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The association between dietary inflammatory index and dietary total antioxidant capacity and Hashimoto's thyroiditis: a case-control study

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Abstract

Background Hashimoto's thyroiditis (HT) is an inflammatory disease characterized by increased reactive oxygen species. Diets rich in anti-inflammatory and antioxidant properties may be linked to a reduced risk of developing HT. The aim of this study was to investigate the association between the dietary inflammatory index (DII) and dietary total antioxidant capacity (DTAC) with HT in Iranian adults.

Methods The study was a hospital-based case-control study conducted on 230 participants (115 cases and 115 controls). Dietary intake was assessed using a food frequency questionnaire (FFQ). The FFQ data were used to calculate DII and DTAC scores. Anthropometric measurements, thyroid function, and antibody tests were evaluated using standard methods. Multivariable logistic regression analysis was performed in both raw and adjusted models to determine the association between DII and DTAC scores with HT.

Results The average age of the participants was 39.76 ± 9.52 years. The mean body mass index in the case and control groups was 28.03 ± 6.32 and 26.43 ± 5.13 (kg/m^2), respectively ($P = 0.036$). In the HT group, the DII level was higher ($P < 0.001$) and the DTAC level was lower than those in the healthy group ($P = 0.047$). In the multivariable logistic regression model, after adjusting for confounding factors, subjects in the last tertile of DII had a nonsignificantly higher HT risk than those in the first tertile (OR = 1.75; 95% CI = 0.83–3.65; $P = 0.130$). Regarding DTAC, the subjects in the last tertile of DTAC had a significantly decreased risk of HT (OR = 0.47; 95% CI = 0.23–0.98; $P = 0.043$) compared to those in the first tertile. The DII had a positive correlation with anti-thyroid peroxidase antibody (anti-TPO), thyroglobulin antibodies (TG-Ab) and thyroid-stimulating hormone, while DTAC had a negative correlation with anti-TPO and TG-Ab ($P < 0.050$).

Conclusion The increase in DII is not associated with an increase in the risk of HT, while DTAC can significantly reduce its risk. Having an anti-inflammatory and antioxidative diet can be effective in improving thyroid function. These conclusions should be confirmed in additional prospective studies.

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Keywords Dietary inflammatory index, Dietary total antioxidant capacity, Hashimoto's thyroiditis, Food frequency questionnaire

Introduction

Hashimoto's thyroiditis (HT) is the most common autoimmune disorder of the thyroid gland, causing dysfunction, particularly hypothyroidism, through increased inflammatory infiltration over time [1–3]. Many environmental and genetic factors, such as ethnicity, age, and sex, contribute to the development of HT [1–4]. Data shows that up to 79% of predisposition to the disease is due to genetic factors, with the remaining 21% attributed to environmental and sex hormone influences [5].

The global prevalence of HT in adults is estimated to be 7.5%, with a prevalence of 17.5% in women and 6.0% in men. The prevalence of HT varies by geographic region. In a systematic review and meta-analysis study, Africa had the highest prevalence (14.2%), while Asia had the lowest prevalence (5.8%) [6]. It's incidence is estimated to be 0.8 per 1000 per year in men and 3.5 per 1000 per year in women. The disease affecting women 7–10 times more often than men [5, 7].

According to the findings, when cellular immune tolerance is lost, the production of thyroid autoantibodies increases. These autoantibodies cause the destruction of the thyroid and inflammation, leading to the potential destruction of thyroid cells. This process is triggered by an excessive increase in oxidative stress, beyond what is necessary for producing thyroid hormones. This imbalance prevents the complete neutralization of oxygen free radicals, resulting in mitochondrial dysfunction and ultimately increasing chronic inflammation in the body [8, 9].

Inflammation and oxidative stress are potential causes or aggravating factors of autoimmune thyroid diseases. Antioxidants play a crucial role in reducing oxidative stress and, consequently, inflammation. Therefore, a deficiency or excess of antioxidants may lead to thyroid dysfunction or worsen autoimmune diseases [10]. Research has indicated a negative correlation between two antibodies, thyroglobulin antibodies (Tg-Ab) and anti-thyroid peroxidase antibody (anti-TPO), and the total antioxidant status and oxidative stress index [11]. A meta-analysis revealed lower serum levels of certain antioxidants, such as selenium and zinc, in individuals with hypothyroidism compared to healthy individuals [12]. Another study found that vitamin A, which has antioxidant properties, can directly neutralize free radicals and eliminate lipid peroxides and singlet oxygen, thereby regulating thyroid hormone metabolism and inhibiting thyroid-stimulating hormone (TSH) secretion [13].

In addition to the effects of antioxidants on thyroid function, research has also shown the impact of an anti-inflammatory diet on thyroid diseases. A cross-sectional study demonstrated that decreasing the intake of inflammatory foods, such as animal products, can help reduce oxidative disorders associated with thyroid diseases [14]. Furthermore, a case report study highlighted the benefits of following an anti-inflammatory Paleo diet [15, 16] as a potential solution to alleviate the complications of HT [17].

Due to interaction or synergism, evaluating the consumption of one or more specific antioxidant nutrients alone cannot accurately reflect the antioxidant power of a diet. Additionally, not all dietary antioxidants or their inflammatory effects have been comprehensively investigated in HT disease. Therefore, using tools that can measure the overall impact of all antioxidants and nutrients involved in inflammation may be useful to track the effect of diet on HT. To achieve this concept, it may be possible to use the dietary total antioxidant capacity (DTAC) as a suitable tool to assess the effects of dietary antioxidants and the dietary inflammatory index (DII) to assess the level of dietary inflammation.

DTAC was developed as a quantitative tool to assess the number of dietary antioxidants based on tables obtained from serum samples. It can evaluate total dietary antioxidants without the need for blood samples [18, 19]. The DII, another quantitative tool, has been identified to assess the impact of diet on health outcomes, from blood concentrations of inflammatory cytokines to chronic diseases. It can classify a person's diet from the highest level of inflammation (high DII score) to the lowest level (low DII score) [20]. The DII has been established to evaluate the inflammatory potential of a diet based on inflammatory and anti-inflammatory food compounds that interact with six biological factors, including interleukin-4 (IL-4), IL-1B, IL-6, IL-10, CRP, and tumor necrosis factor-α (TNF-α) [20].

Considering the difference between the dietary patterns of Middle Eastern countries and Western countries, and the limited number of studies on the effect of DII and DTAC on autoimmune thyroid diseases, especially HT, the present study was conducted to investigate the relationship between DII and DTAC with HT in an Iranian adult population. The hypothesis of the study was that DII can increase the risk of HT, while DTAC can decrease it. The specific research aims of the study were to determine DTAC and DII scores in individuals with HT and healthy participants. The study also aimed to evaluate the relationship between DTAC and DII scores and serum levels of thyroid functional indices, including Anti-TPO, Tg-Ab, TSH, and free T4 (FT4).

Materials and methods

Study design and population

The study was a case-control study conducted between September and December 2022 on patients referred to the two reference endocrinology clinics in Tehran, Iran. The sample size was determined based on a previous study [21] and by G power software [22].

A total of 840 subjects were assessed for the study. The age range of the participants was 20–65 years. The age range of 20–65 years was selected because previous studies have indicated that autoimmune thyroid disorders are age-related [2]. The study subjects (cases and controls) were selected by an endocrinologist after a physical examination and necessary tests (TSH, FT4, TG-Ab, and anti-TPO) to diagnose HT or rule out thyroid diseases. The inclusion criteria were as follows: not having infectious diseases, not using drugs or supplements that change the oxidant and antioxidant status of the body, not taking a higher dose of nonsteroidal anti-inflammatory drugs (>300 mg/day), and not having any other autoimmune diseases. Healthy subjects were selected from individuals referred to the clinics for thyroid examination. All inclusion criteria were as confounding factors in the study variables. Because of age-related feature of the HT, the subjects in the two groups were matched based on their age.

Before the start of the study and after fully justifying the objectives and methods of the study, written informed consent was obtained from all participants. The study protocol was approved by the Medical Ethics Committee at Tabriz University of Medical Sciences (Registration No: IR.TBZMED.REC.1401.583). All stages of the research were conducted in accordance with the Helsinki Declaration.

Anthropometric measurements

Weight measurements were taken with minimal clothing and without shoes, using a calibrated Seca scale with an accuracy of 0.1 kg. The subject's height was measured in a standing position, looking forward, without shoes, and with heels against the wall, using a Seca stadiometer with an accuracy of 0.1 cm. Body mass index (BMI) was calculated by dividing weight (kg) by the square of height (m^2). Waist circumference was measured with a body measuring tape with an accuracy of 0.1 cm without imposing any pressure on the body at the narrowest point between the last rib and iliac crest at the end of natural exhalation. Hip circumference was measured using a body measuring tape with an accuracy of 0.1 cm in a condition where the person was in a standing position, without additional covering, and measured parallel to the ground at the head of the femur, which is equivalent to the largest circumference of the hips. The waist to hip ratio (WHR) was then calculated by dividing the waist circumference (cm) by the hip circumference (cm). All anthropometric measurements were conducted by a trained and skilled individual.

Assessment of food intake and calculation of DII and DTAC

To determine the DII and the amount of antioxidants consumed in the diet, the individual's food intake over the past year was assessed using a semiquantitative food frequency questionnaire (FFQ). The FFQ consists of 168 food items that were designed according to the Willett method and were adapted to include Iranian foods. The validity and reliability of this questionnaire have been tested and confirmed [23]. The average size of each food item in the FFQ was explained to every participant in the study. They were then asked to indicate how often they consumed each food item. After noting the frequency of consumption (per day, week, month, or year) for each item in the questionnaire, all the scales were converted to grams using a household scale guide. The energy, macronutrient, and micronutrient content of each food item were analysed using nutritionist IV software.

To calculate the DII, the average global food intake was subtracted from the average daily intake and divided by the global standard deviation. The resulting Z scores were converted into percentiles. The obtained number was multiplied by the inflammatory effect score, and then all the values were added together [20]. Based on scoring, a higher score indicates an inflammatory state, a lower score suggests an anti-inflammatory state, and a zero score indicates a neutral state.

In this study, 33 out of the 45 food parameters listed in the DII table were calculated. These parameters included various vitamins such as A, D, E, B1, B2, B3, B6, B12, C, beta-carotene, caffeine, carbohydrates, total fat, trans fat, saturated fat, protein, cholesterol, polyunsaturated fatty acids (PUFAs), monounsaturated fatty acids (MUFAs), omega 3, omega 6, fiber, energy, magnesium, iron, zinc, selenium, and foods like garlic, onion, tea, pepper, and spices.

The Ferric Reducing Ability of Plasma (FRAP) method was used to calculate DTAC. FRAP values for each food item, were determined using tables from previous studies. The frequency of consumption for each food item per person was converted to grams, then multiplied by the corresponding antioxidant capacity values, and expressed as mmol per 100 g of food (mmol/100 g). The total values were then summed to calculate the dietary total antioxidant capacity for each participant. For Iranian foods which come in various types, such as bread, the overall average consumption was taken into account [24].

Biochemical assessments

Information related to biochemical indices such as TSH, FT4, anti-TPO, and Tg-Ab was collected through tests

requested by an endocrinologist or from the last recorded tests in the individuals' medical files. TSH was measured using a sandwich Enzyme-Linked Immunosorbent Assay (ELISA). Anti-TPO and Tg-Ab were assessed using a sequential ELISA. FT4 levels were determined using an Enzyme Immunoassay (EIA). All tests were performed in a laboratory using laboratory kits from the Monokit brand of Saman Tajhiz Noor, Iran.

Physical activity

To assess the physical activity of participants, the subjects were divided into two groups: those engaging in appropriate physical activity, performing 150–300 min of aerobic activity with moderate intensity, along with muscle strengthening activities of moderate intensity or higher, at least twice a week; and sedentary subjects engaging in physical activity less than the defined amount [25].

Statistical analysis

Means and standard deviations were used for continuous variables, while frequencies and percentages were used for categorical variables. The Kolmogorov–Smirnov test was employed to assess the normality of the data. Multivariate logistic regression was conducted to examine the association between HT risk among tertiles of DII and DTAC in the crude model and two adjusted models. Model 1 was adjusted for age (years), sex (male/female), and energy, while model 2 further adjusted for BMI, physical activity, and waist circumference.

To calculate the P trend for the odds ratio among DII and DTAC tertiles, the index was considered as a rank variable. Statistical analysis of the data was conducted using IBM SPSS Statistics for Windows, Version 26.0 (IBM Corporation, Armonk, NY, USA), with a P value of <0.050 considered significant.

Results

The flow chart of the study is presented in Fig. 1. A total of 230 subjects aged between 20 and 65 took part in the study, and their data were analyzed (115 controls and 115 HTs). The mean age and BMI of the participants were 39.76 ± 9.52 years and 27.23 ± 5.8 kg/m^2, respectively. In Table 1, the baseline characteristics of the study participants are shown. There were no significant differences between the two groups in terms of mean age, weight, smoking status, WHR, or FT4. However, differences in gender, height, BMI, physical activity, waist and hip circumferences, as well as anti-TPO, TSH, Tg-Ab levels, DII and DTAC were found to be significant. The number of subjects engaging in appropriate physical activity was significantly higher in the healthy group compared to the HT group ($P<0.001$). The mean of DII was higher and DTAC was lower in the case group than in the control group ($P<0.001$ and $P=0.047$, respectively).

In Table 2, dietary intakes in the two groups are shown. The total energy intake in the case group was significantly higher than that in the control group ($P<0.040$). The two groups did not have significant differences in protein, carbohydrate, and fat intake. The intake of fiber, vitamin A, vitamin E, vitamin C, vitamin B_1, vitamin B_3, vitamin B_6, vitamin B_9, iron, and magnesium in the control group was significantly higher than that in the HT group. In comparison, the intake of omega 6, vitamin B_{12}, and vitamin D in the group with HT was significantly higher than that in the control group. The consumption of fruits, vegetables, legumes, and refined grains in the control group was significantly higher than that in the HT group. The group with HT had a higher consumption of fish and chichen compared to the control group.

In Table 3, dietary intakes across tertiles of DII and DTAC in the two groups are displayed. As the tertile of DII increased, there was a significant increase in the intake of carbohydrates, fiber, vitamin B_1, vitamin B_3, vitamin B_9, iron, magnesium, and selenium, while energy intake decreased. For DTAC, the intake of 7 parameters, including carbohydrate, vitamin B_3, vitamin B_9, magnesium, zinc, nuts, and red meat was significantly higher in the third tertile of DTAC compared to the first tertile.

The odds ratios of HT in the DII and DTAC tertiles are shown in Table 4. In both the crude and adjusted models, no significant relationship was found between DII and the risk of HT. Similarly, in both the crude and adjusted model 1, no significant association between DTAC and HT risk was found. However, after further adjusting for BMI, waist circumference, and physical activity, the odds of developing HT in the highest DTAC tertile decreased by 53% compared to the lowest tertile (OR=0.47; 95% CI=0.23–0.98; $P<0.043$).

A positive correlation was observed between DII and anti-TPO, Tg-Ab, and TSH. In contrast, a negative correlation was observed between DTAC and anti-TPO and Tg-Ab (Table 5).

Discussion

The results of the current study showed that the mean DTAC was lower in individuals with HT, and that a decrease in DTAC was associated with an increased risk of HT. While the mean DII was higher in HT subjects compared to the control group, there was no statistically significant relationship between DII and HT after adjusting for various confounding variables (Tables 1 and 4).

There are few studies on the relationship between DII and thyroid diseases. Two case-control studies conducted on patients with thyroid cancer showed a positive and significant relationship between thyroid cancer and DII [26, 27]. In the present study, although no correlation was found between DII and the risk of HT disease, a significant and positive correlation was observed between

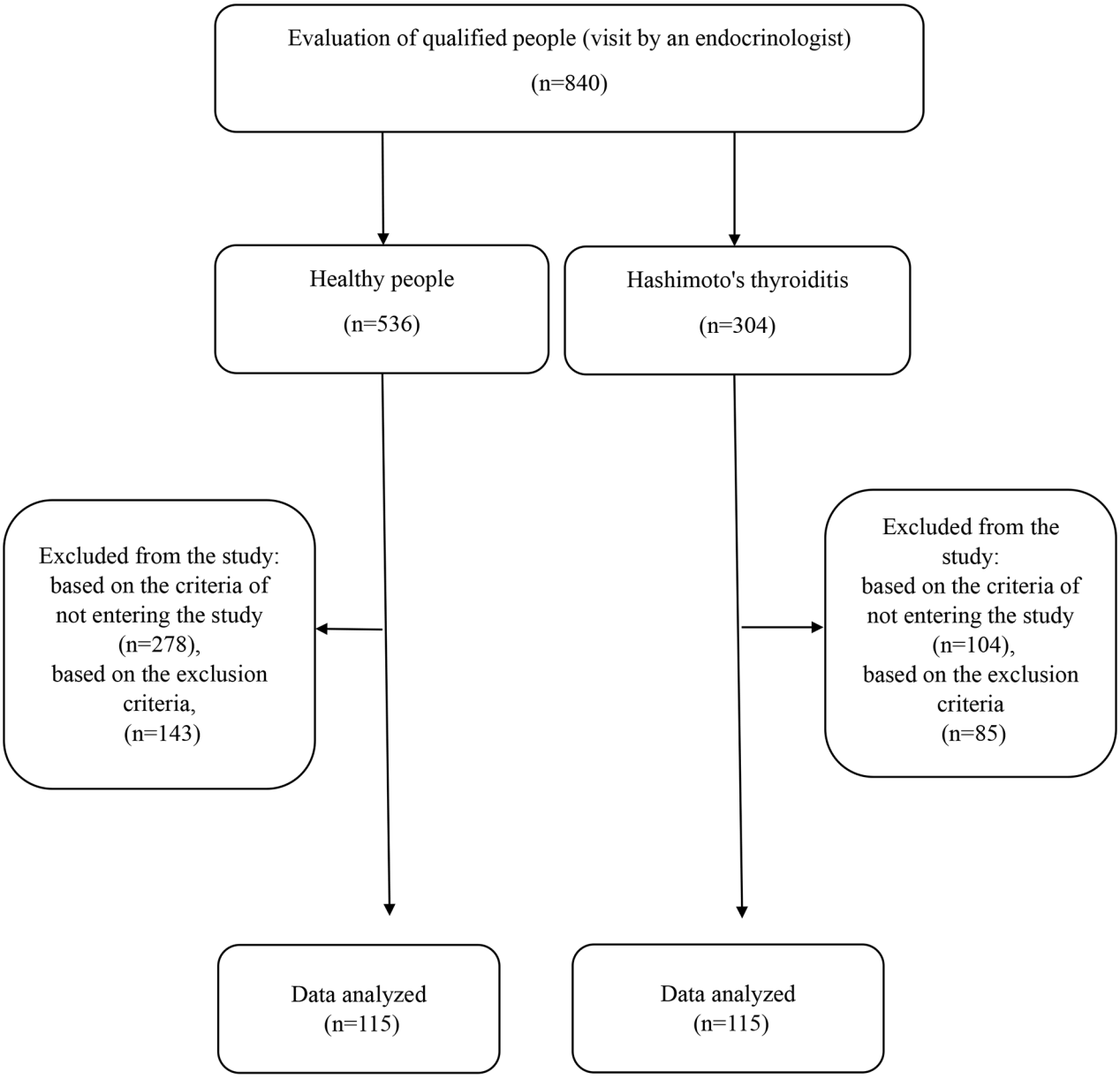

Fig. 1 Flow chart of the study

serum thyroid indices (anti-TPO and Tg-Ab, TSH) and DII. This suggests that DII is significantly related to thyroid function and that following an anti-inflammatory diet can help regulate thyroid function in individuals with HT.

These results were similar to those of a cross-sectional study that demonstrated a significant positive relationship between the DII and total T4, T3, FT4, and TSH in a group with iodine deficiency [21]. Chen et al. in a cross-sectional study using data from the National Health and Nutrition Examination Survey (NHANES: 2007 to 2012) database, showed that DII was positively correlated with thyroid function tests such as total T4, and TSH [28].

The association between different dietary patterns and thyroid function has been assessed in many studies. Alkhatib et al. in a study using data from three cycles of the NHANES (2007–2012), showed that dietary patterns such as fat–processed grains–sugars–meats, and oils–nuts–potatoes–low-fat meats are related to hypothyroidism in the U.S. adult population [29]. Additionally, Matana et al., in a study of 1887 participants with and without elevated plasma TPO-Ab and/or Tg-Ab, found that frequent consumption of animal fats and butter-as pro-inflammatory foods- was associated with positive plasma TPO-Ab and/or Tg-Ab. Conversely, frequent consumption of vegetables, dried fruit, nuts, and muesli-as

Table 1 General and biochemical indices of the study population.[a]

	Case ($n=115$)*	Control ($n=115$)	*P* value**
Age (year)	40.27 ± 10.05	39.4 ± 8.97	0.415
Gender/female	102 (54.5%)	85 (45.5%)	0.004
Weight (kg)	73.77 ± 12.39	72.76 ± 16.12	0.595
Height (m)	1.62 ± 0.09	1.65 ± 0.09	0.034
Body mass index (kg/m^2)	28.03 ± 6.32	26.43 ± 5.13	0.046
Smoking[b]	19 (46.3%)	22(53.7%)	0.365
Physical activity levels (moderate intensity aerobic exercise)[c]	57 (49.6%)	94(81.7%)	0.001
Waist circumference (cm)	85.04 ± 14.73	77.96 ± 15.25	0.001
Hip circumference (cm)	109.34 ± 15.14	98.90 ± 21.13	0.001
Waist to hip ratio	0.77 ± 0.04	0.79 ± 0.07	0.634
Anti-TPO (IU/ml)	397.02 ± 306.25	36.78 ± 70.43	0.001
TSH (mIU/l)	7.51 ± 3.24	1.77 ± 1.18	0.001
FT4 (ng/dl)	0.70 ± 0.43	0.77 ± 0.25	0.173
TG-Ab (IU/ml)	175.62 ± 52.07	67.93 ± 25	0.001
Dietary inflammatory index	0.33 ± 2.02	-0.86 ± 1.82	0.001
Dietary total antioxidant capacity (mmol/d)	20.68 ± 5.86	22.10 ± 4.86	0.047

[a]. Quantitative values are reported as the mean ± standard deviation, qualitative values are reported as n (%)

[b]. Smokers number and percentage of people who use cigarettes

[c]. People who do moderate intensity aerobic exercise 3–4 times a week and between 30–40 min each time

*. Case: People with Hashimoto's thyroidits. Control: Healthy age-matched people

**. Obtained from t-test for continuous variables and chi-square test for categorical variables

Anti-TPO, Antithyroid peroxidase antibody; cm, Centimeter; FT4, Free thyroxin; IU/ml, International units per mililier; kg, Kilogram; m, Meter; mIU/l, Milli-international units per litre; mmol/d, Millimole per day; ng/dl, Nanograms per deciliter; TG-Ab, Thyroglobulin antibodies; TSH, Thyroid stimulating hormone

anti-inflammatory foods- was linked to negative findings of TPO-Ab and/or Tg-Ab [30]. In our study, the consumption of fruits, vegetables, legumes, and refined grains in the control group was significantly higher than that in the HT group. Conversely, the HT group consumed more fish and chicken (Table 2). Similar to our findings, Ruggeri et al. showed that HT subjects consumed more meat, fish, and dairy products than the control group, while the control group had a higher intake of legumes, fruits, vegetables, and nuts than the HT group [14]. In contrast to our results on food intake in the HT and control groups, Kalicanin et al. [31] reported that the consumption of red meat and whole grains was higher in healthy individuals than in HT patients. Their study found that HT patients consumed more processed meat than the control group [31].

Building on the current study and past research, the precise influence of specific dietary patterns on thyroid function has yet to be fully established. However, the role of dietary elements such as vitamins and micronutrients in inflammation and thyroid function is well understood. According to the results of the studies, some foods, such as dried fruits, reduce the expression of the IL-6 gene and inhibit the differentiation of T helper-17 (Th17) cells that intervene in the pathogenesis of autoimmune thyroid disease. On the other hand, foods rich in saturated fatty acids (SFA) and carbohydrates lead to an excessive release of inflammatory cytokines (such as IL-6, IL-17, TNF-α), while decreasing anti-inflammatory cytokines such as IL-10 and IL-4. This disrupts the immune balance and increases oxidative stress by $CD4^+$ helper T cells acting against regulatory T cells. Immune system imbalance and oxidative stress ultimately lead to increased inflammation and, consequently, thyroid disorders [32–35]. Fruits and vegetables, as part of a healthy diet, are rich in fiber, carotene, folate, phytochemicals, various polyphenols, and vitamins B, C, and E. Their antioxidant properties are crucial for reducing inflammation and regulating the immune system in the body [36, 37].

The lack of correlation between DII and HT disease in our study and discrepancies in the results of the effect of dietary patterns on thyroid function could be due to the multifactorial nature of HT. It is important to note that diet is just one of many factors that affect inflammatory processes and thyroid function. Other factors, such as race, climate, age, food composition, and cooking methods, can also impact how different types of food affect thyroid function and thyroid diseases. Additionally, the interplay between environmental factors, and genetic factors can also play a significant role in the development of autoimmune diseases.

Based on the results of the studies, oxidative stress in patients with HT is significantly higher than in healthy individuals, which contributes to increasing inflammation and the oxidative vicious cycle [38, 39]. Reactive oxygen species (ROS) are necessary for the initial stages of thyroid hormone production through iodide oxidation [40, 41]. In other words, ROS play a crucial role in

Table 2 Selected dietary and nutrients intake among case and control groups.[a]

	Case ($n=115$)*	Control ($n=115$)	*P* value**
Total energy intake (kcal/d)	2067.78 ± 427.66	2014.4 ± 449.94	0.040
Protein (g/d)	61.55 ± 13.93	59.01 ± 16.09	0.371
Carbohydrate (g/d)	249.88 ± 45.61	244.48 ± 62.49	0.566
Fat (g/d)	91.26 ± 23.77	88.92 ± 26.89	0.820
Fiber (g/d)	17.99 ± 5.61	21.34 ± 5.97	0.001
Omega-3 (g/d)	1.31 ± 0.62	1.19 ± 0.53	0.224
Omega-6 (g/d)	0.16 ± 0.18	0.072 ± 0.09	0.001
MUFA (g/d)	28.94 ± 9.52	30.64 ± 10.43	0.074
PUFA (g/d)	18.65 ± 8	19.35 ± 8.27	0.245
vaitamin A (RAE/d)	518.47 ± 170.54	584.27 ± 237.75	0.023
vaitamin D (µg/d)	2.91 ± 1.76	2.13 ± 1.37	0.001
vaitamin E (mg/d)	14.2 ± 5.51	16.44 ± 5.86	0.002
vaitamin C (mg/d)	56.1 ± 18.06	87.40 ± 45.16	0.001
Vitamin B1(mg/d)	1.17 ± 0.30	1.29 ± 0.37	0.003
vitamin B2(mg/d)	1.59 ± 0.47	1.55 ± 0.47	0.651
vitamin B3(mg/d)	15.17 ± 3.47	16.12 ± 4.17	0.025
vaitamin B6(mg/d)	1.25 ± 0.32	1.43 ± 0.39	0.001
vitamin B9(µg/d)	379.61 ± 77.65	416 ± 97.66	0.002
vaitamin B12(µg/d)	4.33 ± 1.72	3.77 ± 1.87	0.019
Ca (mg/d)	780.53 ± 278.18	747.831 ± 272.16	0.513
Iron (mg/d)	10.75 ± 2.51	11.92 ± 3.02	0.001
Magnesium (mg/d)	286.99 ± 79.67	305.71 ± 74.16	0.028
Zinc(mg/d)	8.30 ± 2.47	8.38 ± 2.16	0.494
Selenium(µg/d)	87 ± 23.63	89.47 ± 27.55	0.429
Fruit (g/d)	125.98 ± 62.72	236.93 ± 160.87	0.001
Vegtbele (g/d)	218.21 ± 83.35	259.13 ± 96.47	0.001
Nuts (g/d)	9.24 ± 5.74	7.36 ± 7.23	0.433
Legumes (g/d)	8.6 ± 3.9	13.24 ± 8.4	0.001
Red meat (g/d)	7.03 ± 0.39	7.04 ± 3.25	0.549
Fish and chicken (g/d)	32.64 ± 20.1	23.8 ± 19.09	0.004
Whole grains (g/d)	52.48 ± 47.46	58.16 ± 51.57	0.347
Refined grains (g/d)	234.61 ± 91.13	277.55 ± 124.05	0.012

a. All values are reported as the mean ± standard deviation. Energy intake is adjusted for age and gender; other values are adjusted for age, gender, and energy intake

*. Case: People with Hashimoto's thyroidits. Control: Healthy age-matched people

**. Obtained from Analysis of covariance

g/d, Grams per day; kcal/d, Kilocalorie per day; mg/d, Milligrams per day; MUFA, Mono unsaturated fatty acids; PUFA, Poly unsaturated fatty acids; RAE/d, Retinol activity equivalent per day; µg/d, Micrograms per day

maintaining normal thyroid function. To prevent excessive ROS production, thyroid cells release oxidases that catalyze ROS production. Additionally, the repair system activated by ROS-induced damage helps in the processes of autophagy and apoptosis to eliminate damaged cells. However, research indicates that elevated levels of oxidative stress may be a key factor in the development or worsening of autoimmune thyroid symptoms [8, 42].

The mechanisms of increased oxidative stress in HT and other autoimmune thyroid diseases are not well understood. Several studies suggest that excessive production of free radicals and reactive oxygen species, as well as apoptosis and necrosis, are the main causes of thyroid diseases. Over time, these factors can lead to the failure and malfunction of the thyroid gland [43]. The accumulation of ROS may cause oxidative changes in DNA, proteins, and lipids, acting as an oxidant and predisposing a person genetically to disrupt the oxidative balance and create autoimmune processes with destructive effects on the patient's body [44]. Furthermore, inflammation can increase oxidative stress through the peroxidation of thyroid epithelial cells and activation of the NOX enzyme (nicotinamide adenine dinucleotide phosphate (NADPH) oxidase). This creates a vicious cycle, where inflammation disrupts the redox balance, and vice versa [45, 46].

There are two mechanisms to combat oxidative stress in our body: enzymatic and nonenzymatic mechanisms. Both mechanisms are related to the food macro- and micro nutrients. Enzymatic systems involve antioxidants

Table 3 Selected ditary and nutrients intake among tertiles of the dietary inflammatory index and dietary total antioxidant capacity.[a]

DII tertiles					**DTAC tertiles**			
	T1 (-2.60 ± 0.76)	T2 (-0.5 ± 0.45)	T3 (1.82 ± 1.04)	P trend*	T1 (15.099 ± 3.12)	T2 (21.77 ± 1.35)	T3 (27.23 ± 1.67)	P trend*
Total energy intake (kcal/d)	2115.49 ± 504.01	2083.91 ± 376.85	1924.84 ± 407.89	0.024	2005.86 ± 404.35	2045.51 ± 444.23	2071.44 ± 468.28	0.001
Protein (g/d)	58.78 ± 17.81	59.48 ± 13.60	60.94 ± 14.63	0.082	56.23 ± 13.41	62.6 ± 17/09	60.34 ± 14.96	0.140
carbohydrate (g/d)	222.48 ± 55.45	240.12 ± 59.73	237.11 ± 61.75	0.019	217.98 ± 52.42	241.98 ± 57.34	239.69 ± 65.13	0.041
Fat (g/d)	87.96 ± 31.45	91.92 ± 27.22	85.13 ± 20.81	0.806	84.91 ± 23.88	90.76 ± 33.39	89.29 ± 21.87	0.479
Fiber (g/d)	18.34 ± 5.21	20.39 ± 6.20	20.24 ± 6.43	0.013	18.65 ± 5.46	20.46 ± 5.89	19.85 ± 6.59	0.313
Omega-3 (g/d)	1.16 ± 0.60	1.12 ± 0.52	1.02 ± 0.41	0.435	1.15 ± 0.59	1.27 ± 0.61	1.32 ± 0.54	0.108
Omega-6 (g/d)	0.11 ± 0.19	0.11 ± 0.12	0.12 ± 0.12	0.541	0.112 ± 0.119	0.116 ± 0.19	0.12 ± 0.19	0.665
MUFA (g/d)	29.89 ± 11.24	31.14 ± 10.79	28.35 ± 7.5	0.861	29.01 ± 9.06	30.34 ± 11.98	30.01 ± 8.71	0.776
PUFA (g/d)	19.49 ± 9.35	19.58 ± 8.37	17.93 ± 6.39	0.666	18.17 ± 7.61	19.69 ± 10	19.12 ± 6.38	0.636
vitamin A (RAE/d)	527.32 ± 164.98	580.84 ± 260.63	545.64 ± 188.17	0.246	535.424 ± 199.55	569.5 ± 223.99	548.98 ± 204.02	0.950
vitamin D (µg/d)	2.60 ± 1.71	2.31 ± 1.71	2.64 ± 1.43	0.555	2.19 ± 1.46	2.88 ± 1.46	2.48 ± 1.69	0297
vitamin E (mg/d)	15.44 ± 6.02	15.92 ± 6.53	14.60 ± 4.65	0.810	15.04 ± 5.6	15.4 ± 6/02	15.52 ± 5.79	0.824
vitamin C (mg/d)	70.11 ± 39.60	72.13 ± 35.85	72.99 ± 38.11	0.453	66.73 ± 36.37	76.95 ± 34.6	71.51 ± 41.64	0.621
Vitamin B1(mg/d)	1.15 ± 0.30	1.27 ± 0.33	1.26 ± 0.38	0.007	1.19 ± 0.31	1.27 ± 0.37	1.24 ± 0.34	0.507
Vitamin B2 (mg/d)	1.57 ± 0.53	1.51 ± 0.43	1.62 ± 0.45	0.160	1.47 ± 0.45	1.68 ± 0.49	1.55 ± 0.46	0.414
Vitamin B3 (mg/d)	14.98 ± 3.99	16.02 ± 3.46	15.92 ± 4.06	0.024	14.66 ± 3.21	16.28 ± 4.33	15.99 ± 3.79	0.044
vaitamin B6 (mg/d)	1.3 ± 0.41	1.37 ± 0.32	1.36 ± 0.38	0.127	1.27 ± 0.3	1.43 ± 0.47	1.32 ± 0.3	0.451
Vitamin B9 (µg/d)	374.25 ± 82.65	408.90 ± 93.78	410.74 ± 89.43	0.002	363 ± 86.25	413.74 ± 85.11	416.16 ± 89.7	0.001
vaitamin B12 (µg/d)	4.08 ± 2.04	4.06 ± 1.73	4.02 ± 1.68	0.618	3.95 ± 1.67	4.13 ± 1.81	4.07 ± 1.97	0.933
Ca (mg/d)	777.69 ± 320.57	723.41 ± 230.40	791.61 ± 266.20	0.275	694.88 ± 233.57	831.81 ± 286.28	764.95 ± 287.68	0.126
Iron (mg/d)	10.72 ± 2.50	11.77 ± 3	11.51 ± 2.91	0.010	10.91 ± 2.6	11.56 ± 2.78	11.53 ± 3.1	0.304
Magnesium (mg/d)	287.44 ± 81.30	294.54 ± 70.02	306.96 ± 80.08	0.026	267.6 ± 68.15	310.38 ± 73.08	310.71 ± 82.92	0.001
Zinc (mg/d)	8.17 ± 2.46	8.31 ± 2.12	8.53 ± 2.36	0.066	7.75 ± 1.87	8.69 ± 2.31	8.57 ± 2.61	0.045
Selenium (µg/d)	83.04 ± 23.15	90.39 ± 26.32	91.19 ± 26.81	0.008	85.69 ± 25.32	90.57 ± 26.39	88.4 ± 25.29	0.657
Fruit (g/d)	170.16 ± 96.20	189.5 ± 144.40	184.57 ± 154.41	0.534	153.29 ± 86.79	196.82 ± 112.40	193.90 ± 181.03	0.084
Vegtbele (g/d)	229.04 ± 95.44	250.85 ± 91.03	236 ± 90.13	0.473	231.83 ± 92.81	247.05 ± 93.06	237.04 ± 91.47	0.845
Nuts (g/d)	8.70 ± 9.75	7.44 ± 11.25	8.76 ± 15.2	0.849	5.48 ± 5.41	8.48 ± 11.3	10.9 ± 16.76	0.006
Legumes (g/d)	10.81 ± 5.15	12 ± 9.68	10.08 ± 4.80	0.633	10.78 ± 10.13	10.64 ± 4.45	11.47 ± 4.84	0.678
Red meat (g/d)	6.82 ± 3.63	7.43 ± 2.97	6.85 ± 3.32	0.687	6.18 ± 2.85	7.52 ± 2.85	7.39 ± 3.95	0.023
Fish and chicken (g/d)	28.59 ± 22.32	27.71 ± 17.06	28.37 ± 20.83	0.993	65.20 ± 53	56.24 ± 90.35	55.83 ± 27.95	0.121
Whole grains (g/d)	51.43 ± 43.63	57.13 ± 50.60	57.35 ± 54.14	0.325	55.91 ± 53.11	57.47 ± 49.48	53.81 ± 46.58	0.748
Refined grains (g/d)	231.99 ± 97.48	280.81 ± 125.69	252.13 ± 102.09	0.137	239.71 ± 105.62	255.25 ± 109.79	270.07 ± 115.25	0.130

[a]. All values are reported as the mean ± SD. Energy intake is adjusted for age and gender; other values are adjusted for age, gender, and energy intake

*. Obtained from Analysis of covariance

g/d, Grams per day; kcal/d, Kilocalorie per day; mg/d, Milligrams per day; MUFA, Mono unsaturated fatty acids; PUFA, Poly unsaturated fatty acids; RAE/d, Retinol activity equivalent per day; µg/d, Micrograms per day

Table 4 Risk of Hashimoto's thyroiditis in dietary inflammatory index and dietary total antioxidant capacity tertiles

		Reference (T1)	**T2**	**T3**	***P* trend ***
Dietary inflammatory index	Crude model (CI 95%)	1	1.41(0.74–2.67)	1.83 (0.96–3.48)	0.064
	Model 1 (CI 95%)	1	1.37(0.71–2.65)	1.96(1 -3.87)	0.050
	Model 2 (CI 95%)	1	1.20(0.59–2.44)	1.75(0.83–3.65)	0.138
Dietary total antioxidant capacity(mmol/d)	Crude model (CI 95%)	1	0.51(0.27–0.98)	0.54(0.28–1.03)	0.064
	Model 1 (CI 95%)	1	0.54(0.25–1.05)	0.55(0.28–1.07)	0.083
	Model 2 (CI 95%)	1	0.52(0.25–1.07)	0.47(0.23–0.98)	0.043

For Dietary inflammatory index, model 1: adjusted for the effect of age (y), gender (male/female), and energy

Model 2: adjusted more for BMI, waist circumference(cm) and physical activity

For Dietary total antioxidant capacity, model 1: adjusted for the effect of age (y), gender (male/female), and energy

Model 2: adjusted more for body mass index, waist circumference (cm) and physical activity

*P trend with binary regression

Table 5 The correlation between dietary inflammatory index and dietary total antioxidant capacity with laboratory findings

	Dietary inflammatory index		Dietary total antioxidant capacity(mmol/d)	
	r*	P value**	r*	P value**
Anti TPO (IU/ml)	0.20	0.001	-0.15	0.023
TG-Ab (IU/ml)	0.21	0.001	-0.13	0.044
FT4 (ng/dl)	-0.12	0.070	-0.03	0.631
TSH (mIU/l)	0.19	0.004	-0.07	0.283

*. Pearson Correlation

**. Obtained from Analysis of variance

Anti-TPO, Antithyroid peroxidase antibody; FT4, Free thyroxin; IU/ml, International units per mililier; mIU/l, Milli-international units per litre; mmol/d, Millimole per day; ng/dl, Nanograms per deciliter; TG-Ab, Thyroglobulin antibodies; TSH, Thyroid stimulating hormone

such as superoxide dismutase, catalase, glutathione peroxidase, and thioredoxin. Non-enzymatic mechanisms include the action of molecules with strong antioxidant and anti-inflammatory properties, such as catechin, curcumin, ascorbic acid, retinol, carotenoids, tocopherol and other antioxidants [47, 48].

Dietary components play a significant role in the oxidant/antioxidant and inflammatory/anti-inflammatory status of the body [14, 47]. In autoimmune thyroiditis, the total antioxidant capacity of serum is reduced [49], so dietary antioxidants can help the body fight against this condition. In a study on euthyroid women with HT, Ginnakou et al. showed that fruit and vegetable consumption reduces oxidative stress [50].

To date, the overall impact of antioxidants on oxidative stress caused by HT disease is not well defined. It is evident that the body's antioxidant defense systems against the harmful effects of ROS operate at different levels [47, 51]. Antioxidants can neutralize free radicals by accepting or donating electron(s) to eliminate the free radicals. They have various pathways to target ROS and inhibit oxidative stress. They can scaveng reactive oxygen species, prevent and repair DNA damage, prevent lipid peroxidation, influence and modulate immunue system functions, and modulate signal transduction pathways and gene expression [52–54].

Strengths and limitations

Our study had several strengths. One of them was the use of regression models adjusted for potential confounders and the collection of dietary data with a validated FFQ questionnaire. Another strength was the use of the FRAP method to measure the DTAC. The advantage of this method was the inclusion of a wide variety of food items (approximately 3100 items), such as vegetables, spices, drinks, and medicinal plants, compared to other methods [24]. However, it measures antioxidant capacity in vitro, which might not accurately reflect in vivo conditions like as absorption, metabolism, and distribution in tissues, possibly resulting in over or underestimation. Additionally, we did not have FRAP values specifically for Iranian foods. Therefore, we used an international data base, which may not accurately reflect the antioxidant content of Iranian foods due to differences in geographical location and growing conditions. Due to the case-control design of the study, cause-and-effect relationships cannot be defined.

Conclusion

The risk of HT is not related to DII in HT patients, but there is a positive and significant correlation between serum thyroid function indices and DII. DTAC significantly reduces the risk of HT. Consuming an anti-inflammatory and antioxidative diet can be effective in managing autoimmune thyroid diseases like HT. These conclusions should be confirmed in additional clinical and prospective studies with larger sample sizes.

Abbreviations

Anti-TPO	Anti-thyroid peroxidase antibody
BMI	Body mass index
DTAC	Dietary total antioxidant capacity
DII	Dietary inflammatory index
FFQ	Food frequency questionnaire
FRAP	Ferric reducing ability of plasma
FT4	Free thyroxin
HT	Hashimoto's thyroiditis
ROS	Reactive oxygen species
TG-Ab	Thyroglobulin antibodies
TSH	Thyroid-stimulating hormone
WHR	Waist-to-hip ratio

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Author contributions

B.P.G and S.A designed the research; S.A and M.G implemented the research; SA performed the statistical analyses; B.P.G wrote the article and was responsible for the administration and supervision of the research. All authors read and approved the final manuscript.

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Data availability

No datasets were generated or analysed during the current study.

Declarations

Ethics approval and consent to participate

All participants provided written informed consent before participating in the study. The study protocol was approved by the Medical Ethics Committee at Tabriz University of Medical Sciences (Registration No: IR.TBZMED.REC.1401.583). All research stages were conducted in accordance with the Helsinki Declaration.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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