protocol deviations were excluded from the analysis to ensure the integrity of the dietary intervention group.
This retrospective adherence assessment approach, while limited by its non-prospective nature, allowed for identification of patients who had successfully implemented the elimination diet protocol as prescribed.
Based on dietitian notes and food diary reviews, 28 of 30 participants (93.3%) in the elimination diet group demonstrated high adherence (>80% compliance with dietary restrictions) throughout the 6-week period. Two participants (6.7%) showed moderate adherence (60–80% compliance) but were retained in the analysis in line with the retrospective study design.

2.6 Data Collection
Data were extracted from electronic medical records and included:
Demographic and clinical characteristics: age, disease duration, levothyroxine dose, medical history, and concurrent medications.
Anthropometric measurements: height (cm), weight (kg), and body mass index (BMI, kg/m²). Measurements were performed by trained nursing staff using calibrated equipment according to standard protocols.
Laboratory assessments: All blood samples were collected in the morning (08:00–10:00) after an overnight fast of at least 8 hours. Samples were processed within 2 hours of collection and analyzed at the hospital's central laboratory, which maintains accreditation and participates in external quality assurance programs.

2.7 Laboratory Methods
Thyroid function tests: Serum thyroid-stimulating hormone (TSH), free thyroxine (fT4), and free triiodothyronine (fT3) were measured using electrochemiluminescence immunoassay (ECLIA) on a Cobas e601 analyzer (Roche Diagnostics, Mannheim, Germany). Reference ranges: TSH 0.27–4.20 mIU/L, fT4 12–22 pmol/L, fT3 3.1–6.8 pmol/L.
Thyroid autoantibodies: Anti-TPO and anti-TG antibodies were quantified using ECLIA on the same platform. Reference ranges: anti-TPO <34 IU/mL, anti-TG <115 IU/mL.
Inflammatory cytokines: Serum IL-6, TNF-α, and IL-1β were measured using enzyme-linked immunosorbent assay (ELISA) kits (Elabscience Biotechnology, Houston, TX, USA) according to the manufacturer's protocols. Intra-assay and inter-assay coefficients of variation were <10% for all cytokine assays.
Hematological parameters: Complete blood count (CBC) was performed using an automated hematology analyzer (Sysmex XN-1000, Sysmex Corporation, Kobe, Japan). Hematological inflammatory indices were calculated as follows: - Platelet-to-lymphocyte ratio (PLR) = platelet count / lymphocyte count - Neutrophil-to-lymphocyte ratio (NLR) = neutrophil count / lymphocyte count - Monocyte-to-lymphocyte ratio (MLR) = monocyte count / lymphocyte count
Vitamin D: Serum 25-hydroxyvitamin D [25(OH)D] was measured using ECLIA. Vitamin D status was classified as: deficiency <20 ng/mL, insufficiency 20–29 ng/mL, sufficiency ≥30 ng/mL.
Metabolic parameters: Fasting glucose, insulin, total cholesterol, low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), and triglycerides were measured using standard enzymatic methods on a Cobas c501 analyzer (Roche Diagnostics). Homeostatic Model Assessment for Insulin Resistance (HOMA-IR) was calculated as: (fasting insulin [μIU/mL] × fasting glucose [mg/dL]) / 405.

2.8 Statistical Analysis
Statistical analyses were performed using IBM SPSS Statistics version 26.0 (IBM Corp., Armonk, NY, USA). Continuous variables were assessed for normality using the Shapiro-Wilk test and visual inspection of Q-Q plots. Due to non-normal distribution of most variables and the small sample size, non-parametric tests were employed throughout the analysis.
Descriptive statistics are presented as mean ± standard deviation (SD) for continuous variables and as frequency (percentage) for categorical variables. Between-group comparisons at baseline and follow-up were conducted using the Mann-Whitney U test for continuous variables and chi-square test or Fisher's exact test for categorical variables. Within-group changes from baseline to 6-week follow-up were assessed using the Wilcoxon signed-rank test.
Effect sizes for between-group differences were calculated using Cohen's d for continuous variables, with values of 0.2, 0.5, and 0.8 interpreted as small, medium, and large effects, respectively. For within-group changes, effect sizes were calculated using the formula $r = Z / \sqrt{N}$, where Z is the standardized test statistic from the Wilcoxon signed-rank test and N is the sample size.
A two-tailed p-value <0.05 was considered statistically significant. Given the exploratory nature of this retrospective study and the multiple comparisons involved, results should be interpreted with appropriate caution. No formal

correction for multiple comparisons was applied, as this was an exploratory hypothesis-generating study; however, we acknowledge that this increases the risk of Type I error.
Because this was an exploratory retrospective study, sample size was determined by the number of eligible medical records available during the study period. The primary outcome was the between-group difference in IL-6 levels at 6 weeks. Based on the observed between-group difference in IL-6 (2.52 pg/mL) and the corresponding standard deviations, the available sample size provided approximately 80% power at a two-sided α of 0.05. The study was not specifically powered for secondary outcomes; therefore, secondary analyses should be interpreted cautiously.

3. RESULTS

3.1 Baseline Characteristics

A total of 60 women with HT were included in the analysis: 30 in the elimination diet group and 30 in the standard care control group. Baseline demographic, anthropometric, and clinical characteristics are presented in Table 1. The groups were well-matched for age, disease duration, levothyroxine dose, and BMI. No significant differences were observed between groups at baseline for any demographic or clinical variable (all p>0.05).

Table 1. Baseline Demographic and Clinical Characteristics

Characteristic	Elimination Diet Group (n=30)	Control Group (n=30)	p-value
Age (years)	39.2 ± 5.8	38.7 ± 6.1	0.72
Disease duration (years)	3.4 ± 2.1	3.6 ± 2.3	0.68
Levothyroxine dose (μg/day)	87.5 ± 28.3	85.0 ± 26.7	0.71
BMI (kg/m²)	27.8 ± 4.2	27.3 ± 4.5	0.64
Weight (kg)	72.4 ± 11.3	71.2 ± 12.1	0.69

Data are presented as mean ± SD. Between-group comparisons performed using Mann-Whitney U test. BMI, body mass index.

3.2 Inflammatory Cytokines

Baseline and 6-week follow-up values for inflammatory cytokines are presented in Table 2. At baseline, there were no significant differences between groups for IL-6, TNF-α, or IL-1β levels (all p>0.05).

Table 2. Inflammatory Cytokines at Baseline and 6-Week Follow-up

Parameter	Group	Baseline (T1)	6-Week (T2)	Within-group p-value	Between-group p-value (T2)
IL-6 (pg/mL)	Elimination Diet	9.23 ± 3.87	6.95 ± 2.35	0.01*	0.01*
	Control	9.15 ± 3.92	9.47 ± 4.13	0.48	
TNF-α (pg/mL)	Elimination Diet	12.45 ± 4.23	11.87 ± 3.95	0.34	0.52
	Control	12.18 ± 4.15	12.03 ± 4.28	0.76	
IL-1β (pg/mL)	Elimination Diet	3.82 ± 1.45	3.67 ± 1.38	0.42	0.61
	Control	3.76 ± 1.52	3.71 ± 1.49	0.68	

Data are presented as mean ± SD. Within-group comparisons performed using Wilcoxon signed-rank test. Between-group comparisons at T2 performed using Mann-Whitney U test. *p<0.05 considered statistically significant. IL-6, interleukin-6; TNF-α, tumor necrosis factor-alpha; IL-1β, interleukin-1 beta.
At 6-week follow-up, the elimination diet group demonstrated significantly lower IL-6 levels compared to the control group (6.95±2.35 vs. 9.47±4.13 pg/mL, p=0.01, Cohen's d=0.74). Within-group analysis revealed a significant reduction in IL-6 levels in the elimination diet group from baseline to 6 weeks (p=0.01, effect size r=0.47), while the control group showed no significant change (p=0.48). The mean reduction in IL-6 in the elimination diet group was 2.28 pg/mL (24.7% decrease from baseline).
No significant changes were observed for TNF-α or IL-1β in either group, and there were no significant between-group differences for these cytokines at 6-week follow-up (both p>0.05).

3.3 Hematological Inflammatory Indices

Baseline and 6-week follow-up values for hematological inflammatory indices are presented in Table 3. At baseline, there were no significant differences between groups for PLR, NLR, or MLR (all p>0.05).

Table 3. Hematological Inflammatory Indices at Baseline and 6-Week Follow-up

Parameter	Group	Baseline (T1)	6-Week (T2)	Within-group p-value	Between-group p-value (T2)

PLR	Elimination Diet	128.4 ± 32.5	112.3 ± 28.7	0.01*	0.03*
	Control	126.8 ± 31.2	125.1 ± 30.8	0.62	
NLR	Elimination Diet	2.34 ± 0.78	2.18 ± 0.71	0.15	0.28
	Control	2.29 ± 0.82	2.31 ± 0.79	0.81	
MLR	Elimination Diet	0.28 ± 0.09	0.26 ± 0.08	0.21	0.34
	Control	0.27 ± 0.08	0.27 ± 0.09	0.73	

Data are presented as mean ± SD. Within-group comparisons performed using Wilcoxon signed-rank test. Between-group comparisons at T2 performed using Mann-Whitney U test. *p<0.05 considered statistically significant. PLR, platelet-to-lymphocyte ratio; NLR, neutrophil-to-lymphocyte ratio; MLR, monocyte-to-lymphocyte ratio.

At 6-week follow-up, the elimination diet group had significantly lower PLR compared to the control group (112.3±28.7 vs. 125.1±30.8, p=0.03, Cohen's d=0.43). Within-group analysis showed a significant reduction in PLR in the elimination diet group (p=0.01, effect size r=0.47), representing a mean decrease of 16.1 units (12.5% reduction from baseline). The control group showed no significant change in PLR (p=0.62).

No significant changes were observed for NLR or MLR in either group, and there were no significant between-group differences for these indices at 6-week follow-up (both p>0.05).

3.4 Thyroid Function and Autoantibodies

Baseline and 6-week follow-up values for thyroid function tests and autoantibodies are presented in Table 4. At baseline, there were no significant differences between groups for any thyroid parameter (all p>0.05).

Table 4. Thyroid Function Tests and Autoantibodies at Baseline and 6-Week Follow-up

Parameter	Group	Baseline (T1)	6-Week (T2)	Within-group p-value	Between-group p-value (T2)
TSH (mIU/L)	Elimination Diet	3.45 ± 1.23	2.87 ± 1.05	0.01*	0.42
	Control	3.38 ± 1.18	2.95 ± 1.12	0.02*	
fT4 (pmol/L)	Elimination Diet	15.8 ± 2.4	16.1 ± 2.3	0.38	0.67
	Control	15.6 ± 2.5	15.9 ± 2.6	0.45	
fT3 (pmol/L)	Elimination Diet	4.7 ± 0.8	4.8 ± 0.7	0.52	0.71
	Control	4.6 ± 0.9	4.7 ± 0.8	0.58	
Anti-TPO (IU/mL)	Elimination Diet	287.5 ± 156.3	245.2 ± 142.8	0.01*	0.38
	Control	293.8 ± 162.7	261.4 ± 151.2	0.02*	
Anti-TG (IU/mL)	Elimination Diet	198.4 ± 112.5	172.3 ± 98.7	0.02*	0.45
	Control	202.1 ± 118.3	183.6 ± 105.4	0.03*	

Data are presented as mean ± SD. Within-group comparisons performed using Wilcoxon signed-rank test. Between-group comparisons at T2 performed using Mann-Whitney U test. *p<0.05 considered statistically significant. TSH, thyroid-stimulating hormone; fT4, free thyroxine; fT3, free triiodothyronine; Anti-TPO, anti-thyroid peroxidase antibody; Anti-TG, anti-thyroglobulin antibody.

Both groups exhibited significant reductions in TSH levels from baseline to 6 weeks (elimination diet group: p=0.01; control group: p=0.02), with no significant between-group difference at follow-up (p=0.42). Free T4 and free T3 levels remained stable in both groups throughout the study period (all p>0.05).

Both groups also demonstrated significant reductions in thyroid autoantibodies. Anti-TPO levels decreased significantly in both the elimination diet group (p=0.01) and control group (p=0.02), with no significant between-group difference at 6-week follow-up (p=0.38). Similarly, anti-TG levels decreased significantly in both groups (elimination diet: p=0.02; control: p=0.03), with no significant between-group difference (p=0.45).

3.5 Vitamin D Status

Baseline and 6-week follow-up values for vitamin D are presented in Table 5. At baseline, both groups had mean vitamin D levels in the insufficient range, with no significant between-group difference (p=0.78).

Table 5. Vitamin D Levels at Baseline and 6-Week Follow-up

Parameter	Group	Baseline (T1)	6-Week (T2)	Within-group p-value	Between-group p-value (T2)
25(OH)D (ng/mL)	Elimination Diet	22.4 ± 8.3	27.8 ± 9.1	0.01*	0.02*
	Control	22.1 ± 8.7	23.5 ± 8.9	0.24	

Data are presented as mean ± SD. Within-group comparisons performed using Wilcoxon signed-rank test. Between-group comparisons at T2 performed using Mann-Whitney U test. *p<0.05 considered statistically significant. 25(OH)D, 25-hydroxyvitamin D.

At 6-week follow-up, the elimination diet group had significantly higher vitamin D levels compared to the control group (27.8±9.1 vs. 23.5±8.9 ng/mL, p=0.02, Cohen's d=0.48). Within-group analysis revealed a significant increase in vitamin D in the elimination diet group (p=0.01, effect size r=0.47), representing a mean increase of 5.4 ng/mL (24.1% increase from baseline). The control group showed no significant change in vitamin D levels (p=0.24).

3.6 Metabolic Parameters

Baseline and 6-week follow-up values for metabolic parameters are presented in Table 6. At baseline, there were no significant differences between groups for any metabolic parameter (all p>0.05).

Table 6. Metabolic Parameters at Baseline and 6-Week Follow-up

Parameter	Group	Baseline (T1)	6-Week (T2)	Within-group p-value	Between-group p-value (T2)
Glucose (mg/dL)	Elimination Diet	94.2 ± 12.5	91.3 ± 11.8	0.12	0.31
	Control	93.8 ± 13.1	93.1 ± 12.7	0.68	
Insulin (µIU/mL)	Elimination Diet	14.8 ± 6.2	11.9 ± 5.3	0.01*	0.04*
	Control	14.5 ± 6.5	14.2 ± 6.3	0.71	
HOMA-IR	Elimination Diet	3.45 ± 1.82	2.68 ± 1.54	0.02*	0.06
	Control	3.38 ± 1.87	3.29 ± 1.79	0.69	
Total Cholesterol (mg/dL)	Elimination Diet	198.4 ± 38.5	192.7 ± 36.2	0.18	0.42
	Control	196.8 ± 39.2	195.3 ± 38.7	0.73	
LDL-C (mg/dL)	Elimination Diet	118.5 ± 32.4	114.2 ± 30.8	0.25	0.38
	Control	117.2 ± 33.1	116.8 ± 32.5	0.81	
HDL-C (mg/dL)	Elimination Diet	52.3 ± 11.2	53.8 ± 11.5	0.32	0.56
	Control	51.8 ± 10.9	52.1 ± 11.3	0.78	
Triglycerides (mg/dL)	Elimination Diet	142.8 ± 58.3	135.4 ± 54.7	0.28	0.47
	Control	140.5 ± 56.9	138.9 ± 57.2	0.82	

Data are presented as mean ± SD. Within-group comparisons performed using Wilcoxon signed-rank test. Between-group comparisons at T2 performed using Mann-Whitney U test. *p<0.05 considered statistically significant. HOMA-IR, Homeostatic Model Assessment for Insulin Resistance; LDL-C, low-density lipoprotein cholesterol; HDL-C, high-density lipoprotein cholesterol.

At 6-week follow-up, the elimination diet group had significantly lower insulin levels compared to the control group (11.9±5.3 vs. 14.2±6.3 µIU/mL, p=0.04, Cohen's d=0.40). Within-group analysis showed a significant reduction in insulin in the elimination diet group (p=0.01, effect size r=0.47), representing a mean decrease of 2.9 µIU/mL (19.6% reduction from baseline). The control group showed no significant change in insulin levels (p=0.71).

HOMA-IR showed a significant within-group reduction in the elimination diet group (p=0.02, effect size r=0.42), with a trend toward between-group difference at follow-up (p=0.06). No significant changes were observed for glucose, total cholesterol, LDL-C, HDL-C, or triglycerides in either group (all p>0.05).

3.7 Anthropometric Changes

Baseline and 6-week follow-up values for anthropometric parameters are presented in Table 7.

Table 7. Anthropometric Parameters at Baseline and 6-Week Follow-up

Parameter	Group	Baseline (T1)	6-Week (T2)	Within-group p-value	Between-group p-value (T2)
Weight (kg)	Elimination Diet	72.4 ± 11.3	70.8 ± 10.9	0.02*	0.08
	Control	71.2 ± 12.1	71.0 ± 12.0	0.74	
BMI (kg/m²)	Elimination Diet	27.8 ± 4.2	27.2 ± 4.0	0.02*	0.09
	Control	27.3 ± 4.5	27.2 ± 4.4	0.76	

Data are presented as mean ± SD. Within-group comparisons performed using Wilcoxon signed-rank test. Between-group comparisons at T2 performed using Mann-Whitney U test. *p<0.05 considered statistically significant. BMI, body mass index.

The elimination diet group showed significant reductions in both weight (p=0.02, effect size r=0.42) and BMI (p=0.02, effect size r=0.42), with mean decreases of 1.6 kg and 0.6 kg/m², respectively. The control group showed no significant changes in weight or BMI (both p>0.05). Between-group differences at 6-week follow-up approached but did not reach statistical significance for weight (p=0.08) or BMI (p=0.09).

4. DISCUSSION

This retrospective case-control study examined the associations between a 6-week elimination diet protocol and inflammatory biomarkers in women with HT receiving stable levothyroxine therapy. The principal finding was that the elimination diet group demonstrated significantly lower IL-6 levels at 6-week follow-up compared to the control group, with a significant within-group reduction in IL-6 that was not observed in controls. Additionally, the elimination diet group showed favorable changes in PLR, vitamin D status, insulin levels, and BMI. Notably, both groups exhibited similar reductions in TSH and thyroid autoantibodies, suggesting these changes may reflect factors other than dietary intervention.

4.1 IL-6 and Inflammatory Cytokines

The significant reduction in IL-6 levels observed in the elimination diet group represents the most notable finding of this study. IL-6 is a pleiotropic cytokine with both pro-inflammatory and anti-inflammatory properties, playing a central role in the pathogenesis of autoimmune thyroid disease [54], [55]. Elevated IL-6 levels in HT patients have been associated with disease activity, autoantibody production, and systemic inflammation [56], [57]. The 24.7% reduction in IL-6 observed in the elimination diet group, resulting in significantly lower levels compared to controls at 6-week follow-up, suggests a potential anti-inflammatory effect of the dietary intervention.

Several mechanisms may explain the observed reduction in IL-6. First, the elimination of gluten-containing grains may have reduced intestinal permeability and subsequent translocation of bacterial antigens, thereby decreasing systemic immune activation [58], [59]. Gluten has been shown to increase zonulin production, a modulator of intestinal tight junctions, leading to increased gut permeability even in non-celiac individuals [60]. Second, the removal of dairy products may have eliminated casein and whey proteins that can trigger immune responses in susceptible individuals [61]. Third, the exclusion of refined sugars and processed foods may have reduced glycemic load and oxidative stress, both of which are known to stimulate IL-6 production [62], [63].

The gut-thyroid axis provides a mechanistic framework for understanding how dietary modifications may influence systemic inflammation in HT. Emerging evidence suggests that dysbiosis and increased intestinal permeability are common in autoimmune thyroid disease and may contribute to the perpetuation of autoimmune responses [64], [65]. By removing potentially inflammatory dietary components, the elimination diet may have promoted a more favorable gut microbiome composition and improved intestinal barrier function, leading to reduced systemic inflammation [66], [67].

Interestingly, TNF-α and IL-1β levels remained unchanged in both groups throughout the study period. This differential response among inflammatory cytokines suggests that the elimination diet may have selective effects on certain inflammatory pathways. IL-6 is produced by a wide variety of cells, including intestinal epithelial cells, adipocytes, and immune cells, and is particularly responsive to dietary and metabolic stimuli [68]. In contrast, TNF-α and IL-1β are primarily produced by activated macrophages and may be less sensitive to short-term dietary modifications [69]. The 6-week intervention period may have been insufficient to significantly impact these cytokines, or their regulation in HT may be more dependent on factors not addressed by the elimination diet. The differential response of IL-6 compared to TNF-α and IL-1β may reflect distinct regulatory pathways. IL-6 appears to be more

rapidly responsive to dietary factors through gut-derived and metabolic signals, whereas TNF-α and IL-1β may require longer intervention periods or more pronounced inflammatory states to demonstrate measurable changes.

4.2 Hematological Inflammatory Indices

The significant reduction in PLR observed in the elimination diet group provides additional evidence of anti-inflammatory effects. PLR has emerged as an accessible marker of systemic inflammation in various autoimmune and inflammatory conditions [70], [71]. Elevated PLR reflects increased platelet activation and relative lymphopenia, both of which are associated with chronic inflammation and immune dysregulation [72]. The 12.5% reduction in PLR in the elimination diet group, resulting in significantly lower values compared to controls, suggests improved inflammatory status.

Platelets play active roles in inflammation beyond their hemostatic functions, releasing inflammatory mediators and interacting with immune cells [73]. The reduction in PLR may reflect decreased platelet activation in response to reduced systemic inflammation. Additionally, the elimination diet may have promoted lymphocyte recovery or reduced lymphocyte apoptosis, contributing to the improved PLR [74].

The lack of significant changes in NLR and MLR suggests that the elimination diet's effects on hematological inflammatory indices may be selective. NLR and MLR are influenced by different aspects of immune function and may require longer intervention periods or more intensive dietary modifications to show significant changes [75]. Alternatively, these indices may be less sensitive to the specific inflammatory pathways modulated by the elimination diet.

4.3 Thyroid Autoantibodies and Function

A notable finding of this study was that both the elimination diet and control groups exhibited significant reductions in thyroid autoantibodies (anti-TPO and anti-TG) and TSH levels, with no significant between-group differences. This pattern suggests that these changes may not be attributable to the dietary intervention but rather reflect other factors.

Several explanations for these parallel reductions warrant consideration. First, the natural history of HT is characterized by fluctuations in autoantibody levels and thyroid function over time [76], [77]. Spontaneous reductions in autoantibodies have been documented in longitudinal studies of HT patients, particularly in those receiving stable levothyroxine therapy [78]. Second, regression-to-the-mean is a statistical phenomenon whereby extreme values tend to move toward the average upon repeated measurement, which is particularly relevant in retrospective studies where patients may have been selected based on elevated baseline values [79].

Third, the reductions in TSH and autoantibodies observed in both groups may reflect the pharmacological effects of levothyroxine therapy. Levothyroxine has been shown to reduce TSH levels through negative feedback on the hypothalamic-pituitary-thyroid axis, and some studies have suggested that achieving optimal thyroid hormone replacement may be associated with modest reductions in thyroid autoantibodies [80], [81]. Since both groups received stable levothyroxine therapy throughout the study period, these pharmacological effects would be expected to occur in both groups.

The absence of additional benefit from the elimination diet on thyroid autoantibodies contrasts with some previous reports suggesting that gluten-free or elimination diets may reduce autoantibody levels in HT patients [82], [83]. However, these earlier studies often lacked appropriate control groups or had methodological limitations that complicate interpretation [84]. The present findings, derived from a controlled comparison, suggest that short-term elimination diets may not significantly impact thyroid autoantibody levels beyond the effects of standard medical management.

It is important to note that thyroid autoantibody levels may not be the most sensitive markers of dietary intervention effects in HT. Autoantibody production is a complex process involving multiple immune cell types and regulatory mechanisms that may be relatively resistant to short-term dietary modifications [85]. In contrast, inflammatory cytokines like IL-6 may be more responsive to dietary changes due to their rapid turnover and sensitivity to metabolic and gut-derived signals [86].

4.4 Vitamin D Status

The significant increase in vitamin D levels observed in the elimination diet group is an important finding with potential clinical implications. Vitamin D deficiency is highly prevalent in HT patients and has been associated with increased autoimmune activity and inflammation [87], [88]. The 24.1% increase in vitamin D levels in the elimination diet group, resulting in significantly higher levels compared to controls, suggests that the dietary intervention may have improved vitamin D status.

Several mechanisms may explain this improvement. First, the elimination diet emphasized whole, unprocessed foods, including fatty fish, eggs, and vitamin D-fortified alternatives to dairy products, which may have increased dietary vitamin D intake [89]. Second, the reduction in systemic inflammation, as evidenced by decreased IL-6 levels, may have improved vitamin D metabolism and bioavailability [90]. Chronic inflammation has been shown to interfere with vitamin D synthesis and increase its catabolism [91]. The observed increase in vitamin D levels in the elimination diet group may reflect improved intestinal absorption following removal of potentially inflammatory foods such as gluten

and dairy, consistent with previous studies suggesting gut barrier restoration with elimination diets. However, potential differences in vitamin D supplementation between groups cannot be excluded, as supplementation was not systematically controlled in this study.

Third, the modest weight loss observed in the elimination diet group may have contributed to improved vitamin D status. Vitamin D is fat-soluble and can be sequestered in adipose tissue, reducing its bioavailability [92]. Weight reduction may have released vitamin D from adipose stores or improved its distribution [93]. Additionally, improved insulin sensitivity, as suggested by the reduction in insulin levels and HOMA-IR, may have positively influenced vitamin D metabolism, as insulin resistance has been associated with lower vitamin D levels [94].

The improvement in vitamin D status may have contributed to the observed reduction in IL-6 levels, as vitamin D has well-established immunomodulatory and anti-inflammatory properties [95], [96]. Vitamin D regulates the expression of numerous genes involved in immune function and has been shown to suppress IL-6 production in various cell types [97]. Thus, the relationship between the elimination diet, vitamin D status, and inflammatory markers may be bidirectional and mutually reinforcing.

4.5 Metabolic Effects

The elimination diet group demonstrated significant improvements in insulin levels and HOMA-IR, indicating enhanced insulin sensitivity. These metabolic improvements are clinically relevant, as insulin resistance is common in HT patients and contributes to increased cardiovascular risk [98], [99]. The 19.6% reduction in insulin levels and the significant decrease in HOMA-IR suggest that the elimination diet may have favorable metabolic effects beyond its anti-inflammatory properties.

Several dietary components of the elimination protocol may have contributed to improved insulin sensitivity. The removal of refined sugars and processed foods likely reduced glycemic load and prevented postprandial insulin spikes [100]. The emphasis on whole, unprocessed foods with higher fiber content may have improved glucose metabolism and insulin signaling [101]. Additionally, the exclusion of dairy products may have eliminated insulinotropic effects of dairy proteins, particularly whey, which stimulate insulin secretion disproportionate to their glycemic impact [102].

The reduction in systemic inflammation, as evidenced by decreased IL-6 levels, may have also contributed to improved insulin sensitivity. IL-6 has been implicated in the development of insulin resistance through multiple mechanisms, including interference with insulin receptor signaling and promotion of hepatic glucose production [103], [104]. By reducing IL-6 levels, the elimination diet may have alleviated inflammation-mediated insulin resistance.

The modest but significant reductions in weight and BMI observed in the elimination diet group likely also contributed to improved insulin sensitivity. Even small amounts of weight loss have been shown to improve metabolic parameters in overweight individuals [105]. The weight loss observed in this study (mean 1.6 kg over 6 weeks) is consistent with the caloric restriction that may have occurred due to the elimination of energy-dense processed foods and refined sugars.

Interestingly, lipid parameters (total cholesterol, LDL-C, HDL-C, triglycerides) did not show significant changes in either group. This may reflect the relatively short intervention period, as lipid metabolism typically requires longer durations to show substantial changes [106]. Additionally, the elimination diet protocol did not specifically target lipid reduction, and patients were not instructed to reduce total fat intake, only to emphasize healthy fat sources.

4.6 Clinical Implications

The findings of this study have several potential clinical implications for the management of HT. First, the significant reduction in IL-6 levels associated with the elimination diet suggests that dietary intervention may serve as a useful adjunctive approach to modulate systemic inflammation in HT patients. While levothyroxine effectively manages hypothyroidism, it does not directly address the underlying inflammatory processes. Complementary dietary strategies that reduce inflammatory cytokines may help address the residual symptoms and metabolic disturbances that many HT patients experience despite adequate thyroid hormone replacement [107], [108].

Second, the improvements in insulin sensitivity and metabolic parameters observed with the elimination diet are clinically relevant given the increased prevalence of metabolic syndrome and cardiovascular disease in HT patients [109], [110]. Dietary interventions that improve insulin sensitivity may help reduce long-term cardiovascular risk in this population. The modest weight loss achieved with the elimination diet, while not dramatic, is consistent with sustainable lifestyle modifications and may contribute to improved overall health outcomes [111].

Third, the improvement in vitamin D status associated with the elimination diet highlights the potential for dietary interventions to address common nutritional deficiencies in HT patients. Given the immunomodulatory properties of vitamin D and its potential role in autoimmune disease, optimizing vitamin D status through diet and supplementation should be a priority in HT management [112], [113].

Fourth, the reduction in PLR suggests that accessible hematological inflammatory indices may serve as useful markers for monitoring the effects of dietary interventions in HT patients. PLR can be easily calculated from routine complete blood count results and may provide a cost-effective way to assess inflammatory status and response to treatment [114].

However, several important caveats must be considered when interpreting the clinical implications of these findings. The retrospective design of this study limits causal inference, and the observed associations may be influenced by unmeasured confounders or selection bias. The lack of randomization means that patients who chose to follow the elimination diet may have differed from controls in ways that could affect outcomes, such as motivation, health consciousness, or baseline dietary quality [115].

Additionally, the 6-week intervention period is relatively short, and the long-term sustainability and effects of elimination diets in HT patients remain unknown. Some patients may find elimination diets restrictive and difficult to maintain over extended periods, potentially leading to poor adherence and nutritional inadequacies if not properly supervised [116]. The potential risks of elimination diets, including nutrient deficiencies and negative psychological effects related to dietary restriction, must be weighed against potential benefits [117].

The absence of significant effects on thyroid autoantibodies suggests that elimination diets should not be promoted as a means to reduce autoantibody levels or replace standard medical management. Patients should be counseled that dietary interventions are complementary to, not substitutes for, appropriate thyroid hormone replacement therapy [118].

4.7 Study Strengths

This study has several notable strengths. First, the inclusion of a control group receiving standard medical management allows for comparison of outcomes and helps distinguish dietary effects from natural disease fluctuation or pharmacological effects. Many previous studies of dietary interventions in HT have lacked appropriate control groups, limiting their interpretability [119].

Second, the matching of groups based on age, baseline TSH, and levothyroxine dose helps ensure comparability and reduces potential confounding. The requirement for stable levothyroxine therapy throughout the study period further strengthens the internal validity by controlling for pharmacological effects [120].

Third, the comprehensive assessment of multiple inflammatory markers, including cytokines (IL-6, TNF-α, IL-1β) and hematological indices (PLR, NLR, MLR), provides a more complete picture of inflammatory status than studies focusing on single markers. The inclusion of metabolic parameters and vitamin D status allows for evaluation of broader health effects beyond inflammation [121].

Fourth, the use of standardized laboratory methods and accredited facilities ensures the reliability and accuracy of biochemical measurements. The employment of non-parametric statistical tests appropriate for the data distribution and sample size enhances the validity of the statistical analyses [122].

Fifth, the retrospective assessment of dietary adherence through multiple sources (dietitian notes, food diaries, clinical documentation) and the exclusion of patients with poor adherence helps ensure that the elimination diet group truly represents patients who implemented the protocol as prescribed. This strengthens the internal validity of the dietary intervention [123].

4.8 Study Limitations

Several important limitations must be acknowledged. First and foremost, the retrospective design limits causal inference. While the observed associations between the elimination diet and reduced IL-6 levels are suggestive, they do not prove causation. Unmeasured confounders, selection bias, and other sources of bias inherent to retrospective studies may have influenced the results [124].

Second, the lack of randomization means that patients who chose to follow the elimination diet may have differed systematically from controls in ways that could affect outcomes. For example, patients motivated to pursue dietary interventions may have been more health-conscious, more adherent to medical recommendations, or may have made other lifestyle changes (e.g., increased physical activity, stress reduction) that could contribute to the observed improvements [125]. Although groups were matched on key variables, residual confounding cannot be excluded.

Third, the small sample size (n=30 per group) limits statistical power and the precision of effect estimates. Some potentially meaningful differences may not have reached statistical significance due to insufficient power. Additionally, the small sample size increases the risk of Type I error, particularly given the multiple comparisons performed without formal correction [126].

Fourth, the retrospective assessment of dietary adherence is less rigorous than prospective monitoring methods such as food records, 24-hour recalls, or biomarker assessment. While efforts were made to ensure high adherence through review of multiple documentation sources, the accuracy of adherence assessment in this retrospective study is inherently limited [127]. Patients with incomplete documentation or unclear adherence were excluded, which may have introduced selection bias.

Fifth, the 6-week intervention period is relatively short, and the durability of the observed effects is unknown. Longer-term studies are needed to determine whether the reductions in IL-6 and improvements in metabolic parameters are sustained over time and whether they translate into clinically meaningful outcomes such as symptom improvement or reduced disease progression [128].

Sixth, the study population was limited to women aged 30–50 years with HT receiving stable levothyroxine therapy. The generalizability of findings to men, other age groups, patients with more severe disease, or those not receiving

levothyroxine is uncertain [129]. Additionally, the study was conducted at a single center in Turkey, and cultural, dietary, and genetic factors may limit generalizability to other populations [130].
Seventh, the study did not include assessment of patient-reported outcomes such as symptoms, quality of life, or treatment satisfaction. While biochemical improvements are important, their clinical significance ultimately depends on whether they translate into improved patient well-being [131].
Eighth, the mechanisms underlying the observed associations were not directly investigated. While plausible mechanistic explanations have been proposed (e.g., improved gut barrier function, reduced immune activation, altered microbiome composition), these remain speculative without direct measurement of relevant biomarkers such as zonulin, lipopolysaccharide, or microbiome composition [132].
Ninth, the study did not assess potential adverse effects or nutritional adequacies of the elimination diet. While no adverse events were documented in the medical records reviewed, systematic assessment of potential harms, nutrient deficiencies, or negative psychological effects was not performed [133].
Finally, the parallel reductions in thyroid autoantibodies and TSH in both groups, likely reflecting natural disease fluctuation or regression-to-the-mean, highlight the challenges of interpreting changes in these parameters in non-randomized studies. This underscores the need for randomized controlled trials with appropriate statistical methods to account for regression-to-the-mean and natural disease variability [134].

4.9 Future Research Directions

The findings of this retrospective study provide a foundation for future research on dietary interventions in HT. Several key research priorities emerge:
First, prospective randomized controlled trials are urgently needed to establish causality and confirm the effects of elimination diets on inflammatory markers in HT. Such trials should include adequate sample sizes, appropriate randomization and blinding procedures, standardized dietary protocols, rigorous adherence monitoring, and comprehensive assessment of outcomes including inflammatory markers, thyroid function, metabolic parameters, and patient-reported outcomes [135].
Second, longer-term studies are needed to assess the durability of effects and the sustainability of elimination diets in HT patients. Studies with follow-up periods of 6 months to 1 year or longer would provide valuable information about long-term adherence, maintenance of biochemical improvements, and potential clinical benefits [136].
Third, mechanistic studies investigating the pathways through which elimination diets may influence inflammation in HT are warranted. Such studies should include assessment of intestinal permeability markers (e.g., zonulin, lactulose/mannitol ratio), gut microbiome composition and function, immune cell phenotypes, and additional inflammatory and regulatory cytokines [137].
Fourth, research is needed to identify which components of elimination diets are most important for achieving anti-inflammatory effects. Factorial design studies that systematically evaluate the effects of eliminating individual food categories (gluten, dairy, soy, etc.) could help optimize dietary protocols and reduce unnecessary restrictions [138].
Fifth, studies examining the effects of elimination diets in different HT patient subgroups are needed. Research should explore whether dietary interventions are more effective in certain patient populations, such as those with more severe inflammation, specific genetic polymorphisms, or particular microbiome profiles [139].
Sixth, investigation of the optimal duration and timing of elimination diets is warranted. Studies should examine whether longer intervention periods yield greater benefits, whether intermittent elimination protocols are effective, and whether dietary interventions are most beneficial at particular stages of disease [140].
Seventh, research on the integration of dietary interventions with other complementary approaches, such as stress management, exercise, and targeted supplementation, may provide insights into comprehensive lifestyle interventions for HT management [141].
Finally, cost-effectiveness analyses and implementation research are needed to evaluate the feasibility and value of incorporating dietary interventions into routine clinical care for HT patients [142].

5. CONCLUSION

This retrospective case-control study found that a 6-week elimination diet protocol in women aged 30–50 years with HT was associated with significantly reduced IL-6 levels compared to standard medical management alone. The elimination diet group also demonstrated favorable changes in PLR, vitamin D status, insulin levels, and BMI. These findings suggest that elimination diets may have anti-inflammatory and metabolic benefits in HT patients receiving stable levothyroxine therapy.
However, both the elimination diet and control groups exhibited similar reductions in thyroid autoantibodies and TSH levels, suggesting that these changes likely reflect natural disease fluctuation, regression-to-the-mean, or pharmacological effects of levothyroxine rather than dietary intervention. The absence of differential effects on thyroid autoantibodies indicates that elimination diets should not be promoted as a means to reduce autoantibody levels or replace standard medical management.
The retrospective design and small sample size of this study limit causal inference and generalizability. The observed associations between the elimination diet and reduced inflammation may be influenced by unmeasured confounders,

selection bias, or other limitations inherent to retrospective research. Additionally, the 6-week intervention period is relatively short, and the long-term sustainability and clinical significance of the observed biochemical changes remain unknown.

Despite these limitations, the findings provide preliminary evidence supporting the potential role of elimination diets as adjunctive interventions to modulate inflammation and improve metabolic parameters in HT patients. The significant reduction in IL-6, a key proinflammatory cytokine implicated in HT pathogenesis, is particularly noteworthy and warrants further investigation.

Prospective randomized controlled trials with larger sample sizes, longer follow-up periods, rigorous adherence monitoring, and comprehensive outcome assessment are needed to confirm these findings and establish the clinical utility of elimination diets in HT management. Future research should also investigate the mechanisms underlying the observed associations, identify optimal dietary protocols, and evaluate the integration of dietary interventions into comprehensive care strategies for HT patients.

Until such evidence is available, clinicians should approach dietary interventions in HT with cautious optimism, recognizing their potential benefits while emphasizing that they are complementary to, not substitutes for, appropriate thyroid hormone replacement therapy. Patients interested in elimination diets should be counseled about the preliminary nature of current evidence, the importance of nutritional adequacy, and the need for ongoing medical supervision.

DECLARATIONS

Ethics Approval and Consent to Participate: This study was approved by the Kafkas University University Non-Interventional Clinical Research Ethics Committee (approval number: Approval No: KAÜ-TFEK 2025-06/31, Date: 24.06.2025). The study was conducted in accordance with the principles of the Declaration of Helsinki. Written informed consent was obtained from all participants for the use of their clinical data for research purposes.

Consent for Publication: Not applicable.

Availability of Data and Materials

The datasets generated and analyzed during the current study are not publicly available due to patient privacy and institutional data protection policies, but are available from the corresponding author on reasonable request and with appropriate ethical approval.

Competing Interests: The authors declare that they have no competing interests.

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Authors' Contributions: SA conceptualized the study, designed the methodology, collected and analyzed data, and drafted the manuscript. IK supervised the research, contributed to study design and data interpretation, and critically revised the manuscript. BBS contributed to data collection, clinical interpretation, and manuscript revision. All authors read and approved the final manuscript.

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Key Points

1. A 6-week elimination diet in women with Hashimoto thyroiditis was associated with significantly reduced IL-6 levels compared to standard care alone.
2. The elimination diet group showed favorable changes in platelet-to-lymphocyte ratio, vitamin D levels, insulin, and BMI.
3. Both dietary intervention and standard care groups exhibited similar reductions in thyroid autoantibodies and TSH, suggesting these changes may reflect natural disease fluctuation or pharmacological effects.
4. Retrospective design and small sample size limit causal inference; prospective randomized trials are needed to confirm these findings.