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Dietary Iodine Intake and Urinary Iodine Excretion in Patients with Thyroid Diseases

Jung-Yeon Kim[1] and Kyung-Rae Kim[2]

Abstract

This study was conducted to examine the usual iodine intake in patients with thyroid diseases and to compare iodine status with normal subjects. The dietary iodine intake was assessed using a semi-quantitative food frequency questionnaire, and urinary iodine excretion was measured in 184 patients diagnosed with thyroid diseases and 207 normal subjects. The average usual iodine intake of patients with thyroid diseases was 673.8±794.9 ug/day and that of normal subjects was 468.9±481.9 ug/day. Among the patients with thyroid diseases, higher values were found in the patients with thyroid cancer (1460.6±1044.8 ug/day) and lower values were found in patients with simple goiter (443.5±470.4 ug/day). The urinary iodine excretions of patients and normal subjects were 4.33±5.70 mg/L and 2.11±0.69 mg/L, respectively. The iodine intake and urinary iodine excretion of patients with thyroid diseases were significantly higher than those of normal subjects ($p<0.05$). The dietary iodine intake and urinary excretion of patients with thyroid cancer were significantly higher than other patients with thyroid diseases and normal subjects because of the use of seaweed or seaweed-containing dietary supplements ($p<0.01$). This study suggests that the habitual ingestion of seaweed-containing dietary supplements in addition to dietary iodine intake will have adverse effects due to its excessive iodine intake.

Key Words: Iodine intake, urinary iodine excretion, thyroid diseases, seaweed-based dietary supplements

INTRODUCTION

Recent studies have documented the importance of iodine intake levels for the prevalence rate of various thyroid abnormalities.[1-6] These studies have demonstrated that both low and high iodine intake levels correlate to a high prevalence rate of thyroid abnormalities. But the types of abnormalities are different according to the iodine intake.[1,6] There is an increased prevalence of goitre and thyroid nodules, and hyperthyroidism of non-autoimmune origin in old age seems to be more frequent when iodine intake is relatively low.[5,7] On the other hand, hypothyroidism occurs more frequently when iodine intake is relatively high.[5,6,8] These facts have supported the view that the iodine intake level is a major determinant of which types of thyroid abnormalities are common.

Although excess iodine may not be the sole factor in determining the presence of autoimmune thyroid diseases, epidemiological and experimental studies have also suggested a link between the level of iodine intake and the development of autoimmune thyroid diseases.[9-13] Thus, knowing the iodine intake level of an area is valuable for understanding the pattern of thyroid abnormalities and for planning the care of thyroid disorders.[6]

There have been numerous reports on iodine intake and the prevalence of thyroid diseases in iodine-deficient areas,[14-17] but only a few surveys have been reported for areas with high iodine intakes.[11,18]

There have been several reports on urinary iodine excretion of patients with thyroid diseases in Korea, which is a peninsula bounded by the ocean on three sides and whose people generally consume sufficient amounts of iodine through the intake of seaweed.[19-21]

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[1]Department of Food and Nutrition, College of Human Ecology, [2]Department of Internal Medicine, Yonsei University College of Medicine, Seoul, Korea.
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Address reprint request to Dr. K. R. Kim, Department of Internal Medicine, Yongdong Severance Hospital, Yonsei University College of Medicine, Youngdong P.O. Box 1217, Seoul 135-270, Korea. Tel: 82-2-3497-3315, Fax: 82-2-3463-3882, E-mail: kimkr96@yumc.yonsei.ac.kr

The measurement of iodine concentrations in spot or 24-hr urine samples is the method most commonly used for epidemiological investigation of iodine status in an area because the assessment of iodine intake by food analysis is difficult.[22-25] The urinary iodine excretion reflects current iodine status, but the manifestation of thyroid diseases may be affected by the previous iodine intake. One of the dietary assessment methods, the semi-quantitative food frequency method, has been a common way to estimate usual dietary intake (chronic iodine deficiency or excess).[26] Therefore, we conducted this study to investigate the usual iodine intake as well as urinary iodine excretion in patients with thyroid diseases, and to compare the iodine status in patients of thyroid diseases with that of normal subjects.

MATERIALS AND METHODS

Subjects

The 184 patients who were diagnosed with thyroid diseases at Yongdong Severance Hospital in Seoul, Korea, from June 1997 to July 1998, were selected for this study. A clinical examination and measurement of plasma thyroid hormones were performed for diagnosis of thyroid diseases. Additional tests were performed for some cases, including thyroid antibodies to thyroglobulin and thyroid peroxidase (TPO), 24-hour radioactive iodine uptake test, and nuclear scans with technetium or computed tomography (CT).

Simple goiter was diagnosed by euthyroid diffuse goiter without any evidence of inflammatory or neoplastic process. Hyperthyroidism was diagnosed by high levels of free thyroxine and decreased levels of TSH, and positive TSH receptor antibody. All of them were Graves' disease. Hashimoto's thyroiditis was diagnosed by positive antiTPO antibody and/or antithyroglobulin antibody and the presence of diffuse firm goiter with chronicity. Painless thyroiditis was diagnosed by increased levels of serum thyroid hormones for less than 3 months, and later development of transient hypothyroidism, and/or low radioactive iodine uptake and antithyroid antibody. Subacute thyroiditis was diagnosed by typical symptoms including anterior neck pain, firm, tender goiter, elevated ESR and low radioactive iodine uptake. All of them were in the acute stage. Benign thyroid nodule was diagnosed via fine needle aspiration biopsy, and all thyroid cancer was diagnosed by pathology results after surgery.

To compare measurements, 207 normal subjects without thyroid disease were also selected voluntarily. The investigation involved an interview on previous or present diseases, pregnancies, health status, medication, possible sources of extra iodine intake, and main area of residence. Subjects with intake of iodine containing medication and with recent radiographic investigations involving iodine containing contrast media were excluded for this study. Also, subjects who had already been diagnosed at other clinic and had increased or decreased their iodine intake at their option were excluded.

Methods

Measurement of dietary iodine intake: A semi-quantitative food frequency questionnaire was designed to estimate a usual iodine intake of subjects during 1 year. The questionnaire contained questions regarding the average usual food frequency and the amounts of intake. The food items included those with a relatively high iodine content and those which Koreans generally consume. The interview was conducted by a trained nutritionist, while food models, measuring tools, and photographs were provided to decrease the variation as much as possible between the interviewer and interviewee. The dietary iodine intake level was calculated as follows:

$$I = \sum_{i=1}^{n} F_i \times Q_i \times C_i$$

(I: dietary iodine intake, F: frequency per day, Q: amount of serving size /frequency, C: iodine content in the food, i: food items, n: number of food items)

The iodine content table for Korean foods analyzed by Moon et al.[27] was used.

Determination of urinary iodine excretion: Morning spot urine samples were collected for the analysis of urinary iodine concentration on the day the subjects were interviewed. Urine iodine concentration was measured with an iodide selective electrode. The interassay C.V. (Coefficient of Variation) was 20.7%.

An Orion EA 940 ion meter (Orion Research, Boston, MA, USA), equipped with an Orion 94-53 iodide-specific ion electrode and an Orion 90-03 double-junction reference electrode, was used for determination of iodine. The standard solution was 0.1M NaI and the ionic strength adjuster used was 5M $NaNO_3$.

Statistical analysis: All the materials were analyzed by the Statistical Analysis System (SAS) package. The averages and standard deviations of all results were calculated, while ANOVA and t-tests were also obtained. A probability level of <0.05 was regarded as significant. When there were statistically significant differences, LSD and SNK tests were used.

RESULTS

In the current study, one subject among normal controls and 9 patients with thyroid diseases had a history of habitual ingestion of sea tangle or seaweed-containing food supplements. Their average urinary iodine excretion was 25 mg/L (ranging from 10.7 mg/L to 47.2 mg/L). Two of them were excluded for estimation of usual dietary iodine intake because their frequency of intake was irregular and couldn't identify the iodine contents in these products.

The mean ± SD age of the patients and normal subjects were 42 ± 13 and 43 ± 12 years, respectively. Among the 184 patients examined (16 males and 168 females), 17 had simple goiter, 42 had hyperthyroidism (all of them were Graves' diseases), 15 had hypothyroidism, 15 had subacute thyroiditis in the acute stage, 12 had painless thyroiditis, and 36 had Hashimoto's thyroiditis. In patients with Hashimoto's thyroiditis, 38.9% were hypothyroid and remainder were euthyroid state.

Thirty-six had benign thyroid nodule, with 31 cases of single nodule and 5 cases of multiple nodule. Eleven patients had thyroid cancer and all thyroid malignancy were papillary carcinoma (Table 1).

The results of usual iodine intake of the subjects are summarized in Table 2. The average usual dietary iodine intake for patients with thyroid diseases was estimated at 673.8 ug daily (range from 40.3 ug to 5,305.7 ug daily) and normal subjects at 468.9 ug daily (range from 60.7 ug to 4,085.8 ug daily). Forty-one patients with thyroid diseases (22.3%) had a usual iodine intake level of more than 1,000 ug/day, and 15 of them (8.2%) above 2,000 ug/day. Among the normal subjects, 19 (9.2%) had an iodine intake level of more than 1,000 ug/day, and 4 (1.9%) were above 2,000 ug/day. In particular, the subjects who took seaweed-containing dietary supplements had a high usual iodine intake of 4026 ± 3475 ug/day.

On the other hand, only 2 patients with thyroid diseases had a usual iodine intake level of less than 50 ug/day.

Among the patients with a diagnosis of thyroid diseases, the usual iodine intake level of simple goiter patients was the lowest (443.5 ± 470.4 ug/day) and it was highest in patients with thyroid cancer (1,460.6 ± 1,044.8 ug/day). The patients with thyroid

Table 1. Etiology of Thyroid Diseases in 184 Subjects

	No. of subjects		
	Males	Females	Total
Simple goiter	2	15	17
Hyperthyroidism	9	33	42
Hypothyroidism	2	13	15
Subacute thyroiditis	0	15	15
Painless thyroiditis	0	12	12
Hashimoto's thyroiditis	3	33	36
Benign thyroid nodule	0	36	36
Thyroid cancer	0	11	11
Total	16	168	184

Table 2. Usual Dietary Iodine Intakes of Patients with Thyroid Diseases and Normal Subjects

	Iodine intake (μg/day)	
	Mean ± SD	Range
Thyroid diseases	673.8 ± 794.9*	40.3 – 5305.7
Simple goiter	443.5 ± 470.4	76.7 – 1888.8
Hyperthyroidism	600.7 ± 623.2	82.1 – 3112.4
Hypothyroidism	600.8 ± 697.5	102.3 – 2541.3
Subacute thyroiditis	594.0 ± 982.0	40.3 – 3519.5
Painless thyroiditis	633.3 ± 562.6	143.9 – 1791.4
Hashimoto's thyroiditis	623.5 ± 667.9	57.8 – 3296.0
Benign thyroid nodule	622.0 ± 694.5	51.4 – 2823.9
Thyroid cancer	1460.6 ± 1044.8†	141.4 – 3374.9
Normal subjects	468.9 ± 481.9	60.7 – 4085.8

Significantly different from normal subjects at * p=0.05, † p=0.01.

Table 3. Contribution of Food Sources to the Total Iodine Intakes of Subjects

	Normal		Thyroid diseases	
	Food item	(%*)	Food item	(%*)
1	Sea mustard	(27.3)	Sea tangle	(35.8)
2	Sea tangle	(24.5)	Sea mustard	(25.6)
3	Laver	(14.6)	Milk & dairy products	(11.0)
4	Milk & dairy products	(11.1)	Fish	(9.3)
5	Fish	(9.0)	Laver	(8.5)
6	Beef	(2.4)	Egg	(2.6)
7	Egg	(2.0)	Beef	(2.3)

* % of total iodine intake.

Table 4. Urinary Iodine Excretion of Patients with Thyroid Diseases and Normal Subjects

	Urinary iodine excretion (mg/L)	
	Mean ± SD	Range
Thyroid diseases	4.33 ± 5.70*	0.33 − 34.9
Simple goiter	2.88 ± 1.69	1.26 − 6.43
Hyperthyroidism	4.90 ± 7.48*	1.01 − 34.9
Hypothyroidism	4.57 ± 3.97*	1.17 − 12.75
Subacute thyroiditis	4.69 ± 5.39*	0.93 − 17.45
Painless thyroiditis	3.46 ± 3.42	0.75 − 10.65
Hashimoto's thyroiditis	4.14 ± 3.87*	0.33 − 15.50
Benign thyroid nodule	2.95 ± 2.05	0.75 − 9.75
Thyroid cancer	6.18 ± 4.77†	1.10 − 14.35
Normal subjects	2.11 ± 0.69	0.70 − 5.04

Significantly different from normal subjects at * p=0.05, † p=0.01.

diseases had a significantly higher iodine intake than normal subjects ($p<0.05$). However, only patients with thyroid cancer had a significantly higher iodine intake than normal subjects and other patients with thyroid diseases ($p<0.01$). The majority of patients with thyroid cancer (82%) had a history of habitual ingestion of sea tangle soup or sea tangle powder as food supplements.

The food sources of iodine intake in patients with thyroid diseases were sea tangle, sea mustard, milk & dairy products, and fish (Table 3). The sources of dietary iodine were sea mustard, sea tangle, laver, and milk & dairy products in normal subjects. The normal subjects did not show any difference in major sources of iodine intake. The ratio of seaweed to the total iodine intake was 70% with thyroid diseases and 66% with normal subjects.

We measured urinary iodine concentrations in spot urine samples. The mean urinary iodine concentration (S.D.) of patients and normal subjects were 4.33 (5.70) mg/L and 2.11 (0.69) mg/L. The urinary iodine results are summarized in Table 4. The spot urinary iodine concentration in patients with thyroid diseases was significantly higher than in normal subjects ($p<0.05$). The normal subjects and patients with simple goiter, painless thyroiditis and thyroid nodule did not show any significant difference in their urinary iodine concentrations, but the patients with hyperthyroidism, hypothyroidism, subacute thyroiditis, Hashimoto's thyroiditis, and thyroid cancer had significantly higher urinary iodine concentrations than normal subjects ($p<0.05$). The patients with benign thyroid nodule and thyroid cancer showed significant differences in both usual dietary iodine intake level and urinary iodine excretion ($p<0.01$).

DISCUSSION

This study was performed to investigate the usual dietary iodine intake over 1 year using a semi-quantitative food frequency questionnaire in subjects with and without thyroid diseases. The urinary iodine excretion that reflects current iodine status was also measured on the day subjects were interviewed.

It was noted that the dietary iodine intake and urine iodine concentration in the study population were considerably higher than that in other studies.[28,29]

The average usual dietary iodine intake was estimated at 469 ug daily for subjects without thyroid diseases and ranging from 440 ug to 1,460 ug daily in patients with thyroid diseases. In the case of normal subjects, this value was higher than the amounts reported for Americans[30] and Europeans,[6,31] but it was comparable to that of the Japanese.[32,33]

A major source of dietary iodine intake of Korean subjects was seaweed, such as sea tangle, sea mustard, and laver. The iodine content of seaweed ranged from 3,570 to 179,060 ug/100 g.[27]

Our data indicated that the iodine intake of subjects with and without thyroid diseases depended on the amount of seaweed consumption. Konno et al.

reported that there was considerable variation in the prevalence of high urinary iodine excretion in the Japanese, showing that the amount of kelp consumption may vary among the areas studied.[18]

In this study, the subjects who used seaweed-containing dietary supplements had a usual iodine intake level above 4 mg/day. Occasionally, dietary iodine intakes in the order of 1～10 mg/day have been reported as a result of the consumption of seaweed products.[34] In most healthy subjects, iodine intakes of ～1 mg/day are well tolerated. The upper limit was set at 1 mg/day iodine, although negative effects were indicated in individual subjects at lower intakes.[34] There is little information on the safety of seaweed-based health supplements. This study suggests that the habitual ingestion of seaweed-containing dietary supplements in addition to dietary iodine intake will have negative effects on thyroid diseases in an iodine-sufficient region.

It is well known that excessive intake of iodine may induce thyroid diseases.[5,8,9,11,18,35,36] In China, endemic goitre associated with excessive iodine intake has been reported in numerous locations.[37] Recent studies from Hong Kong documented a high incidence of childhood Graves' disease and it may be related to the increase dietary iodine intake in children.[36]

It has been reported that excessive iodine intake may cause hypothyroidism in patients with underlying thyroid diseases such as chronic thyroiditis, as well as in the absence of apparent underlying thyroid disease.[8,11,18,38,39]

In Laurberg et al's study, the high prevalence rate of subclinical hypothyroidism in Iceland could be caused by the high iodine intake, and their major source of iodine intake was iodine in dairy products caused by feeding cattle with fish meal.[6] Konno et al also reported that the prevalence of hypothyroidism in iodine sufficient areas, e.g. Japan, may be associated with the amount of iodine ingested, and that hypothyroidism is more prevalent and marked in subjects consuming further excessive amounts of iodine.[18] They suggested that an excessive intake of iodine should be considered an etiology of hypothyroidism in addition to chronic thyroiditis in these areas.[18] It was noted that thyroid function spontaneously returned to normal with only iodine restriction in some cases.[11,18,38]

In Hashimoto's thyroiditis, a high iodine intake also correlated with an increase in thyroid dysfunction. Iodine seems to be an important environmental factor in the development of thyroid autoimmunity in genetically susceptible individuals.[3] Therefore, iodine appears to be an immune stimulant as well as a substrate for the biosynthesis of thyroid hormone, and greater exposure to iodine may increase autoimmune thyroid disease.[10,13]

Postpartum thyroid dysfunction is characterized by transient hyperthyroidism, followed by transient hypothyroidism.[40] Iodine intake may also have an impact on the severity of the thyroidtoxic and hypothyroid phases of autoimmune postpartum thyroiditis.[9] In Korea, it is customary to serve large quantities of seaweed soup to lactating mothers during their lying-in period. Recently, Moon et al. reported that the dietary iodine intake and the iodine content of breast milk of Korean lactating mothers were much higher than in other countries.[41] However, little information is available on the effects of the excessive iodine intake during lactation on the development of postpartum thyroiditis in Korea. Further studies on postpartum thyroid function in our populations with the consumption of seaweed soup may define the precise role of iodine for the clinical expression of autoimmune postpartum thyroiditis.

In the current study, all thyroid malignancy was for cases of papillary carcinoma. Their usual iodine intake and urinary iodine excretion were significantly higher than other patients with thyroid diseases ($p < 0.01$).

A number of observations support the suggestion that a high dietary intake of iodine may be associated with a high frequency of papillary carcinoma.[4] Papillary carcinoma is the predominant type of thyroid malignancy in areas with a naturally high iodine intake and has also increased in frequency in iodine-deficient areas since iodine prophylaxis.[4]

The current study provides evidence of the relation of papillary carcinoma to dietary iodine intake. But the number of cases with clinically significant thyroid tumors were relatively small. Further studies, therefore, are required to evaluate the patients with thyroid cancer, in relation to their dietary iodine intake in iodine sufficient area to clearly define the etiology of thyroid cancer.

There have been many reports on the beneficial and negative effects of iodine prophylaxis in iodine-deficient areas, with or without preexisting thyroid diseases.[42-49] Several studies have reported the increased incidence of hyperthyroidism and thyroiditis following iodine prophylaxis.[3,4,42] Careful monitoring of populations given iodine supplementation is essential to be sure that adequate but not excessive iodine intake is being maintained.[47]

The differences in iodine intake levels may have a considerable impact on the pattern of thyroid diseases seen in an area. Laurberg et al. compared 68-year-old subjects from Denmark (low iodine intake) and Iceland (high iodine intake) and found that in the region with low iodine intake, goitre and subclinical hyperthyroidism were more common, whereas in Iceland there were more cases with subclinical hypothyroidism.[6]

Accordingly, assessing the iodine status of the entire population is important both in the aspect of planning of care and in the prevention of thyroid diseases.

This study provides information on the usual iodine intake of patients of thyroid diseases in an iodine sufficient area. Further studies are required to determine the effects of the usual iodine intake on the manifestation of thyroid disease and the prevalence rate of various thyroid diseases in our population.

REFERENCES

1. Laurberg P, Pedersen KM, Vestergard H, Sigurdsson G. High incidence of multinodular goitre in the elderly population in a low iodine intake area versus high incidence of Graves' diseases in the young in a high iodine area. J Intern Med 1991;229:415-20.
2. Boyages SC. Iodine deficiency disorders. J Clin Endocrinol Metab 1993;77:587-91.
3. Laurberg P. Iodine intake-What are we aiming at? J Clin Endocrinol Metab 1994;79:17-9.
4. Harach HR, Williams ED. Thyroid cancer and thyroiditis in the goitrous region of Salta, Argentina, before and after iodine prophylaxis. Clin Endocrinol 1995;43:701-6.
5. Szabolcs I, Podoba J, Feldkamp J, Dohan O, Farkas I, Sajgo M, et al. Comparative screening for thyroid disorders in old age in areas of iodine deficiency, long-term iodine prophylaxis and abundant iodine intake. Clin Endocrinol 1997;47:87-92.
6. Laurberg P, Pedersen KM, Hreidarsson A, Sigfusson N, Iversen E, Knudsen PR. Iodine intake and the pattern of thyroid disorders: A comparative epidemiological study of thyroid abnormalities in the elderly in Iceland and in Jutland, Denmark. J Clin Endocrinol Metab 1998;83: 765-9.
7. Szabolcs I, Kovacs ZS, Gonczi J, Kakosy T, Goth M, Dohan O, et al. Prevalence of thyroid dysfunction in different geriatric subpopulations from a moderately iodine-deficient Hungarian region. Comparative clinical and hormonal screening. Eur J Endocrinol 1995;133:294-9.
8. Tajiri J, Higashi K, Morita M, Umeda T, Sato T. Studies of hypothyroidism in patients with high iodine intake. J Clin Endocrinol Metab 1986;63:412-7.
9. Jansson R, Safwenberg J, Dahlberg PA. Influence of the HLA-DR4 antigen and iodine status on the development of autoimmune postpartum thyroiditis. J Clin Endocrinol Metab 1985;60:168-73.
10. Hall R, Lazarus JH. Changing iodine intake and the effect on thyroid disease. Br Med J 1987;294:721-2.
11. Konno N, Yurl K, Taguchi H, Miura K, Taguchi S, Hagiwara K, et al. Screening for thyroid diseases in an iodine sufficient area with sensitive thyrotrophin assays, and serum thyroid autoantibody and urinary iodide determinations. Clin Endocrinol 1993; 38:273-81.
12. Mooij P, Wit HJ, Bloot AM. Iodine deficiency induces thyroid autoimmune reactivity in Wistar rats. Endocrinology 1993;133:1197-204.
13. Mooij P, Wit HJ, Drexhage HA. An excess of dietary iodine accelerates the development of a thyroid-associated lymphoid tissue in autoimmune prone BBrats. Clin Immunol Immunopathol 1993;69:189-98.
14. Delange F, Burgi H. Iodine deficiency disorders in Europe. WHO Bulletin 1989;67:317-25.
15. Maberly GF. Iodine deficiency disorders: Contemporary scientific issues. J Nutr 1994;124:1473S-8S.
16. Baltisberger BL, Minder CE, Burgi H. Decrease of incidence of toxic nodular goitre in a region of Switzerland after full correction of mild iodine deficiency. Eur J Endocrinol 1995;132:546-9.
17. Reinhardt W, Luster M, Rudorff KH, Heckmann C, Petrasch S, Lederbogen S, et al. Effect of small doses of iodine on thyroid function in patients with Hashimoto's thyroiditis residing in an area of mild iodine deficiency. Eur J Endocrinol 1998;139:23-8.
18. Konno N, Makita H, Yuri K, Iizuka N. Association between dietary iodine intake and prevalence of subclinical hypothyroidism in the costal regions of Japan. J Clin Endocrinol Metab 1994;78:393-7.
19. Park HY, Lee SI, Kim WB, Kim SY, Cho BY, Lee HK, et al. A study on the urinary iodine excretion in normal subjects and patients with thyroid disease. J Korean Soc Endocrinol 1995;10;386-94.
20. Cho YW, Kim YS, Baick SH, Oh DY, Kim WJ. Analysis of daily intake and urinary excretion of iodine in normal control and patients with thyroid disease. J Korean Soc Endocrinol 1994;9;307-17.
21. Kim HM, Lee HC, Park KS, Ju HY, Kim KR, Hong CS, et al. A study on the urinary iodide excretion in normal subjects and patients with thyroid disease. Korean J Intern Med 1985;29;625-631.
22. Furnee CA, Van der Haar F, West CE, Hautvast JG. A critical appraisal of goiter assessment and the ratio of urinary iodine to creatinine for evaluating iodine status. Am J Clin Nutr 1994;59:1415-7.
23. Delange F, Benker G, Caron PH, Eber O, Ott W, Peter

F, et al. Thyroid volume and urinary iodine in European schoolchildren: standardization of values for assessment of iodine deficiency. Eur J Endocrinol 1997;136:180-7.
24. Pardede LVH, Hardjowasito W, Gross R, Dillon DHS, Totoprajogo OS, Yosoprawoto M, et al. Urinary iodine excretion is the most appropriate outcome indicator for iodine deficiency at field conditions at district level. J Nutr 1998;128:1122-6.
25. Wong GWK, Lam CWK, Kwok MY, Mak TWL, Ahuja AT, Chow CC, et al. Childhood goitre and urinary iodine excretion in Hong Kong. Eur J Pediatr 1998;157:8-12.
26. Thompson FE, Byers T. Dietary assessment resource manual. J Nutr 1994;124:2245S-61S.
27. Moon SJ, Kim JY, Chung YJ, Chung YS. The iodine content in common Korean foods. Korean J Nutr 1998;31: 206-12.
28. Ali O, Muda K, Khalid B. Iodine content in urine samples among Malays and aborigines. Acta Med Okayama 1994; 48:289-92.
29. Pedersen KM, Iversen E, Laurberg P. Urinary iodine excretion and individual iodine supplementation among elderly subjects: A cross-sectional investigation in the commune of Randers, Denmark. Eur J Endocrinol 1995;132: 171-4.
30. Pennington JA, Young BE. Total diet study: Nutrients elements, 1982－1989. J Am Diet Assoc 1991;91:179-83.
31. Lee SM, Lewis J, Buss DH. Iodine in British foods and diets. Br J Nutr 1994;72:435-46.
32. Suzuki M, Tamura T. Iodine intakes of Japanese male university student: Urinary iodine excretion of sedentary and physically active students and sweat iodine excretion during exercise. J Nutr Sci Vitaminol 1985;31:409-15.
33. Katamine S, Mamiya Y, Sekimoto K, Hoshino N, Totsuka K, Naruse U, et al. Iodine content of various meals currently consumed by urban Japanese. J Nutr Sci Vitaminol 1986;32:487-95.
34. Sandstrom B. Toxicity considerations when revising the Nordic nutrition recommendations. J Nutr 1998;128:372S-4S.
35. Pennington JA. A review of iodine toxicity reports. J Am Diet Assoc 1990;90:1571-81.
36. Wong GWK, Kwok MY, Ou Y. High incidence of Juvenile Graves' disease in Hong Kong. Clin Endocrinol 1995;43:697-700.
37. Li M, Liu D, Qu C, Zhang P, Qian Q, Zhang C, et al. Endemic goitre in central China caused by excessive iodine intake. Lancet 1987;2:257-8.
38. Yoshinari M, Okamura K, Tokuyama T, Shiroozu A, Nakashima T, Inoue K, et al. Clinical importance of reversibility in primary goitrous hypothyroidism. Br Med J 1983;287:720-2.
39. Takeda S, Michigishi T, Takazakura E. Iodine-induced hypothyroidism in patients on regular dialysis treatment. Nephron 1993;65:51-5.
40. Lazarus JH. Prediction of postpartum thyroiditis. Eur J Endocrinol 1998;139:12-3.
41. Moon SJ, Kim JY. Iodine content of human milk and dietary iodine intake of Korean lactating mothers. Int J Food Sci Nutr 1999;50:165-71.
42. Fradkin JE, Wolff J. Iodide-induced thyrotoxicosis. Medicine 1983;62:1-20.
43. Leisner B, Henrich B, Knorr D, Kantlehner R. Effects of iodide treatment on iodine concentration and volume of endemic non-toxic goitre in childhood. Acta Endocrinol 1985;108:44-50.
44. Phillips DIW, Nelson M, Barker DJP, Morris JA, Wood TJ. Iodine in milk and the incidence of thyrotoxicosis in England. Clin Endocrinol 1988;28:61-6.
45. Delange F. Correction of iodine deficiency: benefits and possible side effects. Eur J Endocrinol 1995;132:542-3.
46. Elnagar B, Eltom M, Karlsson A, Ermans AM, Medhin MG, Bourdoux PP. The effects of different doses of oral iodized oil on goiter size, urinary iodine, and thyroid-related hormones. J Clin Endocrinol Metab 1995;80: 891-7.
47. Braverman LE. Adequate iodine intake-the good far outweighs the bad. Eur J Endocrinol 1998;139:14-5.
48. Ojea AR, Menendez R, Terry B, Vega L, Abreu Y, Diaz Z. Low levels of urinary iodine excretion in schoolchildren of rural areas in Cuba. Eur J Clin Nutr 1998;52:372-5.
49. Todd CH, Allain T, Gomo ZAR, Ndiweni M, Oken E. Increase in thyrotoxicosis associated with iodine supplements in Zimbabwe. Lancet 1995;346:1563-4.