The association between inflammatory potential of diet and newly diagnosed hypothyroidism among Isfahan adults: A case-control study

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Abstract

Background: The effective role of the dietary inflammatory index (DII) on the risk of endocrine disorders has been known. The aim of the current study was to assess the possible association between DII and hypothyroidism.

Methods: This is a case-control study that recruited 360 participants (case: 120/ control: 240). A validated 148-item food frequency questionnaire was used to determine the dietary intake of participants. Hypothyroidism was assessed by thyroid stimulating hormone (TSH), which its Serum concentration was measured by immunoradiometric assay. Energy-adjusted dietary inflammatory index (E-DII) scores were calculated based on 30 food and nutrient components. The association of the inflammatory potential of diet with the risk of developing hypothyroidism was analyzed by logistic regression in different models.

Results: People with hypothyroidism had higher DII scores (more pro-inflammatory diet) compared to the control group (0.72± 1.16 vs. -0.56± 1.29; $p < 0.001$). A higher intake of the pro-inflammatory diet (DII > 0.34) was associated with a higher risk of developing hypothyroidism (Adjusted odds ratio (OR) = 6.90; 95% CI (confidence interval) = 2.66–17.86) compared to the anti-inflammatory diet intake, as referent category (DII < -0.83). This positive association was also observed when DII was considered a continuous variable (Adjusted OR = 1.61; 95% CI = 1.24–2.10).

Conclusion: There is a possible link between the inflammatory potential of diet and the development of hypothyroidism, as subjects with a higher intake of pro-inflammatory diet (higher DII scores) were at higher odds of hypothyroidism.

Introduction

Hypothyroidism is a common endocrine disorder in the world, especially in females and those of advanced age. [1–5]. The prevalence of hypothyroid disease in two-thirds of the world's adults is calculated at 1–2% [6]. Furthermore, the prevalence of subclinical and overt hypothyroidism is computed to be 5.5 and 2% in Iran, respectively [7, 8]. According to previous studies conducted in Isfahan, Iran; an iodine-replete area, hypothyroidism is a prevalent thyroid disorder in Isfahan, which has been reported to be 12.8% in women and 4.7% in men [9, 10]. The annual incidence of overt hypothyroidism was 2.7 per 1000 adults in Isfahan [9, 10]. Hypothyroidism seems to exert adverse effects on various parts of the body, including the cardiovascular, endocrine, gastrointestinal, musculoskeletal, neurological, and psychiatric system; as it has been known to cause secondary hypertension, arterial atherosclerosis and myocardial infarction, thyroid cancer, and depression [11–13].

The prevalence and incidence of hypothyroidism are associated with several factors, including genetic predisposition, geographic areas, ethnicity, and a number of environmental factors such as iodine intake, smoking habits, and alcohol consumption [14–18]. Several studies have observed elevated pro-inflammatory cytokines such as high-sensitivity C-reactive protein (hs-CRP), Interleukin-6 (IL-6), and alpha necrosis tumor factor (TNF-a) in patients with hypothyroidism [19, 20]. Recently, a study by Savas et al, suggested that inflammation plays an important role in the pathogenesis of thyroid disorders, regardless of autoimmune and non-autoimmune thyroid dysfunction [21]. Now, it is well-accepted that the inflammation starts in the early stages of hypothyroidism before levothyroxine replacement therapy [20, 22]. On the other hand, Ruggeri RM, et al study [23], recently revealed the role of nutritional patterns in thyroid autoimmunity by regulating redox balance and consequent oxidative stress-related disorders.

Despite the fact that the exact mechanism is not known, there is growing evidence that declares diet acts as a strong moderator in the regulation of chronic inflammation [24–26]. Some evidence shows that Western (red meat, processed meat, and fat intake) and Mediterranean (fruit, vegetable, and fiber intake) dietary patterns are associated with higher and lower levels of inflammatory cytokines; respectively [25, 26]. While, the Mediterranean diet; as a healthy food pattern, has a protective effect on Hashimoto's thyroiditis [23].

As a result, we suggest that the pro-inflammatory diet; as an environmental risk factor, may regulate the inflammation in the early stages of hypothyroidism and subsequently may play a role in its pathogenesis. The Diet's role in the development of inflammation can be measured using the dietary inflammatory index (DII) [27]. So, recognizing the effective factors of the inflammatory potential of diet will declare a new approach to the preventive role of diet in hypothyroidism and its complications.

Therefore, we hypothesized that the DII might be higher in hypothyroidism compared to the normal condition. Accordingly, the current case-control study was designed to assess the potential association of DII with hypothyroidism in a sample of adults.

Materials and methods

Study design and participants

The present study is an unmatched case-control study conducted at the Isfahan Endocrine and Metabolism Research Center (IEMRC), Isfahan, Iran, between April and December 2019. This study was approved by the Ethics Committee of Isfahan University of Medical Sciences (ID: IR.MUI.MED.REC.1398.646). All subjects provided written and informed consent and were reassured that their information would be kept confidential. All methods were carried out in accordance with the relevant guidelines and regulations.

Participants were recruited from patients referred to IEMRC. The case group included 120 patients newly diagnosed with hypothyroidism. At the same time, 240 healthy subjects were selected randomly by a physician from eligible people who presented to the clinic of IEMRC without any history of thyroid medications or disease (two control subjects per case subject). Inclusion criteria for all participants at recruitment were as follows: age ≥ 20 years, hypothyroidism for the case group, and normal blood TSH levels for the control group. Hypothyroidism was defined as high TSH (TSH greater than 5.5 µUI/mL) and FT4 level within or below the reference range (0.89 to 1.76 ng/dl). Normal TSH was defined as TSH between 0·60 and 5.5 µUI/mL. The exclusion criteria were included for both groups: pregnancy, autoimmune diseases, people taking blood sugar-lowering drugs, and people with a history of stroke, cancer, liver disorders, kidney disease or other severe chronic diseases, thyroid nodules disease, goitre, and hyperthyroidism. This study was approved by the ethics committee of Isfahan University of Medical Sciences, Isfahan, Iran. By the protocol required acceptable range [28] participants were excluded from the final analysis if they had unexplained energy intake (< 800 kcal/d or > 4200 kcal/d*).*

Data gathering

A socio-demographic questionnaire including personal information (age, sex, marital status, education level, physical activity, and smoking), and other information such as prior nutritional treatment, use of medications that may influence body inflammation status of subjects (e.g. g, anti-inflammatory drugs, hormone therapy, weight loss drugs, and others) and consumption of supplements (vitamins, minerals) was used to acquire basic data. The weight and height of subjects were determined with an accuracy of 0.1 kg and 0.5 cm; respectively. Blood pressure was measured using a Mercury sphygmomanometer while subjects were in a seated position two times with at least a 30-second interval between measurements. The mean of two measurements was recorded as the subject's blood pressure. The results of anti-thyroperoxidase antibodies (TPOAb) were provided from individual health cases that differentiate types of hypothyroidism (autoimmune or non-autoimmune).

Dietary Assessment and Calculation of the DII

In the present study, the whole diet (the average consumption of whole grains, fruits, vegetables, aromatic herbals, oils, nuts, cocoa, and tea) of participants was assessed using a validated and reliable 148-item semi-quantitative food frequency questionnaire (SQ-FFQ) that included a list of foods (with standard serving sizes) commonly consumed by Iranians which was designed and developed to measure the intake of common food groups, energy, and nutrients over the previous year [29]. The FFQ was interviewer-administered which a trained dietitian asked participants to designate their intake frequency for each food item, consumed during the past year on a daily (e.g., bread), weekly (e.g., rice or meat), or monthly (e.g., fish) basis. The portion sizes of consumed foods were reported in household measures and then converted to grams. For all food items in the FFQ, the frequency of consumption is converted to daily intake. As the Iranian food composition table (FCT) is incomplete (limited to only raw materials and a few nutrients), each food and beverage was analyzed for energy and nutrient intake using the US Department of Agriculture's (USDA) FCT. For mixed dishes, nutrients were calculated according to their ingredients. The energy and macronutrients of bread and fruits are almost similar to alternative food items in the USDA FCT, with a correlation > 0.9. We used the Iranian FCT only for food items like '*kashk*' which was not listed in the USDA FCT (the manual for household measures, cooking yield factors, and edible portions of food) [30].

The DII is a tool to quantify the inflammatory potential of a diet. The design and development of DII have been described, elsewhere [31]. The DII was based on data reported in 1943 research articles examining the relationship between various dietary constituents (referred to as food parameters) and inflammation to develop an article score for each food parameter. Dietary parameters were scored positive (+ 1) if the effect was pro-inflammatory, negative (-1) if the effect was anti-inflammatory, or zero if these parameters produced no significant change in inflammatory biomarkers. Theoretically, the DII can range from the most anti-inflammatory score of (-8.87) to the most pro-inflammatory score of (7.98). To calculate the DII score, we used the method previously reported by Shivappa et al [32], which these steps were briefly done in this study in order. Firstly, it was obtained a robust estimate of the mean and standard deviation for each parameter; in the second step, computed z-score which expresses an individual's exposure relative to the "standard global mean"; and then accounted for the centered percentile score (To minimize the effect of "right skewing"). Thereafter this score for each food parameter for each individual was then multiplied by the respective food parameter effect score, which is derived from the literature review, in order to obtain a food parameter-specific DII score for an individual; finally summed the food parameter-specific DII scores to create the overall DII score for every participant in the study. In this study, 24 of the 45 food parameters were available from the FFQ to calculate DII. These included pro-inflammatory components (energy, carbohydrate, protein, fat, saturated fat, cholesterol, Trans fat, iron) and anti-inflammatory components (fiber, mono-unsaturated fat, poly-unsaturated fat, niacin, thiamin, riboflavin, magnesium, zinc, selenium, vitamin A, vitamin C, vitamin E, vitamin D, folic acid, cobalamin, beta-carotene). Energy adjustment was performed using the residual method [33]. Due to the lack of a defined cut-off point for DII, low power, and sample size of the study, DII was categorized according to tertile values.

Statistical Analysis

Statistical analysis was performed with SPSS version 25 (SPSS, Inc., Chicago, IL, USA). Continuous and categorical variables were reported as mean ± Standard Deviation (SD) and frequency (percentage). The normality of continuous data was evaluated by using the Smirnov-Kolmogorov test and Q-Q plot. Non-normality positively skewed data were subjected to logarithmic transformation. Continuous and categorical basic variables were compared between study groups using independent samples t-test and chi-squared test, respectively.

Binary Logistic regression was used to evaluate the association of DII with the risk of hypothyroidism in different models. Firstly, the DII values were categorized into tertiles, the lowest tertile was considered as the reference category, and the risk of being affected by hypothyroidism was compared between people who were in the second and third tertile compared with those who were in the first tertile and odds ratio (OR) with 95% confidence interval (CI) was computed in the framework of the logistic regression model. In addition, DII was also treated as a continuous variable and its association with the risk of hypothyroidism was reflected in the OR with 95% CI. P-value < 0.05 was considered a statistically significant level in main statistical analyses.

Results

At baseline, 360 subjects were enrolled in the study. Twenty-three participants with < 800 or ≥ 4200 Kcal dietary intake for DII assessment were excluded from the study. Overall, 337 participants were included in the study. The average age of the participants was 37.43 ± 11.63 (mean ± SD) years. The characteristics of 102 newly diagnosed hypothyroidism (72% female, 28% male) were compared to 235 healthy subjects (54.5% female, 45.5% male) (Table 1). The case group was significantly older than the control group (41.4 ± 12.4 vs. 35.7 ± 1.9, $p < 0.001$). Gender ($P = 0.06$) and BMI ($P = 0.071$) were marginally different between groups. The DII scores in this study ranged from − 3.28 (most anti-inflammatory score) to + 3.37 (most pro-inflammatory score). Educational levels and marital status were significantly distributed between the two groups ($P < 0.001$). Also, the mean value of systolic blood pressure DII was significantly higher in hypothyroidism than in the control group ($P < 0.001$). The overall diet was significantly more pro-inflammatory in hypothyroidism compared with healthy subjects (Table 1).

Table 1
General characteristics of the study subjects at baseline

Characteristics		**Group**		**P-value** [a]
		Hypothyroidism	**control**	
No. of participants		102	235	
Age (years)		41.42 ± 12.35	35.69 ± 10.89	< 0.0001
Gender	Female/ Male	74 / 28	146 / 89	0.065
Marital Status	Single/ Married	14/ 88	79/ 156	< 0.0001
Educational level	Under diploma	38 (37.30)	47 (20.00)	< 0.0001
	Diploma	32 (31.40)	60 (25.50)	
	Collegiate	32 (31.40)	128 (54.50)	
Smoking (Yes/No)		21/81	62/173	0.261
Physical activity	less or never	20 (19.60)	44 (18.72)	0.672
	Moderate	76 (74.50)	178 (75.74)	
	High	6 (5.88)	13 (5.53)	
Drug use (Yes/No)		26/76	58/177	0.133
Supplement use (Yes/No)		42/60	110/125	0.542
BMI (kg/m^2)		25.87 ± 4.48 [b]	26.90 ± 4.92	0.071
SBP (mmHg)		118.18 ± 13.92	114.63 ± 56.30	< 0.0001
DBP (mmHg)		76.81 ± 8.85	87.17 ± 7.64	0.155

[a] Independent samples t Test for continuous variables and chi-squares test for categorical variables.

[b] Values are expressed as number (%) or mean ± SD. Abbreviations: Body mass index (BMI), Systolic blood pressure (SBP), Diastolic blood pressure (DBP)

Table 2 shows the mean intake of different dietary components in both case and control groups, in which the majority of nutrients were differently distributed between the two groups. While the intake of energy, carbohydrates, cholesterol, total, and different types of fat was higher in the case group, participants in the control group consumed more protein, magnesium, selenium, and zink. No significant difference was observed between groups in terms of other nutrients. In addition, People in the highest tertile of DII consumed more energy and fat made more proportion of their energy intake, while they intake less fiber and carbohydrates, and protein compromised less percentage of energy intake in comparison with people in the lowest tertile. Moreover, a higher following of a diet with a higher score of DII was related to a lower intake of fruits, vegetables, whole grains, and red meat and a higher intake of legumes and soy (Table 3).

Table 2
The mean values of different dietary intakes in both groups [a]

	Group		P-value [b]
	Hypothyroidism	Control	
DII	0.72 ± 1.16	− 0.56 ± 1.29	< 0.0001
Energy (Kcal/ day)	3246.10 ± 526.40	2659.00 ± 765.80	< 0.0001
Carbohydrate (g/day)	378.90 ± 82.90	375.10 ± 109.40	0.756
Protein (g/day)	69.38 ± 22.42	92.17 ± 26.14	< 0.0001
Cholesterol (g/day)	308.70 ± 300.00	257.10 ± 135.80	0.030
Total fat (g/day)	134.88 ± 35.01	104.90 ± 31.39	< 0.0001
Saturated fat (g/day)	30.01 ± 10.30	26.90 ± 10.30	< 0.0001
Iron (mg/day)	20.45 ± 9.82	19.72 ± 6.06	0.489
Fiber (g/day)	41.20 ± 20.92	40.00 ± 10.67	0.486
PUFA (g/day)	46.50 ± 18.70	21.70 ± 16.80	< 0.0001
MUFA (g/day)	60.80 ± 21.50	33.20 ± 19.10	< 0.0001
Magnesium (mg/day)	363.39 ± 127.62	504.86 ± 118.46	< 0.0001
Selenium (mg/day)	108.13 ± 59.01	153.37 ± 49.70	< 0.0001
Zinc (mg/day)	9.71 ± 3.68	14.12 ± 3.53	< 0.0001
β.caroten	3560.70 ± 3116.40	3656.60 ± 2664.10	0.774
Vitamins c (mg/day)	2219.85 ± 1529.10	2042.89 ± 391.08	0.252

[a] Values are expressed as mean ± SD.

[b] Independent samples t Test for continuous variables

[c] Anti- Inflammatory vitamins (B1,2,3, 6, 9,12 A, C, D, E).

Abbreviations: Dietary inflammatory index (DII), Polyunsaturated fat (PUFA), Monounsaturated fat (MUFA).

Table 3

dietary intakes of participants across tertiles of dietary inflammatory index [a]

Variables	Tertiles of dietary inflammatory index			P value
	1 (< -0.831)	2 (-0.83 to 0.34)	3 (> 0.34)	
Nutrients a				
Energy (kcal/d)	2921.36 ± 664.96	2662.37 ± 737.44	2925.61 ± 819.27	0.013
Carbohydrates (% of total daily energy)	59.39 ± 6.33	55.49 ± 6.85	46.84 ± 9.28	< 0.0001
Fat (% of total daily energy)	28.68 ± 6.50	32.56 ± 7.45	43.95 ± 11.35	< 0.0001
Protein (% of total daily energy)	14.82 ± 2.62	13.26 ± 3.55	8.99 ± 3.33	< 0.0001
Fiber (g/d)	48.60 ± 13.62	40.22 ± 16.20	32.88 ± 15.91	< 0.0001
Food groups				
Fruit (g/d)	403.49 ± 198.36	251.74 ± 132.20	230.68 ± 101.75	< 0.0001
Vegetables (g/d)	333.76 ± 177.55	195.70 ± 100.91	196.15 ± 120.47	< 0.0001
Refined grains (g/d)	295.15 ± 164.09	283.23 ± 130.12	246.48 ± 126.68	0.260
Whole grains (g/d)	275.19 ± 159.03	189.13 ± 113.31	111.05 ± 103.19	< 0.0001
White meat (g/d)	51.66 ± 43.46	51.26 ± 46.42	44.99 ± 39.52	0.454
Red meat (g/d)	31.43 ± 21.60	27.95 ± 24.13	17.42 ± 16.02	0.004
Nuts (g/d)	10.42 ± 10.42	9.50 ± 14.23	7.39 ± 9.10	0.470
legumes and soy(g/d)	81.81 ± 59.47	101.71 ± 104.32	130.49 ± 115.81	0.022
Vegetable oil (g/d)	8.43 ± 4.52	8.01 ± 5.53	6.56 ± 4.45	0.055
solid oil (g/d)	7.99 ± 8.77	9.08 ± 10.53	7.93 ± 11.11	0.460

[a] Analysis of covariance (ANCOVA) and energy was considered as the absolute amount per day. Nutrients except energy were adjusted for age and total energy intake (kcal), while energy only for age.

The association of DII with the risk of hypothyroidism was evaluated in both types, i.e., continuous and categorical in logistic regression analysis. Considering DII as a continuous variable, there was a positive association between higher score of DII and the risk of hypothyroidism in crude (OR = 2.18, 95% CI:1.76–2.70; P < 0.001) and after adjustment for potential confounding variables, including age, sex, BMI, blood pressure, smoking, and history of diseases (Adjusted OR (AOR) = 1.61, 95% CI: 1.24–2.10; P < 0.001). In the categorical analysis of DII, participants who were at the highest DII tertile had a higher risk of developing hypothyroidism in the crude model (OR = 13.42, 95% CI: 6.18–29.15). This association remained significant in the fully adjusted model (OR = 6.90, 95% CI: 2.66–17.86) (Table 4).

Table 4

Associations between the dietary inflammatory index (DII) and hypothyroidism †

Dietary Inflammatory Index						
	Tertile 1 (< -0.831)	Tertile 2 (-0.83 to 0.34)	Tertile 3 (> 0.34)	$P_{-\text{ value}}$	Continuous	$P\text{-}_{\text{value}}$
No. Cases/Controls	9/103	32/81	61/51			
Model 1	1.0 (ref.)	4.58 (2.07–10.14)	13.42 (6.18–29.15)	< 0.0001	2.18 (1.76–2.70)	< 0.0001
Model 2	1.0 (ref.)	4.60 (2.04–10.35)	10.66 (4.79–23.69)	< 0.0001	2.01 (1.60–2.52)	< 0.0001
Model 3	1.0 (ref.)	4.52 (1.71–11.99)	6.90 (2.66–17.86)	< 0.0001	1.61 (1.24–2.10)	< 0.0001
Data are presented as odds ratio (95% confidence interval) Abbreviations; DII, dietary inflammatory index; ref, reference						
Model 1: Crude						
Model 2: Adjusted for age, sex, BMI,						
Model3: Adjusted for age, sex, BMI, blood pressure, smoking and history of diseases						

Discussion

This current case-control study; as a first study, evaluated the association between dietary inflammatory index and hypothyroidism. Our findings showed that newly diagnosed hypothyroidism subjects had significantly higher pro-inflammatory diet scores in comparison with the control group.

These results approved our hypothesis that there is an association between a more pro-inflammatory diet (higher DII score) and an increased risk of hypothyroidism. Although there is no previous evidence that investigated the relationship between the DII and the risk of hypothyroidism, nevertheless our finding is in line with other studies [34–36], that examined the effect of the pro-inflammatory potential of diet on the development of other metabolic diseases. As the study by Paquet et al, has revealed that there is a significant association between higher DII scores; as reflected in the more pro-inflammatory diet, and a higher risk of differentiated thyroid carcinoma [34].

The DII has been previously shown to be associated with various inflammatory markers including hs-CRP, IL-6, TNF-a, and homocysteine [31, 37, 38]. The pro-inflammatory diet, as indicated by higher DII scores, is associated with higher systemic levels of inflammatory cytokines, while the anti-inflammatory diet, as indicated by lower DII scores, is accompanied by lower levels of these factors. The dietary inflammation index can predict the levels of various inflammatory markers [24, 31, 37]. Our findings showed a significant positive association between a higher pro-inflammatory score of DII and hypothyroidism, which was representative of the probable presence of systemic inflammation. This finding is in line with prior literature that reported elevated levels of CRP, TNF-a, and IL-6 in the early stage of hypothyroidism [19, 20, 39–43]. Recently, the possible role of this systematic inflammation in the pathogenesis of hypothyroidism has been proposed [21]. To this evidence, the pro-inflammatory diet can be proposed as a reason for emerging chronic inflammation in the pathogenesis of hypothyroidism.

Aging is also closely linked with raised systemic inflammatory markers such as CRP, IL-6, and TNF-α [44, 45]. Previous studies have shown that a higher pro-inflammatory diet (i.e. higher DII score) is associated with old age [46, 47]. Aging is known as a contributing factor to diet-induced inflammation [44, 45, 48]. The exact mechanism of this contribution is still under investigation, but there is convincing evidence that shows dietary changes accompanied by aging may promote inflammation [45, 49]. Therefore, older people’s pro-inflammatory diet might be a possible reason for the higher risk of hypothyroidism in advanced age.

Previous studies have indicated that elevated pro-inflammatory cytokines such as CRP, TNF-a, and IL-6 increase the risk of developing cardiovascular disease (CVD) in hypothyroidism [40, 50]. In other words, chronic inflammation has been known as a cause of high CVD and its mortality among hypothyroidism. The significant effect of a pro-inflammatory diet and the resultant inflammation has been seen in a higher risk of developing cardiovascular disease [51, 52]. These findings are consistent with the proposed role of diet in the occurrence of inflammation, which plays a role in hypothyroidism complications.

Further studies with a large sample size are needed to prove the relationship between DII and hypothyroidism. Future research can also study the effects of changing the inflammatory potential of diet on chronic inflammation, the risk of hypothyroidism, and its complications.

The strengths of this study could be mentioned in this case. Firstly, the enrollment of subjects with newly diagnosed hypothyroidism, as a study group, and conducted an assessment of dietary intake before they started levothyroxine treatment, which reduces the recall bias. Secondly, limited measurement errors by considering the various confounding factors such as intake of anti-inflammatory drugs and hormone replacement therapy that may modify the inflammation status in subjects. There was some limitation in this study, such as information bias due to the nature of the study which was a case-control study. Also, of 45 food parameters to calculate DII 21 items remained non-available. Another limitation could be that the type of hypothyroidism (autoimmune or non-autoimmune) was not determined, so further studies are required to identify the association of dietary inflammatory index across different types of hypothyroidism.

Conclusion

Subjects who consumed a more pro-inflammatory diet were at increased risk of hypothyroidism compared to those who consumed a more anti-inflammatory diet. This finding shows the possible role of the inflammatory potential of diet assessed by DII in the risk of hypothyroidism and its complications. Therefore, we suggest that changing dietary habits to a less pro-inflammatory pattern may be a good strategy for reducing the risk of hypothyroidism and its complications. This change in dietary habits could be taking more anti-inflammatory dietary factors (e.g. foods containing high concentrations of omega-3 fatty acids and plant-based) or less pro-inflammatory factors (foods rich in saturated fat or Trans fatty acids).

Abbreviations

BMI: Body mass index; CI: Confidence intervals; DII: Dietary inflammatory index; FFQ: Food frequency questionnaire; hs-CRP: high-sensitivity C-reactive protein; IEMRC: Isfahan Endocrine and Metabolism Research Center; IL-6: Interleukin 6; ORs: Odds ratios; SQFFQ: Semi-quantitative food frequency questionnaire; TNF-a: Tumor necrosis factor-alpha; TSH: Thyroid stimulate hormone.

Declarations

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Authors’ contributions

MS and AA designed the project's idea, and supervised the study, and the manuscript. ST and MS were involved in patients’ recruitment and clinical assessments. AF, BZ, and FF were involved in the data acquisition and analysis of the data. MA, BZ, MS, and MA wrote the paper. All authors approved the final manuscript.

Competing interests

The authors declare that they have no conflict of interest.

Consent publishing

Not applicable

Availability of data and materials

The datasets used and analyzed during the current study are available by contacting the corresponding author upon reasonable request.

Ethics approval and consent to participants

This study was approved by the Ethics Committee of Isfahan University of Medical Sciences (ID: IR.MUI.MED.REC.1398.646). All subjects provided written and informed consent and were reassured that their information would be kept confidential.

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