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Comparison of Knowledge and Behavior of High-Iodine Food Consumption Among Patients With Graves' Disease and Healthy Adults in Iodine-Sufficient Area

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Background: Iodine is a required dietary supplement to solve iodine deficiencies; however, many food products may have an excessive amount of iodine. This excess may be causing unexpected iodine-induced Graves' disease.

Objective: To investigate the impact of high-iodine diets on adults diagnosed with Graves' disease and healthy adults.

Methods: A case-control study was performed among 200 patients with Graves' disease and 200 healthy participants in Chon Buri, Thailand, using cluster random sampling from November 2019 to March 2020. Data on iodine-rich food consumption were collected using a questionnaire. Data were analyzed using a chi-square test and multiple logistic regression.

Results: Patients with Graves' disease significantly less knew of high-iodine food than the control group ($P < .05$), particularly in eggs, processed foods, ready-to-eat food, cod liver oil, and high-iodine vegetables. A frequent consumption of high-iodine food items, including fermented food (OR, 2.20; 95% CI, 1.20 - 4.02), ready-to-eat food (OR, 2.08; 95% CI, 1.02 - 4.22), high-iodine vegetables (OR, 1.72; 95% CI, 1.13 - 2.61), bakery (OR, 1.99; 95% CI, 1.10 - 3.64), iodine-supplemented sauces (OR, 1.79; 95% CI, 1.18 - 2.72), and iodized salts (OR, 1.62; 95% CI, 1.02 - 2.56) was higher in Graves' disease patients.

Conclusions: In iodine sufficiency area, patients with Graves' disease less knew and more frequently consumed high-iodine foods than healthy participants.

Keywords: High-iodine food, Graves' disease, Iodine-sufficient area

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Introduction

In the past, various populations faced deficiency in dietary iodine, which is an essential trace element required for thyroid hormones synthesis. Iodine was added as a supplement to various foods. However, modern diets in developed areas often include an overabundance of iodine consumptions. We theorized that this is due not only to the prevalence of dietary iodine, but lack of consumer knowledge of high-iodine food products. Iodine supplementation in salt iodization plays a crucial role in preventing iodine deficiency.[1] However, it could be associated with iodine overload, and increased risk of iodine-induced hyperthyroidism, including Graves' disease.

The effects of iodine on the thyroid gland are complex and incompletely understood.[2] Previous studies showed that thyroid dysfunction occurred not only due to thyroid autoimmunity or genetic factors, but also due to poor health habits, such as smoking, experiencing frequently high stress levels, and high-iodine consumption.[3] Excess iodine intake is considered to be associated with hyperthyroidism[4] and hypothyroidism[5] in some vulnerable individuals.

The incidence of Graves' disease, an autoimmune disorder characterized by hyperthyroidism, has become an increasingly public health problem in Thailand, especially in the working-age population. Among women, the incidence of hyperthyroid disease has been predicted to be 0.1 to 1 per 1000 women per year. The major complications of this disease are heart failure, atrial fibrillation and stroke, and may affect the quality of working life.[6]

In 2013, the Iodine Global Network (IGN) and the World Health Organization[7] reported Thailand to be an iodine-sufficient country. The Eastern Economic Corridor (EEC) of Thailand consists of 3 coastal provinces including Chon Buri, Chachoengsao, and Rayong, and is a developed economic area. Even, there was no report about the iodine status of non-pregnant adults in this region, the iodine status in the pregnant group during 5-year observation (2013 - 2017) showed sufficient level (median urinary iodine concentration [UIC] > 150 µg/L).[8] Moreover, the working population living in this region may exposed to excessive iodine intake due to their urban lifestyles. However, there is no study about this interest issue in Thailand. Monitoring and surveillance initiatives should emphasize the consideration of all high-iodine sources in iodine sufficiency areas.

High-iodine levels were commonly found in seafood, kelp or seaweed, egg yolk, water, dairy products, and iodized salt.[9] Recently, dietary iodine is rising substantially in many food products, such as fermented food, frozen food, and other added iodine diets. It may be causing unexpected incidences of iodine-induced hyperthyroidism, known as "Jod-Basedow phenomenon", which are side effect of iodine supplementation.[10] Some studies have found that excess iodine intake was caused by high-iodine content in drinking water,[11] in salt iodization,[12] and in seaweed.[13] Although, some countries reported excess iodine overload increase in the incidence of Graves' disease,[14-16] there has been no report, based on large case-control study, linking dietary iodine consumption and knowledge about high-iodine food to Graves' hyperthyroidism. In addition, Thailand was no report of iodine pool status in working-age group in the iodine-sufficient area. It could be difficult to create a specific health promotion program to prevent the iodine-induced Graves' disease.

Since 90% of the ingested iodine is excreted in urine, the UIC is considered a sensitive marker of the current iodine intake.[17] According to the World Health Organization, UIC is recommended as an indicator of iodine intake because it is well-accepted, cost-efficient and easily obtainable.[18] This study aims to investigate the knowledge and behavior of high-iodine food consumption, and then evaluate the iodine status as a secondary outcome, among patients with Graves' disease in iodine sufficiency areas.

Methods

Participants

This study included 400 participants aged 18 to 60 years. Of this population, 200 participants had been diagnosed with Graves' disease, and 200 participants had not the disease. All 200 Graves' disease patients visited the thyroid clinics at 2 hospitals in Chon Buri province during the study period. The diagnosis of Graves' disease was made on the presence of Graves' eye disease and/or dermopathy, a symmetrically enlarged thyroid gland, and a lower than normal level of thyroid-stimulating hormone (TSH) and higher levels of thyroid hormones. The control group comprised 200 healthy volunteers, who had same age and sex distribution as the Graves' group. We invited volunteers using the public announcement and randomly selected them from the same public community. The sample size was calculated using G*Power, alpha error probability was 0.05, power was 0.8, and the 2-sided was used.

Ethics

This study was approved by the National Ethics Committee from Burapha University. The number of approval decision was IRB 022/2562 on November 1, 2019. Additionally, the participants signed a written informed consent prior to enrolment in the study.

Study Design

This study was a case and control design between November 2019 and March 2020. Cross-sectional data were collected by the researcher team using a questionnaire, which consists of high-iodine food knowledge and food frequency. This study measured the iodine status in all participants using spot UIC.

Knowledge and Behavior of High-Iodine Food

The high-iodine food knowledge questionnaire was constructed by information from Thailand's Department of Health, Ministry of Public Health. Nine food items were listed, and participants were asked whether they knew if each had iodine supplementation. The list consisted of 4 local items with naturally high in iodine and 5 items supplemented with iodine. Total scores were separated in 3 levels according to Bloom theory; low level (less than 5 scores), moderate level (5 - 7 scores), and high level (8 - 9 scores).[19]

All food items classified into XIV groups; Group I eggs, Group II fresh and dried seafood, Group III cow milk, soy milk, and dairy products, Group IV processed food, Group V ready-to-eat or convenience food, Group VI cod liver oil, Group VII iodine-supplemented food, Group VIII high-iodine fruits, Group IX high-iodine vegetables, Group X bakery, Group XI snacks, Group XII fermented food, Group XIII iodine-supplemented sauces, and Group XIV iodized salts. We defined frequent behaviors of high-iodine food consumption when the total score of the food frequency questionnaire higher than 75 percentiles.

Iodine Status Analysis

Urinary iodine concentration/creatinine ratio (UI/Cr) measurement was used to compare dietary behavior between case and control groups and was expressed in microgram per gram (μg/g). However, UI/Cr was suggested for a measure of iodine intake in people with abnormal thyroid function, which generally affects renal clearance and storage of iodine.[20] Spot urine samples of 20 mL were obtained from each participant. Iodine and creatinine concentration was measured at a laboratory in Health Promotion Center 6 Chon Buri, based on the Sandell-Kolthoff reaction method, which is widely used to determine urinary iodine.[21]

Statistical Analysis

All measurements were performed using SPSS version 16 (SPSS for Windows, Version 16.0. Chicago, SPSS Inc; 2007). In the comparisons between Graves' patient and normal groups, normally distributed variables used an independent *t* test, and a chi-square test was used for category variables. Spot UI/Cr concentration between case and control groups were determined using the Mann-Whitney U test. Overall and each item of high-iodine food knowledge and high-iodine food consumption between case and control were computed the odds ratio (OR) and 95% confidence intervals (CI) by using logistic regression. Modifiable confounding variables were adjusted, including occupations, shift work, workload, and smoking, for OR analysis and $P < .05$ was considered statistically significant.

Results

Participants in case and control groups were characterized, mean (standard deviation, SD) age was 37.9 (12.2) years and females represented about 80.0% of both groups. Patients with Graves' disease had shift work, heavy workload or sleepless (less than 4 hours per day), smoking, and family history with hyperthyroidism significantly higher proportion than healthy participants ($P < .05$). However, healthy participants were more stressed, and they belonged to a significantly different range of jobs compared with patients with Graves' disease ($P < .001$) (Table 1).

Graves' disease patients achieved lower scores on the knowledge questionnaire than healthy participants (mean [SD], 4.57 [2.13]) scores vs 5.39 [2.34] scores, $P < .05$). After adjusted confounding variables, this study found that low level of this knowledge related to Graves' disease about 1.92 times (95% CI, 1.07 - 3.47), particularly in the items of eggs (OR, 1.58; 95% CI, 1.04 - 2.40), processed foods (OR, 1.74; 95% CI, 1.16 - 2.62), ready-to-eat food (OR, 1.75; 95% CI, 1.10 - 2.80), cod liver oil (OR, 1.53; 95% CI, 1.01 - 2.30), and high-iodine vegetables (OR, 1.64; 95% CI, 1.07 - 2.51) (Table 2).

Patients with Graves' disease also consumed more overall high-iodine food and had higher iodine pool (UI/Cr ratio) than those in the healthy group, but the results were not statistically significant. Interestingly, there were several high-iodine food items that were highly consumed in patients with Graves' disease, including ready-to-eat food, high-iodine vegetables, bakery, fermented food, iodine-supplemented sauces and iodized salts ($P < .05$). Surprisingly, patients with Graves' disease consumed fresh and dried seafood less frequent than the healthy group ($P < .05$) (Table 3).

Table 1. Characteristics of Participants in Case and Control Groups

Characteristic	No (%)		*P* Value*
	Case (n = 200)	Control (n = 200)	
Sex			
Male	41 (20.5)	39 (19.5)	.80
Female	159 (79.5)	161 (80.5)	
Age, mean (SD), y	37.9 (12.2)	36.2 (12.9)	.19
Occupation			
Office worker	49 (24.5)	8 (4.0)	< .001
Factory employee	6 (3.0)	0 (0.0)	
Civil servant/state enterprise	21 (10.5)	73 (36.5)	
Health professional and worker	10 (5.0)	33 (16.5)	
Personal business/freelance and services	69 (34.5)	33 (16.5)	
Farmer	3 (1.5)	0 (0.0)	
No occupation/housekeeper	22 (11.0)	7 (3.5)	
Students	20 (10.0)	46 (23.0)	
Working time, mean (SD), h/wk	45.0 (17.3)	43.6 (10.9)	.33
Shift work	37 (18.5)	19 (9.5)	.009
Heavy workload or sleepless	47 (23.5)	31 (15.5)	.04

Table 1. Characteristics of Participants in Case and Control Groups (Continued)

Characteristic	No (%)		*P* Value*
	Case (n = 200)	Control (n = 200)	
Stress	100 (50.0)	131 (65.5)	.002
Smoking	17 (8.5)	3 (1.5)	.001
Family history with hyperthyroidism	57 (28.5)	20 (10.0)	< .001
Family history with hypothyroidism	10 (5.0)	9 (4.5)	.82

Abbreviation: SD, standard deviation.

* The statistically significance was determined at $P < .05$.

Table 2. Knowledge of High Iodine Food Between Case and Control Groups

Category	No. (%)		Crude OR (95% CI)	*P* Value*	Adjusted OR (95% CI)	*P* Value*
	Case (n = 200)	Control (n = 200)				
Knowledge score of high iodine food, mean (SD)	4.57 (2.13)	5.39 (2.34)	-	-	-	-
Low level (< 5 scores)	102 (51.0)	70 (35.0)				
Moderate level (5 - 7 scores)	76 (38.0)	93 (46.5)	1.84 (1.04 - 3.24)	.03	1.92 (1.07 - 3.47)	.03
High level (8 - 9 scores)	22 (11.0)	37 (18.5)				
Group I eggs	64 (32.0)	87 (43.5)	1.64 (1.09 - 2.46)	.01	1.58 (1.04 - 2.40)	.03
Group II fresh and dried seafood	170 (85.0)	180 (90.0)	1.59 (0.87 - 2.90)	.13	1.47 (0.79 - 2.74)	.22
Group III cow milk, soy milk, and dairy products	59 (29.5)	73 (36.5)	1.37 (0.90 - 2.09)	.13	1.35 (0.88 - 2.08)	.16
Group IV processed food	77 (38.5)	103 (51.5)	1.70 (1.14 - 2.52)	.009	1.74 (1.16 - 2.62)	.008
Group V ready-to-eat or convenience food	137 (68.5)	159 (79.5)	1.78 (1.13 - 2.81)	.01	1.75 (1.10 - 2.80)	.02
Group VI cod liver oil	101 (50.5)	122 (61.0)	1.53 (1.03 - 2.21)	.03	1.53 (1.01 - 2.30)	.04
Group VII iodine-supplemented food	182 (91.0)	183 (91.5)	1.07 (0.53 - 2.13)	.86	1.09 (0.53 - 2.20)	.84
Group VIII high-iodine fruits	34 (17.0)	51 (25.5)	1.67 (1.03 - 2.72)	.03	1.59 (0.97 - 2.62)	.06
Group IX high-iodine vegetables	63 (31.5)	84 (42.0)	1.58 (1.05 - 2.37)	.03	1.64 (1.07 - 2.51)	.02

Abbreviations: SD, standard deviation; OR, odds ratio.

* The statistically significance was determined at $P < .05$.

Table 3. High Iodine Food Behavior and Iodine Status in Case and Control Groups

Category	No. (%)		Crude OR (95% CI)	*P* Value*	Adjusted OR (95% CI)	*P* Value*
	Case (n = 200)	Control (n = 200)				
Overall	53 (26.5)	44 (22.0)	1.28 (0.81 - 2.02)	.29	1.19 (0.74 - 1.90)	.48
Group I eggs	53 (26.5)	65 (32.5)	0.75 (0.49 - 1.15)	.19	0.75 (0.48 - 1.17)	.20
Group II fresh and dried seafood	47 (23.5)	72 (36.0)	0.55 (0.35 - 0.85)	.007	0.52 (0.33 - 0.82)	.005
Group III cow milk, soy milk, and dairy products	70 (35.0)	77 (38.5)	0.86 (0.57 - 1.29)	.47	0.72 (0.48 - 1.12)	.15
Group IV processed food	20 (10.0)	23 (11.5)	0.86 (0.45 - 1.61)	.63	0.83 (0.43 - 1.60)	.58
Group V ready-to-eat or convenience food	25 (12.5)	13 (6.5)	2.01 (1.02 - 4.14)	.04	2.08 (1.02 - 4.22)	.04
Group VI cod liver oil	6 (3.0)	14 (7.0)	0.41 (0.15 - 1.09)	.07	0.42 (0.15 - 1.16)	.09
Group VII iodine-supplemented Food	26 (13.0)	29 (14.5)	0.88 (0.50 - 1.56)	.66	0.90 (0.50 - 1.65)	.74
Group VIII high-iodine fruits	54 (27.0)	43 (21.5)	1.35 (0.85 - 2.14)	.20	1.39 (0.87 - 2.23)	.17
Group IX high-iodine vegetables	91 (45.5)	66 (33.0)	1.70 (1.13 - 2.54)	.01	1.72 (1.13 - 2.61)	.01
Group X bakery	35 (17.5)	20 (10.0)	1.91 (1.06 - 3.44)	.03	1.99 (1.10 - 3.64)	.02
Group XI snacks	64 (32.0)	75 (37.5)	0.78 (0.52 - 1.19)	.25	0.76 (0.49 - 1.16)	.20
Group XII fermented food	38 (19.0)	19 (9.5)	2.24 (1.24 - 4.03)	.008	2.20 (1.20 - 4.02)	.01
Group XIII iodine-supplemented sauces	126 (63.0)	99 (49.5)	1.74 (1.17 - 2.59)	.007	1.79 (1.18 - 2.72)	.006
Group XIV iodized salts	62 (31.0)	44 (22.0)	1.59 (1.02 - 2.50)	.04	1.62 (1.02 - 2.56)	.04
UI/Cr, median (Q1, Q3), μg/g	218.23 (135.7, 329.4)	188.10 (133.7, 295.5)	1.36 (0.87 - 2.12)	.17	1.24 (0.78 - 1.95)	.36

Abbreviations: CI, confidence interval; OR, odds ratio; Q1, quartile 1; Q3, quartile 3; UI/Cr, urine iodine to creatinine ratio.

*The statistical significance was determined at $P < .05$

Discussion

In the last decade, local and national authorities strongly supported the use of iodine supplementation as a solution for iodine deficiency-related problems. Sources of iodine include iodized salts, commercial food products, dietary supplements, and multivitamins. Some food supplements have been proven to contain very high doses of iodine (up to more than 40 mg of elemental iodine per kg per day), and actual iodine content can be higher than reported by the product labeling.[22] Additionally, evidence exists for increased levels of iodine-induced thyroid disorders in iodine sufficiency areas as well. Moreover, a recent national survey showed that many countries with "more than adequate" or "excessive" iodine intake have growing number of people at risk for iodine-induced hyperthyroidism.[23]

Patients with Graves' disease in our study had higher levels of iodine in their urine than healthy participants (median UI/Cr, 218.2 μg/g vs 188.1 μg/g) even this result was not statistically significant. Hiraiwa et al[24] found UI/Cr ratio of patients with Graves' disease was more than adequate level (median UI/Cr ratio > 200 μg/g). It may be due to the over-uptake of iodine in thyroid gland. We also found a positive association between higher iodine levels and Graves' disease (adjusted OR, 1.24; 95% CI, 0.78 - 1.95), but this effect was not statistically significant.

For the frequency of high-iodine food consumption, there were some differences between 2 groups. Patients with Graves' disease more frequently consumed fermented food (*P* = .01), ready-to-eat food (*P* = .04), bakery products (*P* = .02), iodine-supplemented sauces (*P* = .006), high-iodine vegetables (*P* = .01), and iodized salts (*P* = .04) than healthy volunteers. These results related to a study by Polumbryk et al,[25] which reported that serum free thyroxine and urine iodine levels were rising in volunteers who consumed fortified sausages for 10 days. The difference in high iodine food consumption between 2 groups may correlate with their working patterns. Patients with Graves' disease had more shift work (18.5% vs 9.5%, *P* = .009), more work loading times (23.5% vs 15.5%, *P* = .04), and most of them worked in an office, their own business, as a freelancer or in another kind of service industry, which made them more likely to consume fermented food, ready-to-eat food, high-iodine vegetables, bakery, and iodine-supplemented sauces than the healthy volunteers. Unexpectedly, all of patients with Graves' disease in our study less consumed fresh and dried seafood than healthy group (*P* = .005) (Table 3). However, only one study reported the non-association between high seafood intake and urinary iodine status.[26] Previous studies have been reported that the restriction of dietary iodine for 6 to 8 weeks significantly decreased free thyroxine,[13] and reversed the high urinary iodine levels among patients with Graves' disease living in an excessive iodine intake area.[24]

Undoubtedly, patients with Graves' disease were less aware of which items contained high iodine foods than healthy volunteers (mean [SD], 4.57 [2.13]) scores vs 5.39 [2.34] scores, *P* < .05). Frequently consumed food items that they did not recognize as high in iodine were ready-to-eat products (*P* = .02), processed foods (*P* = .008), high-iodine vegetables (*P* = .02), eggs (*P* = .03), and cod liver oil (*P* = .04). Hence, the one of important key component of Graves' disease prevention in the EEC region is to educate working-age people about high-iodine food items and advise them to consume the correct amount of dietary iodine. The same information and advice can be given on a national level as well.

Graves' disease is also influenced by other behavioral factors including stress and smoking.[27, 28] We found that patients with Graves' disease more likely to have shift work, an excessive workload, less than 4 hours per day of sleep and a smoking habit than the healthy volunteers (*P* < .05). These other factors should also be discussed in a health promotion program of Graves' disease. In the future, we will evaluate high-iodine consumption behavior in a target population of the EEC region after the launch of a health promotion program.

A particular strength of this study is the investigation of knowledge and consumption behavior of foods relating to a specific disease and a contextually defined area, leading to the practical usefulness of the results for population at risk. Another strong point, to the best of our knowledge, this is the first study to report the iodine status of non-pregnant, working-aged population in Thailand.

However, this study had some limitations. First, the socioeconomic status, such as occupations, shift work, and workload, of participants was different between 2 groups. This may affect to their levels of knowledge and high-iodine food consumption. Second, we lacked exact details of iodine content in each food item studied. Further research should consider this specific data.

Conclusions

In iodine sufficiency area, patients with Graves' disease less knew and more frequently consumed high-iodine foods than healthy participants. This result can inform a preventive program of Graves' disease among the population in this area.

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การเปรียบเทียบความรู้และพฤติกรรมการบริโภคอาหารที่มีไอโอดีนสูงระหว่างผู้ป่วยโรคต่อมไทรอยด์เป็นพิษชนิด Graves และผู้ใหญ่สุขภาพดีในพื้นที่ที่มีไอโอดีนเพียงพอ

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บทนำ: ไอโอดีนถูกนำมาเสริมในอาหารเพื่อต่อสู้กับภาวะขาดสารไอโอดีน อย่างไรก็ตาม ผลิตภัณฑ์อาหารหลายชนิดในปัจจุบันอาจจะมีปริมาณไอโอดีนที่เกิน ซึ่งอาจจะเป็นสาเหตุของการเกิดโรคต่อมไทรอยด์เป็นพิษชนิด Graves โดยไม่คาดคิด

วัตถุประสงค์: เพื่อศึกษาผลกระทบของอาหารที่มีไอโอดีนสูงระหว่างผู้ป่วยโรคต่อมไทรอยด์เป็นพิษชนิด Graves และผู้ใหญ่สุขภาพดี

วิธีการศึกษา: การศึกษาจากผลมาหาเหตุนี้ดำเนินการในผู้ป่วย จำนวน 200 คน และผู้ใหญ่สุขภาพดี จำนวน 200 คน ในจังหวัดชลบุรี ประเทศไทย โดยการสุ่มแบบกลุ่มจากเดือนพฤศจิกายน พ.ศ. 2562 ถึงเดือนมีนาคม พ.ศ. 2563 เก็บข้อมูลด้านพฤติกรรมการบริโภคอาหารที่อุดมไปด้วยไอโอดีนโดยใช้แบบสอบถาม ข้อมูลถูกวิเคราะห์โดยใช้สถิติ Chi-square test และ Multiple logistic regression

ผลการศึกษา: ผู้ป่วยโรคต่อมไทรอยด์เป็นพิษชนิด Graves มีความรู้เรื่องอาหารไอโอดีนสูงน้อยกว่ากลุ่มควบคุมอย่างมีนัยสำคัญ ($P < .05$) โดยเฉพาะอย่างยิ่งหมวดไข่ไก่ อาหารแปรรูป อาหารสำเร็จรูป น้ำมันตับปลาและผักที่มีไอโอดีนสูง หมวดอาหารที่มีไอโอดีนสูงที่ผู้ป่วยบริโภคบ่อยคือ อาหารหมักดอง (OR, 2.20; 95% CI, 1.20 - 4.02) อาหารสำเร็จรูป (OR, 2.08; 95% CI, 1.02 - 4.22) ผักที่มีไอโอดีนสูง (OR, 1.72; 95% CI, 1.13 - 2.61) เบเกอรี่ (OR, 1.99; 95% CI, 1.10 - 3.64) เครื่องปรุงเสริมไอโอดีน (OR, 1.79; 95% CI, 1.18 - 2.72) และเกลือเสริมไอโอดีน (OR, 1.62; 95% CI, 1.02 - 2.56)

สรุป: ผู้ป่วยโรคต่อมไทรอยด์เป็นพิษชนิด Graves มีความรู้น้อยกว่าและบริโภคอาหารที่มีไอโอดีนสูงมากกว่าผู้ที่มีสุขภาพดีในพื้นที่ที่มีไอโอดีนเพียงพอ

คำสำคัญ: อาหารที่มีไอโอดีนสูง โรคต่อมไทรอยด์เป็นพิษชนิด Graves พื้นที่ที่มีไอโอดีนเพียงพอ

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