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Tuber Crops Consumption and Increased Incidence of Solitary Thyroid Nodules among Women Living in Karunagappally, Kerala, India

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Abstract

Background: The prevalence of solitary thyroid nodules (nodules) is higher among the residents of Kerala's coastal region. Diet may contribute to the development of nodules, which can turn into malignant by interfering with thyroid hormone production and function. The purpose of this study is to find potential dietary factors related to thyroid diseases/nodules among women in Karunagappally, India. **Methods:** A questionnaire survey regarding the frequency of the dietary intake was performed along with clinical diagnostic procedures of thyroid diseases in 2012 among asymptomatic and voluntarily participating women in Karunagappally. Logistic regression models adjusted for age and education were used to estimate odds ratios (ORs) and 95% confidence intervals (CIs). Bonferroni correction was applied for multiple comparisons. **Results:** Among the 524 subjects, 75 (14%) were detected with nodules and 145 (28%) with thyroiditis. The logistic regression analyses, adjusting for age and education, revealed that a higher frequency of intake of goitrogenic food, such as cruciferous vegetables and tuber crops, such as roots and tubers were positively associated with the risk of nodules (P for trend 0.024 and 0.002, respectively) and though not statistically significant, tapioca also increased the risk. Consumption of the following meats and seafood at least once a week was significantly associated with the risk of nodules, with odds ratio magnitudes of around two; chicken, mutton, beef, shell, mussel, crab, and sepia. Frequent consumption (1 - 2 times/week) of chicken, mutton, and beef was associated with increased risk of nodules (Bonferroni-adjusted p = 0.012, 0.017, and 0.006, respectively), with beef intake ≥ 3 times/week further elevating risk (p = 0.023). Seafood intake (shellfish, mussels, crab, sepia) and smoked foods were also positively associated with nodule risk. While considered to be a risk factor for other cancers, frequent pickle intake showed a protective role against both the nodules (P for trend 0.022) and thyroiditis (P for trend 0.017) with significant reductions in risk observed at ≥3 times/week. **Conclusion:** The results obtained show dietary factors might be related to the risk of solitary thyroid nodules among women in Karunagappally.

Keywords

Diet, Goitrogenic Foods, Karunagappally, Solitary Thyroid Nodules, Thyroiditis

1. Introduction

The frequency of solitary thyroid nodules (thyroid nodules) is higher in women, and the prevalence of palpable solitary thyroid nodules is as high as—about 12.2%—among the residents of Kerala's coastal regions [1]. Thyroid nodules detection has been rising recently due to greater awareness and usage of ultrasound scans and when thyroid nodules are detected, 7 - 15 % of them pose a risk for malignancy [2].

The development of thyroid nodules and the high prevalence of thyroid cancer may be related to dietary variables [3]. That unpredictability of identifying the problematic food item might also be due to the variations in eating habits, dietary trends, and the accessibility of particular foods. Due to its high degree of food diversity—which is also seen as an indicator of the quality of the diet—Kerala's dietary pattern is renowned for being distinct among Indian diets [4]. In contrast to other regions of India, in Kerala tuber crops are regarded as superfoods, it is a staple meal that are sustainable and accessible throughout nearly the entire year. The most widely eaten tuber crops are Taro (Colocasia esculenta), Elephant Foot Yam (Amophophallus paeoniifolius), Sweet Potato (Ipomoea batatas), and Tapioca/Cassava (Manihot esculenta) [4]. Cruciferous vegetables, in addition to tuber crops, are an essential component of every diet. Despite knowing their immunomodulatory and anticancer properties, some have been suggested to be goitrogens [5] [6]. Nutritional goitrogens are substances that promote both renal excretion of iodine and inhibit its partial absorption [7].

In the current study, we looked at the effect that dietary determinants have on the incidence of thyroiditis and thyroid nodules among female inhabitants of Karunagappally, Kerala, India.

2. Subjects and Methods

2.1. Study Design and Subjects

This is a cross-sectional study. As part of routine health camps, we examined thyroid abnormalities among the female Karunagappally cohort members in 2012. Background of the cohort and study subject's selection criteria in detail are mentioned in our previous paper [8].

This study was approved by Institutional Scientific Review Board and Ethics Committee of Regional Cancer Centre, India and Kagoshima University, Japan.

Our study's subjects were women who live in the cohort region permanently and 900 women in total visited the health clinic; 376 of them were disqualified from the study according to the following standards, leaving 524 subjects (58%): Women who meet one of the following criteria: (i) had a medical history of thyroid illness before the survey; (ii) had more than ten diagnostic X-rays and CT scan imaging procedures performed within the previous five years; (iii) were severely ill to participate in the interview and examination; or (iv) were 75 years of age or older.

2.2. Interview

Social investigators conducted interviews with women who visited the health clinics using a standardized questionnaire in Malayalam, the local language. The questionnaire had questions on previous and present diseases of the thyroid, medical history, past and present residential history, religion, occupation, and lifestyle choices including tobacco and alcohol use. Questions about religion were categorized as Hindu, Muslim, and Christian. Education was categorized into not educated, primary school, middle school, high school, college, and higher. After the occupation was noted, it was categorized into several groups such as elementary occupations, white collar jobs, company workers, housewife's/home makers and jobs not mentioned. Questions about cigarette smoking, bidi smoking, tobacco chewing and water pipe use were asked for. Smoking status was categorized into never smoker, former smoker, and current smoker. Alcohol drinking status was categorized as a drinker and non-drinker. Since the number of subjects who used alcohol and tobacco was very few, no analysis was performed.

2.3. Dietary History Assessment

Questionnaire was used to collect data on eating patterns and the frequency of meals consumed as well. Twenty-two common foods consumed by this demographic were included in the questionnaire. To simplify the data, some food products were categorized into predetermined groupings. For instance, cruciferous vegetables such as cauliflower, cabbage, turnip, radish and so on were a group; instead of the type of fish, any type of fish that was consumed was considered as fish eating; and fruits of all kinds were included in the fruit intake category. Since different kinds of roots and tubers are consumed together, it was grouped together as well. The participants were asked to report how often they consumed an item weekly. In-person interviews were carried out by experienced interviewers who have experience completing these sorts of forms. For every food item from the food categories, the respondents' chosen frequency option was translated into a weekly consumption. Never or less than once a week, once or twice a week, three or four times a week, and five or six times a week were the consumption frequency categories.

2.4. Diagnosis of Thyroid Diseases

Thyroid-stimulating hormone (TSH), anti-thyroxine (FT4), and free thyroxine

(FT4) were measured in the lab using blood samples. The thyroidologist from Regional Cancer Centre, Thiruvananthapuram, made a clinical diagnosis based on the results of clinical examination, ultrasonography, and biochemical assays. In this study, nodules identified through ultrasonographic evaluation and both solitary and multiple were categorized as thyroid nodules. These were further divided into solid and cystic types, with any nodule containing both solid and cystic elements classified as solid. Solid nodules were then assessed for their potential malignancy or benign nature based on ultrasonographic criteria outlined in the National Comprehensive Cancer Network (NCCN) Guidelines for Thyroid Carcinoma. For inclusion in the analysis, only solitary solid nodules measuring 1 cm or more in their longest dimension were considered. Additionally, individuals presenting with diffusely coarse and irregular echotexture on ultrasonography, along with elevated Anti-TG antibody levels exceeding 115 IU/mL, were identified as thyroiditis. The specific diagnostic criteria for thyroiditis and solitary solid nodules are covered in our earlier publication as well [8].

2.5. Statistical Analysis

Odds ratios (ORs) and corresponding 95% confidence intervals (95% CIs) were obtained from logistic regression analysis adjusted for age and education. P values for heterogeneity and trend were obtained using the likelihood ratio test. Group comparisons are done using Chi square test. Bonferroni corrections were applied to adjust for multiple comparisons

3. Results

3.1. Basic Characteristics of the Study Population

Table 1 provides a summary of the research individuals' characteristics. Of the 524 participants, 145 (28%) had thyroiditis and 75 (14%) had solitary solid nodules. Comparison of age groups showed significant differences among thyroiditis cases (P = 0.043) and education groups also showed significant differences among solitary nodules cases (P = 0.030). **Table 2** presents the age-adjusted ORs and 95% CIs for thyroiditis and thyroid nodules based on socioeconomic status factors such as occupation, education, and religion. Women with college degrees had lower chances of thyroiditis (OR = 0.56; CI = 0.29 - 1.06) and nodules (OR = 0.54; CI = 0.20 - 1.42). Women without formal education had a higher risk of isolated thyroid nodules (OR = 2.29; CI = 1.02 - 5.16). Thyroiditis and nodules had no significant correlations with occupation or religion.

Table 1. Characteristics of the study subjects.

Variables	Subjects without thyroid diseases N (%)	Thyroiditis N (%)	P Value*	Solitary thyroid nodules N (%)	P Value*
All subjects (N = 524)	304 (58.0)	145 (27.7)		75 (14.3)	

Continued

Age (years)	Less than 30	51 (16.8)	13 (9.0)		6 (8.0)	
	30 - 39	59 (19.4)	44 (30.3)		15 (20.0)	
	40 - 49	91 (29.9)	43 (29.7)	0.043	22 (29.3)	0.300
	50 - 59	78 (25.7)	36 (24.8)		26 (34.7)	
	60 - 74	25 (8.2)	9 (6.2)		6 (8.0)	
Education level	Illiterate	22 (7.2)	5 (3.5)		13 (17.3)	
	Primary school	46 (15.1)	28 (19.3)		12 (16.0)	
	Middle school	62 (20.4)	28 (19.3)	0.155	16 (21.3)	0.030
	High school	118 (38.8)	66 (45.5)		28 (37.3)	
	College/higher	56 (18.4)	18 (2.4)		6 (8.0)	
Religion	Hindu	228 (75.0)	112 (77.2)		56 (74.7)	
	Muslim	17 (5.6)	12 (8.3)	0.287	5 (6.7)	0.933
	Chritian	59 (19.4)	21 (14.5)		14 (18.7)	
Occupation	Elementary Occupations	36 (11.8)	19 (13.1)		13 (17.3)	
	White collar jobs	28 (9.2)	10 (6.9)		4 (5.3)	
	**Company workers	55 (18.1)	34 (23.5)	0.587	19 (25.3)	0.272
	House wives/Home makers	171 (56.3)	74 (51.0)		37 (49.3)	
	Job not mentioned	14 (4.6)	8 (5.5)		2 (2.7)	

*P values are calculated using Chi square test. **Company workers include cashew nut factory workers and other factories around study area

Table 2. Odds ratios (OR) and 95% confidence interval (CI) for developing solitary thyroid nodules and thyroiditis according to religion, education and occupation.

		OR (95% CI)	
		Thyroiditis	Solitary thyroid nodules
Religion	Hindu	1 (reference)	1 (reference)
	Muslim	1.43 (0.66 - 3.11)	1.09 (0.38 - 3.10)
	Christian	0.73 (0.42 - 1.26)	1.05 (0.54 - 2.03)
P for heterogeneity		0.297	0.981
Education	Illiterate	0. 42 (0.15 - 1.16)	2.29 (1.02 - 5.16)
	Primary school	1.12 (0.62 - 2.01)	0.97 (0.44 - 2.12)
	Middle school	0.82 (0.47 - 1.44)	0.99 (0.49 - 2.00)
	High school	1 (reference)	1 (reference)
	College/higher	0.56 (0.29 - 1.06)	0.54 (0.20 - 1.42)

Continued

P for heterogeneity		0.137	0.135
Occupation	Elementary Occupations	1 (reference)	1 (reference)
	White collar jobs	0.67 (0.26 - 1.72)	0.52 (0.15 - 1.85)
	Company workers	1.17 (0.58 - 2.37)	0.86 (0.37 - 1.97)
	House wifes/Home makers	0.82 (0.44 - 1.52)	0.58 (0.28 - 1.20)
	Job not mentioned	1.08 (0.38 - 3.03)	0.42 (0.08 - 2.11)
P for heterogeneity		0.603	0.464

ORs and 95% CIs were calculated using a logistic regression model after adjusting for age.

3.2. Risks Associated with Food Item Consumption

Table 3 and Table 4 summarize the associations between dietary intake and the risk of thyroiditis and thyroid nodules. After adjusting for age and education, several food groups demonstrated significant associations with thyroid nodules. A positive dose-response relationship was observed for cruciferous vegetables (P for trend = 0.024), roots and tubers (P = 0.002), and fruits (P = 0.028), with the highest risk noted among individuals consuming roots and tubers five or more times per week (OR = 8.41; 95% CI: 2.35 - 30.04). Frequent consumption of animal proteins—including chicken, mutton, and beef—was also associated with increased risk (P for trend < 0.05 for all). These associations remained statistically significant after Bonferroni correction, with 1 - 2 times per week consumption of chicken, mutton, and beef yielding adjusted *p*-values of 0.012, 0.017, and 0.006, respectively. Additionally, beef intake at 3 - 4 times per week or more was significantly associated with elevated risk (P = 0.023). (Table 4)

Table 3. Results of multiple logistic regression analysis for the risk of thyroiditis according to diet consumptions.

Food groups	Controls N = 304	Thyroiditis N = 145	OR	(95% CI)
Fruits and Vegetables				
Cruciferous vegetables				
Never	74	38	1	Reference
1 - 2 times a week	154	77	0.95	0.59 - 1.55
3 - 4 times a week	72	29	0.82	0.45 - 1.49
5 or more times a week	0	0	-	-
Unknown	4	1		
	P for trend	0.546	P for heterogeneity	0.797
Tapioca				
Never	87	42	1	Reference
1 - 2 times a week	174	82	1.02	0.64 - 1.62
3 - 4 times a week	37	17	0.94	0.47 - 1.88

Continued

5 or more times a week	1	1	2.01	0.12 - 33.64
Unknown	5	3		
	P for trend	0.772	P for heterogeneity	0.961
Roots and Tubers				
Never	118	57	1	Reference
1 - 2 times a week	115	59	1.13	0.72 - 1.78
3 - 4 times a week	60	23	0.77	0.43 - 1.38
5 or more times a week	5	3	1.57	0.35 - 7.01
Unknown	6	3		
	P for trend	0.411	P for heterogeneity	0.564
Fruits				
Never	45	21	1	Reference
1 - 2 times a week	180	83	1.01	0.55 - 1.85
3 - 4 times a week	65	36	1.29	0.64 - 2.62
5 or more times a week	10	4	0.89	0.24 - 3.26
Unknown	4	1		
	P for trend	0.566	P for heterogeneity	0.775
Garlic				
Never	45	30	1	Reference
1 - 2 times a week	108	49	0.72	0.40 - 1.30
3 - 4 times a week	131	60	0.75	0.42 - 1.33
5 or more times a week	12	4	0.50	0.15 - 1.73
Unknown	8	2		
	P for trend	0.486	P for heterogeneity	0.601
Onion				
Never/up to 2 times a week	72	29	1	Reference
3 - 4 times a week	160	85	1.35	0.81 - 2.25
5 or more times a week	67	30	1.19	0.64 - 2.21
Unknown	5	1		
	P for trend	0.935	P for heterogeneity	0.503
Pickle				
Never	43	35	1	Reference
1 - 2 times a week	113	54	0.58	0.33 - 1.02
3 - 4 times a week	113	45	0.47	0.26 - 0.84
5 or more times a week	23	8	0.43	0.17 - 1.10
Unknown	10	3		
	P for trend	0.017	P for heterogeneity	0.071

Continued

		Protein sources		
Fish				
Never/1 - 2 times per week	24	11	1	Reference
3 - 4 times a week	87	42	0.98	0.44 - 2.22
5 or more times a week	187	91	0.96	0.45 - 2.07
Unknown	6	1		
	P for trend	0.950	P for heterogeneity	0.992
Shells or Clams				
Never	184	90	1	Reference
1 - 2 times a week	111	49	0.91	0.59 - 1.39
3 - 4 times a week	8	6	1.45	0.48 - 4.38
5 or more times a week	0	0	-	-
Unknown	1	0		
	P for trend	0.742	P for heterogeneity	0.695
Mussel				
Never	209	100	1	Reference
1 or more times a week	86	41	0.98	0.63 - 1.54
3 - 4 times a week	2	3	2.92	0.47 - 18.09
5 or more times a week	0	0	-	-
Unknown	7	1		
	P for trend	0.400	P for heterogeneity	0.499
Crab				
Never	172	82	1	Reference
1 or more times a week	119	58	1.04	0.69 - 1.59
3 - 4 times a week	7	4	1.16	0.33 - 4.14
5 or more times a week	0	0	-	-
Unknown	6	1		
	P for trend	0.513	P for heterogeneity	0.959
Sepia				
Never	209	100	1	Reference
1 or more times a week	84	41	1.00	0.63 - 1.57
3 - 4 times a week	1	3	6.12	0.62 - 60.71
5 or more times a week	0	0	-	-
Unknown	1	1		
	P for trend	0.978	P for heterogeneity	0.237
Egg				
Never	141	65	1	Reference
1 - 2 times a week	133	70	1.20	0.78 - 1.86
3 - 4 times a week	21	7	0.82	0.32 - 2.10

Continued

5 or more times a week	5	1	0.52	0.06 - 4.73
Unknown	4	2		
	P for trend	0.863	P for heterogeneity	0.646
Chicken				
Never	158	74	1	Reference
1 - 2 times a week	139	68	1.09	0.72 - 1.65
3 - 4 times a week	2	1	0.97	0.09 - 10.94
5 or more times a week	0	0	-	-
Unknown	5	2		
	P for trend	0.761	P for heterogeneity	0.916
Mutton				
Never	207	104	1	Reference
1 - 2 times a week	90	40	0.88	0.56 - 1.39
3 or more times a week	0	0	-	-
Unknown	7	1		
			P for heterogeneity	0.590
Beef				
Never	162	81	1	Reference
1 - 2 times a week	135	62	0.98	0.64 - 1.48
3 - 4 times a week	1	1	1.74	0.11 - 28.52
5 or more times a week	0	0	-	-
Unknown	6	1		
	P for trend	0.697	P for heterogeneity	0.920
Smoked food				
Never	230	111	1	Reference
1 - 2 times a week	60	26	0.88	0.52 - 1.47
3 - 4 times a week	5	6	2.87	0.78 - 10.54
5 or more times a week	0	0	-	-
Unknown	9	2		
	P for trend	0.770	P for heterogeneity	0.227

ORs and 95% CIs were calculated using a logistic regression model after adjusting for age and education.

Table 4. Results of multiple logistic regression analysis for the risk of solitary thyroid nodules according to diet consumptions.

Food groups	Controls N = 304	Thyroid nodules N = 75	OR	(95% CI)
		Fruits and Vegetables		
Cruciferous vegetables				
Never	74	11	1	Reference

Continued

1 - 2 times a week	154	44	2.08	1.00 - 4.33
3 - 4 times a week	72	20	2.30	1.00 - 5.29
5 or more times a week	0	0	-	
Unknown	4	0		
	P for trend	0.024	P for heterogeneity	0.081
Tapioca				
Never	87	20	1	Reference
1 - 2 times a week	174	41	1.15	0.62 - 2.14
3 - 4 times a week	37	12	1.44	0.63 - 3.32
5 or more times a week	1	2	9.86	0.83 - 116.37
Unknown	5	0		
	P for trend	0.069	P for heterogeneity	0.269
Roots and Tubers				
Never	118	20	1	Reference
1 - 2 times a week	115	25	1.25	0.65 - 2.42
3 - 4 times a week	60	22	2.20	1.10 - 4.42
5 or more times a week	5	8	8.41	2.35 - 30.04
Unknown	6	0	-	-
	P for trend	0.002	P for heterogeneity	0.003
Fruits				
Never	45	5	1	Reference
1 - 2 times a week	180	49	3.29	1.19 - 9.06
3 - 4 times a week	65	19	4.25	1.39 - 13.01
5 or more times a week	10	2	2.32	0.37 - 14.36
Unknown	4	0	-	-
	P for trend	0.028	P for heterogeneity	0.042
Garlic				
Never	45	12	1	Reference
1 - 2 times a week	108	31	1.14	0.52 - 2.53
3 - 4 times a week	131	25	0.74	0.32 - 1.68
5 or more times a week	12	4	1.12	0.29 - 4.31
Unknown	8	3		
	P for trend	0.870	P for heterogeneity	0.537
Onion				
Never or less than two times a week	72	20	1	Reference*
3 - 4 times a week	160	40	0.87	0.47 - 1.62
5 or more times a week	67	15	0.78	0.36 - 1.68

Continued

Unknown	5	0	-	-
	P for trend	0.623	P for heterogeneity	0.811
Pickle				
Never	43	10	1	Reference
1 - 2 times a week	113	47	1.94	0.88 - 4.29
3 - 4 times a week	115	15	0.62	0.25 - 1.53
5 or more times a week	23	2	0.39	0.08 - 1.95
Unknown	10	1	-	-
	P for trend	0.022	P for heterogeneity	0.001
Protein sources				
Fish				
Less than 2 times a week	24	4	1	Reference
3 - 4 times a week	87	18	1.26	0.38 - 4.19
5 or more times a week	187	53	1.61	0.52 - 4.96
Unknown	6	0	-	-
	P for trend	0.098	P for heterogeneity	0.562
Shells or Clams				
Never	184	34	1	Reference
1 - 2 times a week	111	37	2.11	1.22 - 3.64
3 - 4 times a week	8	4	2.79	0.76 - 10.32
5 or more times a week	-	-	-	-
Unknown	1	0	-	-
	P for trend	0.003	P for heterogeneity	0.016
Mussel				
Never	209	39	1	Reference
1 - 2 times a week	86	33	2.31	1.34 - 4.00
3 - 4 times a week	2	3	7.78	1.19 - 50.91
5 or more times a week	-	-	-	-
Unknown	7	0	-	-
	P for trend	0.0001	P for heterogeneity	0.002
Crab				
Never	172	30	1	Reference
1 - 2 times a week	119	41	2.42	1.38 - 4.23
3 - 4 times a week	7	3	2.20	0.51 - 9.52
5 or more times a week	0	0	-	-
Unknown	6	1	-	-

Continued

	P for trend	0.003	P for heterogeneity	0.006
Sepia				
Never	209	41	1	Reference
1 - 2 times a week	84	32	2.16	1.24 - 3.75
3 - 4 times a week	1	2	13.33	1.14 - 156.57
5 or more times a week	0	0	-	-
Unknown	10	0	-	-
	P for trend	0.073	P for heterogeneity	0.004
Egg				
Never	141	29	1	Reference
1 - 2 times a week	133	40	1.82	1.04 - 3.20
3 - 4 times a week	21	4	1.32	0.40 - 4.38
5 or more times a week	5	2	1.54	0.25 - 9.53
Unknown	4	0		
	P for trend	0.072	P for heterogeneity	0.214
Chicken				
Never	158	28	1	Reference
1 - 2 times a week	139	44	2.21	1.27 - 3.84
3 - 4 times a week	2	3	7.64	1.19 - 49.26
5 or more times a week	0	0	-	-
Unknown	5	0	-	-
	P for trend	0.0003	P for heterogeneity	0.004
Mutton				
Never	207	40	1	Reference
1 - 2 times a week	89	33	2.23	1.29 - 3.85
3 - 4 times a week	1	2	11.31	0.97 - 131.75
5 or more times a week	0	0	-	-
Unknown	7	0		
	P for trend	0.0002	P for heterogeneity	0.003
Beef				
Never	162	33	1	Reference
1 - 2 times a week	135	38	1.64	0.96 - 2.83
3 - 4 times a week	1	4	19.76	2.08 - 187.49
5 or more times a week	0	0	-	-
Unknown	6	0		
	P for trend	0.040	P for heterogeneity	0.004
Smoked food				
Never	230	45	1	Reference

Continued

1 - 2 times a week	60	28	2.34	1.33 - 4.13
3 - 4 times a week	5	2	1.39	0.24 - 8.20
5 or more times a week	0	0	-	-
Unknown	9	0		
	P for trend	0.557	P for heterogeneity	0.015

ORs and 95% CIs were calculated using a logistic regression model after adjusting for age and education.

Consumption of seafood, including shellfish, mussels, crab, and sepia, was also significantly associated with thyroid nodules. Weekly intake of these items at 1 - 2 times per week was linked to increased odds, with Bonferroni-adjusted *p*-values of 0.026, 0.013, 0.006, and 0.028, respectively. Smoked food consumption 1 - 2 times per week was similarly associated with increased risk (OR = 2.34; 95% CI: 1.33 - 4.13; Bonferroni-adjusted P = 0.019), though no clear dose-response trend was observed. In contrast, frequent pickle consumption demonstrated a consistent protective association. Individuals consuming pickles 3 - 4 times or more than 5 times per week had significantly reduced odds of developing thyroid nodules (OR = 0.62; 95% CI: 0.25 - 1.53 and OR = 0.39; 95% CI: 0.08 - 1.95, respectively), with Bonferroni-adjusted P-values of 0.001 and 0.006.

In comparison, thyroiditis showed no significant associations with most dietary components. Cruciferous vegetables, fruits, tubers, meats, seafood, and smoked foods were not significantly associated with thyroiditis risk. However, pickle consumption again emerged as a protective factor, with a significant inverse trend (P for trend = 0.017), suggesting a potential shared dietary mechanism influencing both thyroid conditions. (**Table 3**)

4. Discussion

Diet is seldom studied in relation to thyroid diseases; publications from epidemiological studies are mostly on diet and thyroid carcinoma. The present study suggests the significant role of diet of the risk of developing thyroid nodules and thyroiditis in a population who are not deprived from iodine. High intake of cruciferous vegetables, and tuber crops together with some fatty foods were associated with increased risk of thyroid nodules while no clear patterns of association were found with other dietary components. A 2022 cross-sectional study by Kim *et al.* in South Korea found that high consumption of cruciferous vegetables was associated with increased thyroid nodule prevalence, particularly among individuals with marginal iodine status, suggesting a synergistic effect between dietary goitrogens and iodine availability. Highly educated women showed a decreased risk for nodules similarly in a retrospective study done in China, the risk of thyroid nodules was reduced for the subjects with an education level of post-graduation and above [9].

Already there is clear evidence that cruciferous vegetables are associated with thyroid cancer [10]. Increased consumptions of it increased the risk of thyroid nodules in this study also. Previous studies showed that thiocyanate and goitrogens in cruciferous vegetables have a goitrogenic effect by inhibiting iodine uptake and organification by the thyroid gland [9].

Tapioca together with roots and tubers are called crop tubers. Since tapioca can be also a main meal, separate questions were asked about uptake of tapioca and other roots and tubers. A local cuisine known as "Puzhukku" is made from two to three different varieties of tuber crops, including tapioca, sweet potatoes, taro, and elephant foot yam, that are cooked and mashed. And the intake of these roots and tubers, except tapioca showed a significant dose-dependent positive association with the risk of thyroid nodules (P for trend 0.002). Though the risk increased among tapioca consumers, that was not statistically significant, tapioca contains high concentration of linamarin, a cyanogenic glucoside which can be metabolized to thiocyanate, it has been suspected as a cause of endemic goiter [11]. Though tapioca is a dietary goitrogen, consumption of it was not independently related to nodular disease among women from high background radiation areas of China [9]. But in French Polynesia, high cassava intake showed an inverse association with thyroid cancer risk as well [12]. Taro root is known in its high content of phytate, a compound which inhibits iodine absorption. Although iron deficiency is primarily caused by insufficient dietary intake, the uptake of these goitrogens like cassava and taro root has been suggested to interfere with the proper functioning of thyroid hormone synthesis and utilization of iodine [6]. Studies aimed at identifying the anti-thyroid effects of other tuber roots are inadequate.

Fruit intake is considered to probably protect against thyroid disease risks, but the results in our studies are not consistent with that notion. One primary reason for this may be because of the low or less intake of the recommended daily servings of fruit. In the study area, the most consumed fruits are homegrown or locally grown bananas and seasonally available Jackfruits and Mangoes. The seasonal changes and local availability will also affect the consumption of fruits [13]. The daily intake and the frequency of fruits were not significantly associated with thyroid cancer risks in women, in a case-control study in South Korea [14].

Although there are many indications of dietary factors of food items that affect thyroid function, an insufficient and contradictory understanding still exists. This study also showed a weak inverse association with the consumption of garlic and onion. Increased consumption of vegetables of the allium class has significantly reduced (17%) the prevalence of thyroid nodules among women from high background radiation areas of China and *in vitro* studies showed that onion and garlic oils inhibit tumor promotion [15] [16].

In a pooled analysis of case-control studies, fish consumption was not associated with thyroid cancer risk, and the same study suggested a possible protective role of fish consumption on thyroid diseases in the iodine-deficient regions [17]. A dietary pattern loaded heavily on fish was positively associated with the risk of the follicular thyroid cancer among Greek population [18]. Though not statistically significant, we also found an increase in risk according to the frequency of consumption. Fish is an important source of iodine and other micronutrients, but it also has some contaminants that may affect the thyroid gland and increase the risk of thyroid diseases. Lack of cold storage and use of poor-quality ice and other preservatives such as sodium benzoate and formalin are potentially harmful and carcinogenic for humans [19]. A Norwegian case-control study also showed that seafood increases the risk of thyroid cancer [20]. Among the seafood, consumption of shell, mussel, crab, and sepia at least once a week was significantly associated with the risk of solitary thyroid nodules, with odds ratio magnitudes of around two which tells us that regular consumption of probably poor-quality seafood may increase the risk for thyroid damage and dysfunction.

More eggs decreased the risk of thyroiditis. Eggs are rich sources of iodine and selenium which are thyroid supportive nutrients. Chicken, mutton and beef also increased the thyroid nodules risk significantly. Red meat processing or cooking at high temperatures is known to generate carcinogenic compounds. Kuwaiti research found a significant correlation between thyroid cancer and high intakes of chicken (OR = 1.7; 95% CI: 1.2 - 2.3) and mutton (OR = 1.8; 95% CI: 1.1 - 2.8) [21]. Furthermore, a 2021 European cohort study by Muller *et al.* identified a positive association between high red meat consumption and thyroid nodule formation, with effect sizes comparable to those observed in our analysis [22].

In this study, frequent pickle consumption demonstrated a consistent protective association. A 2023 study by Zhang *et al.* in a Chinese cohort also reported that frequent intake of pickled vegetables was inversely associated with autoimmune thyroiditis, potentially due to the immunomodulatory effects of fermented foods [23].

The important limitation of our study is that we did not obtain any direct laboratory measure of iodine intake. However, we are confident that limitations do not affect the implications of the associations that we found between thyroid nodules and certain food items. And in this study, we considered seafood consumption frequency check as one of the proxies for iodine uptake measure. While direct biochemical measures of iodine status were not available, we have incorporated goiter prevalence as a proxy indicator of iodine deficiency [24]. A state-wide survey from Kerala shows that consumption of fewer than five grams of salt per day was observed in only 18.3% of the women [25] and in this study population, the prevalence of goiter was 7.3% (38/540), suggesting a relatively low burden of iodine deficiency. Additionally, the study was conducted in coastal regions where dietary iodine intake is generally higher due to seafood availability and widespread awareness of the Government of India's iodine fortification programs [26]-[28]. Given this context, the population is likely to be iodine sufficient, which may attenuate or modify the expected effects of dietary goitrogens.

Another limitation is that we did not enquire about the type of fruits and the quantity of their intake. So, we expect the kinds of intake might not be recorded adequately. Another limitation of our study is that BMI data were available for only 169 of the 524 participants. Although a sensitivity analysis restricted to this subset indicated that adjusting for BMI did not materially change the observed associations, the incomplete availability of anthropometric data may still introduce residual confounding. We also think that our study design has these limitations and hence we cannot make a conclusion of causal association.

5. Conclusion

The results obtained from this study show certain dietary products which can increase the risk of solitary thyroid nodules among women in Karunagappally. Since there is a large intake of tuber crops and it is known that these crops might alter thyroid function, thyroid function should be closely monitored. Eating a balanced diet rich in vitamins and nutrients ensures proper thyroid function and prevents any possible thyroid disorders. Further epidemiologic studies need to be done to investigate the association of other environmental factors with thyroid diseases.

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Informed Consent

Informed consent was signed by all women prior to thyroid investigations.

Conflicts of Interest

The authors declare that they have no conflict of interest.

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