

THYROID SIZE AND IODINE INTAKE IN IODINE-REPLETED PREGNANT WOMEN IN ISFAHAN, IRAN

Hassan Rezvanian, MD, Ashraf Aminorroaya, MD, Mohammad Majlesi, MD,
Amin Amini, MD, Ali Hekmatnia, MD, Ali Kachoie, MD, Masoud Amini, MD,
and Jaber Emami, PharmD

ABSTRACT

Objective: To evaluate the goiter and iodine intake status of pregnant women in Isfahan, after 8 years of iodized salt distribution in Iran.

Methods: Thyroid staging was assessed by clinical examination, thyroid volume was determined by sonography, and urinary iodine (UI) excretion was assessed by the digestion method in 90 healthy pregnant women (30 in each trimester) and 90 age-matched nonpregnant women selected by random sampling in prenatal and primary health-care clinics. The data were reported as mean \pm standard deviation; P values <0.05 were considered statistically significant.

Results: The mean age of the pregnant and the nonpregnant women was 25.3 and 27.5 years, respectively—no significant difference ($P = \text{NS}$). The clinical goiter prevalence in the pregnant and the nonpregnant groups was 37% and 32%, respectively ($P = \text{NS}$). The mean thyroid volume in the pregnant and nonpregnant women was 7.8 ± 3.2 and 7.8 ± 2.8 mL, respectively ($P = \text{NS}$). Urinary iodine (UI) excretion was 20.7 ± 6.9 $\mu\text{g/dL}$ in pregnant women and 23.7 ± 7.6 $\mu\text{g/dL}$ in nonpregnant women ($P = \text{NS}$). The prevalence of goiter assessed by sonography was 29% in pregnant women and 21% in nonpregnant women ($P = \text{NS}$). The mean thyroid size in 26 of 90 pregnant women with goiter (thyroid volume >9.2 mL) was 11.8 ± 2.73 mL and in 19 of 90 nonpregnant women with goiter was 12.36 ± 1.6 mL ($P = \text{NS}$). The mean thyroid volume was 6.0 ± 1.7 , 9.9 ± 1.7 , 11.8 ± 2.2 , and 18.9 ± 2.4 mL in the pregnant women with or without goiter at thyroid stages 0, Ia, Ib, and II, respectively. A strong correlation between goiter staging assessed by clinical examination and thyroid volume determined by sonography was found in pregnant ($r = 0.77$) and nonpregnant ($r = 0.78$) women

(both $P < 0.000001$). Mean UI excretion was 20.9 ± 7.0 , 19.9 ± 6.8 , 20.6 ± 7.5 , and 25.9 ± 2.3 $\mu\text{g/dL}$ in the pregnant women at thyroid stages 0, Ia, Ib, and II, respectively. In the pregnant and the nonpregnant women, no correlation was found between thyroid stage and UI excretion or between thyroid volume and UI excretion.

Conclusion: No iodine deficiency was found in Isfahani pregnant women. Thus, as in most iodine-sufficient areas, thyroid size did not increase during pregnancy. Despite sufficient iodine intake, a moderate prevalence of goiter was noted in pregnant and nonpregnant women. This study also revealed that careful physical examination of the thyroid had diagnostic accuracy similar to sonography. (**Endocr Pract.** 2002;8:23-28)

Abbreviations:

NS = no significant difference; UI = urinary iodine;
WHO = World Health Organization

PMID: 11939756 DOI: 10.4158/EP.8.1.23

INTRODUCTION

During pregnancy, the thyroid is subjected to increased demands associated with a tendency to endogenous iodine deficiency (1). Therefore, in iodine-deficient areas, pregnancy may disclose the underlying iodine restriction, with maternal goiter formation as the most visible consequence—which can easily be prevented by iodine supplementation (2-5). Severe iodine deficiency can result in stillbirth, abortion, congenital defects, endemic cretinism characterized most commonly by mental deficiency, deaf mutism, and spastic diplegia, and lesser degrees of neurologic defects related to fetal iodine deficiency and impaired mental function in children (6,7). Thyroid volume may increase up to 47% during pregnancy (2,5). Thus, the World Health Organization (WHO) recommended daily iodine intake of 100 to 200 μg for pregnant women (2). Iran had been considered iodine deficient until 1989 (8,9). Therefore, this study was designed to evaluate the goiter and iodine intake status of pregnant women in 1997, after 8 years of iodized salt distribution in Isfahan, a city in the central part of Iran.

Submitted for publication February 1, 2001

Accepted for publication July 2, 2001

From the Endocrine Research Center of Isfahan University of Medical Sciences, Isfahan, Iran.

Address correspondence and reprint requests to Dr. Ashraf Aminorroaya, Endocrine Research Center of Isfahan University of Medical Sciences, Isfahan, Iran.

© 2002 AACE.

METHODS

In a cross-sectional study, 90 healthy pregnant women (30 patients in each trimester) and 90 age-matched nonpregnant women (control subjects), with no previous history of thyroid dysfunction or use of medication affecting the thyroid gland, were selected by random sampling in prenatal and primary health-care clinics in three different regions in Isfahan. Approximately 60 women were studied in each region ($N = 180$). Thyroid staging was determined by physical examination and based on WHO criteria (10). Throughout the entire study, thyroid volume was measured with a Dornier scanner (Dornier, Germany) and use of a 7.5-MHz linear transducer by an experienced sonographer (A.H.), who was "blinded" with regard to the findings on physical examination of the women. All study subjects were examined in the supine position with the neck in hyperextension. The volume of each thyroid lobe was calculated on the basis of Brunn's equation, as follows (4): Volume of each thyroid lobe (mL) = length (mm) \times width (mm) \times thickness (mm) \times 0.479. Total thyroid volume was the sum of both thyroid lobes; the isthmus was not included in these calculations.

The thyroid volume of nonpregnant women, who proved not to have goiter on physical examination, was assumed as an index of normal thyroid volume. Any thyroid volume greater than this index was considered as goiter in the pregnant women or in the control subjects.

Urinary iodine (UI) excretion was measured in random urine samples of all 180 subjects by means of the digestion method (11). Results were expressed as micrograms of iodine per deciliter ($\mu\text{g}/\text{dL}$). UI excretion of less than 2.0 $\mu\text{g}/\text{dL}$ was considered severe deficiency, between 2.0 and 4.9 $\mu\text{g}/\text{dL}$ as moderate deficiency, and between 5.0 and 9.9 $\mu\text{g}/\text{dL}$ as mild iodine deficiency. UI excretion of 10.0 $\mu\text{g}/\text{dL}$ or more was assumed to reflect a normal daily iodine intake (10).

Statistical analysis was performed with use of the Student *t* test, analysis of variance, chi-square tests, and

Spearman and Pearson correlation coefficients in SPSS software. *P* values less than 0.05 were considered statistically significant. The data are reported as mean \pm standard deviation, unless otherwise noted.

RESULTS

The mean ages of the two groups (pregnant versus nonpregnant women) were not significantly different ($P = \text{NS}$) (Table 1). In addition, the UI excretion and thyroid volume of the pregnant women did not differ significantly from those of the nonpregnant women ($P = \text{NS}$). In the pregnant women, these values also were not significantly different among the trimesters ($P = \text{NS}$) (Table 1). Clinically, 63% of pregnant women did not have goiter. None of them had a large goiter (stage III) (Table 2 and Fig. 1).

In the nonpregnant women, clinical examination showed that 68% did not have goiter and 32% had mild to moderate goiter (Table 2 and Fig. 1). No statistically significant difference was observed between clinical goiter prevalence in the two groups ($P = \text{NS}$) (Table 2 and Fig. 1). The mean thyroid volume in pregnant and nonpregnant women was 7.8 ± 3.2 mL and 7.8 ± 2.8 mL, respectively ($P = \text{NS}$) (Table 1). The upper limit of the thyroid volume in 61 women in the control group who did not have goiter on physical examination was 9.2 mL. Thus, thyroid volume of more than 9.2 mL was considered an index for goiter. On the basis of this criterion, the prevalence of goiter was 29% in pregnant women and 21% in nonpregnant women ($P = \text{NS}$) (Table 2 and Fig. 2). The mean thyroid size in 26 of 90 pregnant women with goiter (thyroid volume >9.2 mL) was 11.8 ± 2.73 mL and in 19 of 90 nonpregnant women with goiter was 12.36 ± 1.6 mL ($P = \text{NS}$) (Table 2). In the pregnant women with goiter, the difference in the thyroid size assessed by sonography during the three trimesters also did not reach a significant level ($P = \text{NS}$) (Table 2 and Fig. 2).

Table 1
Age, Urinary Iodine Excretion, and Thyroid Volume
in Pregnant and Nonpregnant Women in Isfahan

Group	Age (yr)	Urinary iodine excretion ($\mu\text{g}/\text{dL}$)	Thyroid volume (mL)
Pregnant women* (N = 90)	25.3 \pm 5.1	20.7 \pm 6.9	7.8 \pm 3.2
1st trimester (N = 30)	25.7 \pm 5.4	20.6 \pm 7.0	8.8 \pm 3.5
2nd trimester (N = 30)	25.7 \pm 4.9	23.3 \pm 6.3	7.0 \pm 2.5
3rd trimester (N = 30)	24.6 \pm 4.9	18.4 \pm 6.7	7.6 \pm 3.3
Nonpregnant women† (N = 90)	27.5 \pm 7.8	23.7 \pm 7.6	7.8 \pm 2.8

*Study cases.

†Control group.

Table 2
Relative Prevalence of Goiter
Assessed by Clinical Examination and Sonography
in Pregnant and Nonpregnant Women in Isfahan
and Thyroid Volume in Subjects With Goiter Determined by Sonography

Group	Goiter clinically		Goiter sonographically (TV >9.2 mL)*		Thyroid volume (TV >9.2 mL)*
	No.	%	No.	%	
Pregnant women (N = 90)	33	37	26	29	11.8 ± 2.73
1st trimester (N = 30)	13	43	11	37	12.76 ± 2.3
2nd trimester (N = 30)	9	30	8	27	10.38 ± 1.35
3rd trimester (N = 30)	11	37	7	23	11.94 ± 3.94
Nonpregnant women (N = 90)	29	32	19	21	12.36 ± 1.6

*TV = thyroid volume; 9.2 mL was upper limit of TV in 61 control subjects without goiter on physical examination (see text).

The mean thyroid volume was 6.0 ± 1.7 mL, 9.9 ± 1.7 mL, 11.8 ± 2.2 mL, and 18.9 ± 2.4 mL in pregnant women with or without goiter at thyroid stages 0, Ia, Ib, and II, respectively (Table 3 and Fig. 3). A strong correlation was noted between thyroid staging assessed by clinical examination and thyroid volume determined by sonography in the pregnant women ($r = 0.77$; $P < 0.000001$) and the nonpregnant women ($r = 0.78$; $P < 0.000001$) (Table 2 and Fig. 3). The thyroid size was well correlated with thyroid staging during the different trimesters ($r = 0.79$; $P < 0.000001$) (Table 2 and Fig. 4).

No correlation was found between thyroid stages and UI excretion in the pregnant women ($r = -0.007$; $P = NS$) and the nonpregnant women ($r = -0.1$; $P = NS$) (Table 3). Furthermore, no correlation was observed between thyroid

volume and UI excretion in the pregnant ($r = -0.05$; $P = NS$) and the nonpregnant women ($r = -0.08$; $P = NS$) (Table 3).

DISCUSSION

Investigators who have performed studies in iodine-sufficient areas have concluded that the maternal thyroid gland is able to adapt to the new state of equilibrium associated with the gestational status, without substantial modification in thyroid volume (12-14). During pregnancy, increased thyroid volume can occur but goiter formation is uncommon in iodine-sufficient or iodine-repleted areas (goiter was found in 9% of women at delivery in Belgium) (15). In areas of low iodine intake, however, goiter has

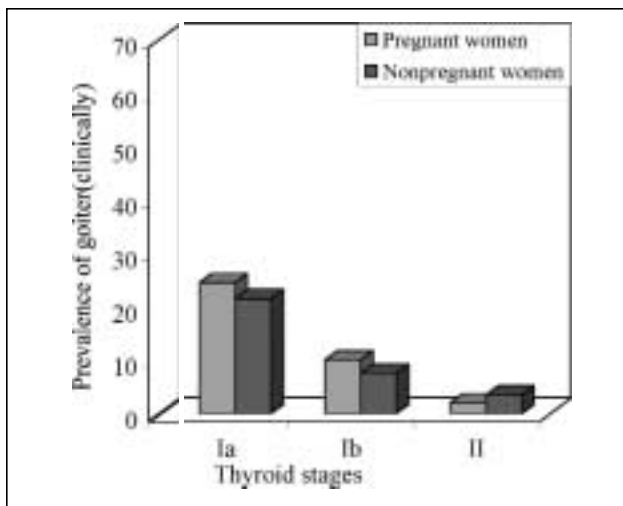


Fig. 1. Prevalence of clinical goiter (%) in pregnant and nonpregnant women in Isfahan, stratified by thyroid stage.

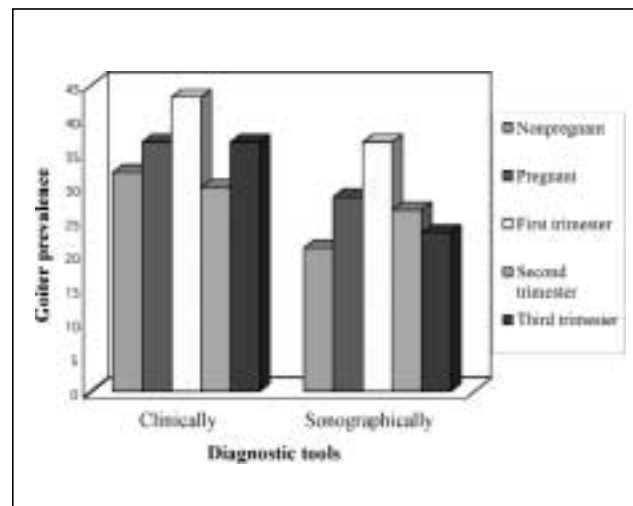


Fig. 2. Prevalence of goiter (%) in nonpregnant and pregnant women in Isfahan, stratified by trimester and by clinical and sonographic diagnosis.

Table 3
Urinary Iodine Excretion and Thyroid Volume
in Pregnant and Nonpregnant Women in Isfahan,
Stratified by Thyroid Stage

Group and thyroid stage	Urinary iodine excretion ($\mu\text{g/dL}$)	Thyroid volume (mL)*
Pregnant women (N = 90)		
0	20.9 \pm 7.0	6.0 \pm 1.7
Ia	19.9 \pm 6.8	9.9 \pm 1.7
Ib	20.6 \pm 7.5	11.8 \pm 2.2
II	25.9 \pm 2.3	18.9 \pm 2.4
Nonpregnant women (N = 90)		
0	23.8 \pm 8.9	6.4 \pm 1.6
Ia	19.5 \pm 8.7	9.6 \pm 1.8
Ib	24.8 \pm 6.5	12.9 \pm 1.8
II	23.7 \pm 6.5	14.1 \pm 0.2

*See text for method of calculation of thyroid volume.

been observed in more than 50% of all pregnant women whose goiter prevalence before pregnancy was 25 to 40% (1). In another study, the increment of the goiter rate was found to be as high as 47% (5), which was not completely reversible after pregnancy (16). In one study in Krakow, 80% of the pregnant women had enlarged thyroid glands (17). In the current study in Isfahan, no statistically significant difference was found between thyroid volume in the pregnant and the nonpregnant women (Table 1 and Fig. 2). Thus, as reported in iodine-sufficient areas, the thyroid size did not increase during pregnancy (2).

Just as the mean thyroid volume during pregnancy in different geographic areas has been reported to vary—from 14.3 mL in Belgium (3) and 16.2 mL in Germany (4) to 26.4 mL in Ireland (5)—likewise the sonographic index of goiter diagnosis has been at variance in different countries. For example, thyroid volumes of 18 mL in Germany and 22 mL in Belgium were considered as the goiter index in pregnant patients (2,4). Therefore, we decided to establish a local criterion for goiter by ultrasonography. Values greater than the upper limit of the thyroid volume range in 61 nonpregnant women without goiter (assessed by physical examination) was considered the goiter index (thyroid volume >9.2 mL). On the basis of Gutekunst's criterion in Germany (4), among all subjects in our study, only one pregnant woman in her third trimester of pregnancy might have had goiter (Fig. 4). This finding would be contrary to expectation in Iran, which had long been considered an area of endemic goiter (8,9,18)—especially because 37% of pregnant women and 32% of nonpregnant women had goiter on the basis of WHO criteria (10) (Table 2 and Fig. 1 and 2). With use of the local criterion established in our current investigation, goiter was present in 29% or 37% of

pregnant women assessed either by sonography or by physical examination, respectively ($P = \text{NS}$) (Table 2 and Fig. 2), whereas in the control (nonpregnant) group, the corresponding goiter prevalences were 21% and 32% ($P = \text{NS}$) (Table 2 and Fig. 2).

The increment in the thyroid stage was well correlated with increasing thyroid volume in the pregnant women (for assessment of the entire pregnancy period as well as each trimester) and in the nonpregnant women (Table 3 and Fig. 3 and 4). Consequently, careful physical examination has almost the same accuracy as sonographic assessment in goiter diagnosis (Fig. 2). The mean increment in thyroid volume in women with iodine supplementation during pregnancy has been reported to range from less than 5% in Italy to 15% in Belgium (2). In the current study, no statistically significant difference was noted in thyroid volume between the pregnant women and the control group (Table 1), similar to findings in a study reported by Italian researchers (2).

The mean UI excretion in both case and control groups was more than 10 $\mu\text{g/dL}$ (Tables 1 and 3). Therefore, daily iodine intake seemed to be sufficient. Thus, we conclude that Iran has been successful in its national program of iodine repletion, despite some reported cases of iodine deficiency in European countries and Australia (4,19,20). The relatively high prevalence of goiter in the pregnant and the nonpregnant women in our study (Table 2 and Fig. 1 and 2) and their sufficient UI excretion (Tables 1 and 3) suggest the possible role of other goitrogens besides iodine deficiency in Isfahan. This finding is similar to the results of other studies conducted in Bangladesh (21) and in Tehran, Iran (8,22,23). An alternative explanation is the possibility of an increased rate of

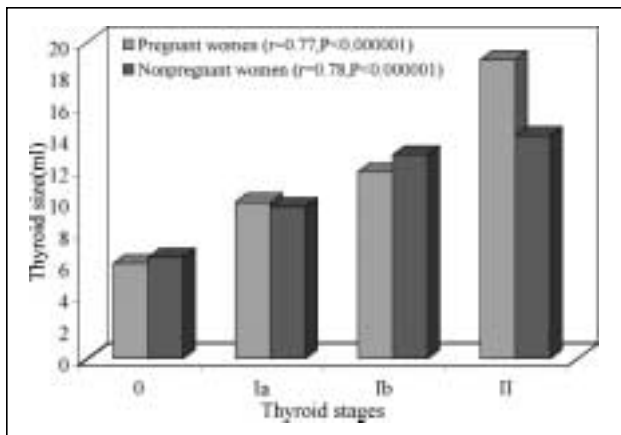


Fig. 3. Mean thyroid size, stratified by thyroid stage, in pregnant and nonpregnant women in Isfahan.

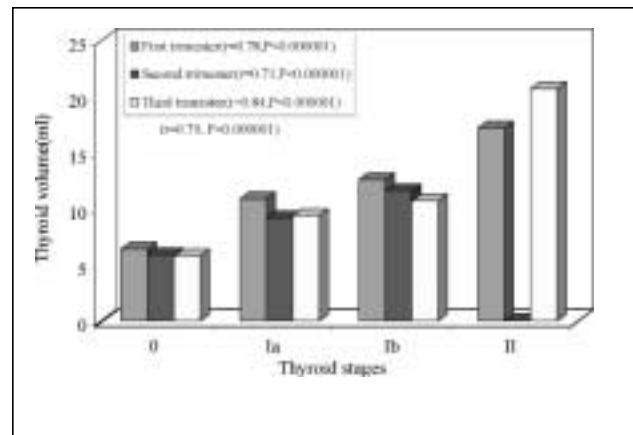


Fig. 4. Mean thyroid volume, stratified by trimester and by thyroid stage, in pregnant women in Isfahan.

occurrence of autoimmune thyroid diseases manifested as goiter in their early stages in iodine-replete areas, even in endemic prevalence (24-27).

CONCLUSION

On the basis of UI excretion, pregnant women in Isfahan did not have iodine deficiency due to insufficient intake of iodine. Thyroid size did not increase significantly during pregnancy, similar to the finding in iodine-sufficient areas. Despite sufficient iodine intake, study subjects had a relatively high prevalence of goiter. Careful physical examination was as valid as sonography in determination of thyroid size.

ACKNOWLEDGMENT

We thank the women in the prenatal and primary health-care clinics who participated in this research study and the Ebnesina Health Center for measurement of UI excretion.

REFERENCES

1. **Bauch K, Meng W, Ulrich FE, et al.** Thyroid status during pregnancy and post partum in regions of iodine deficiency and endemic goiter. *Endocrinol Exp.* 1986;20:67-77.
2. **Glinoe D.** The regulation of thyroid function in pregnancy: pathways of endocrine adaptation from physiology to pathology. *Endocr Rev.* 1997;18:404-433.
3. **Glinoe D, De Nayer P, Delange F, et al.** A randomized trial for the treatment of mild iodine deficiency during pregnancy: maternal and neonatal effects. *J Clin Endocrinol Metab.* 1995;80:258-269.
4. **Liesenkötter KP, Göpel W, Bogner U, Stach B, Grüters A.** Earliest prevention of endemic goiter by iodine supplementation during pregnancy. *Eur J Endocrinol.* 1996;134:443-448.
5. **Smyth PP, Hetherington AM, Smith DF, Radcliff M, O'Herlihy C.** Maternal iodine status and thyroid volume during pregnancy: correlation with neonatal iodine intake. *J Clin Endocrinol Metab.* 1997;82:2840-2843.
6. **Hetzel BS.** Iodine deficiency disorders (IDD) and their eradication. *Lancet.* 1983;2:1126-1129.
7. **Azizi F, Kalani H, Kimiagar M, et al.** Physical, neuro-motor and intellectual impairment in non-cretinous school-children with iodine deficiency. *Int J Vitam Nutr Res.* 1995;65:199-205.
8. **Kimiagar M, Azizi F, Navai L, Yassai M, Nafarabadi T.** Survey of iodine deficiency in a rural area near Tehran: association of food intake and endemic goitre. *Eur J Clin Nutr.* 1990;44:17-22.
9. **Azizi F, Kimiagar M, Nafarabadi MT, Yassai M.** Current status of iodine deficiency disorders in the Islamic Republic of Iran. *EMR Health Serv J.* 1990;8:23-27.
10. **Delange FM, Ermans A.** Iodine deficiency disorders. In: Braverman LE, Utiger RD, eds. *Werner and Ingbar's The Thyroid: A Fundamental and Clinical Text.* 7th ed. Philadelphia: Lippincott-Raven. 1996: 296-312.
11. **May W, Wu D, Eastman C, Bourdoux P, Maberly G.** Evaluation of automated urinary iodine methods: problems of interfering substances identified. *Clin Chem.* 1990;36:865-869.
12. **Berghout A, Endert E, Ross A, Hogerzeil HV, Smits NJ, Wiersinga WM.** Thyroid function and thyroid size in normal pregnant women living in an iodine replete area. *Clin Endocrinol (Oxf).* 1994;41:375-379.
13. **Glinoe D.** What happens to the normal thyroid during pregnancy? *Thyroid.* 1999;9:631-635.
14. **Berghout A, Wiersinga W.** Thyroid size and thyroid function during pregnancy: an analysis. *Eur J Endocrinol.* 1998;138:536-542.
15. **Glinoe D, de Nayer P, Bourdoux P, et al.** Regulation of maternal thyroid during pregnancy. *J Clin Endocrinol Metab.* 1990;71:276-287.
16. **Glinoe D, Lemone M, Bourdoux P, et al.** Partial reversibility during late postpartum of thyroid abnormalities associated with pregnancy. *J Clin Endocrinol Metab.* 1992;74:453-457.
17. **Krzyczkowska-Sendrakowska M, Zdebski Z, Kaim I, Golkowski F, Szybinski Z.** Iodine deficiency in pregnant women in an area of moderate goiter endemicity. *Endokrynol Pol.* 1993;44:367-372.
18. **Emami A, Shahbazi H, Sabzevari M, et al.** Goiter in Iran. *Am J Clin Nutr.* 1969;22:1584-1588.
19. **Mezosi E, Molnar I, Jakab A, et al.** Prevalence of iodine deficiency and goitre during pregnancy in east Hungary. *Eur J Endocrinol.* 2000;143:479-483.

28 Thyroid Size and Pregnancy, Endocr Pract. 2002;8(No. 1)

20. **Gunton JE, Hams G, Fiegert M, McElduff A.** Iodine deficiency in ambulatory participants at a Sydney teaching hospital: is Australia truly iodine replete? *Med J Aust.* 1999;171:467-470.
21. **Filteau SM, Sullivan KR, Anwar US, Anwar ZR, Tomkins AM.** Iodine deficiency alone cannot account for goitre prevalence among pregnant women in Modhupur, Bangladesh. *Eur J Clin Nutr.* 1994;48:293-302.
22. **Salarkia N, Azizi F, Kimiagar M, Zakeri H, Soheilikhah S, Nafarabadi M.** Monitoring iodine following consumption of iodized salt in Tehrani inhabitants. *Int J Vitam Nutr Res.* 2000;70:65-69.
23. **Keyvani F, Yassai M, Kimiagar M.** Vitamin A status and endemic goiter. *Int J Vitam Nutr Res.* 1988;58:155-160.
24. **Vagenakis AG, Roti E.** Effects of excess iodide: clinical aspects. In: Braverman LE, Utiger RD, eds. *Werner and Ingbar's The Thyroid: A Fundamental and Clinical Text.* 7th ed. Philadelphia: Lippincott-Raven, 1996: 316-327.
25. **Medeiros-Neto G.** Iodine deficiency disorders. In: DeGroot LJ, ed. *Endocrinology.* Vol 1. 3rd ed. Philadelphia: WB Saunders, 1995: 821-833.
26. **Premawardhana LD, Parkes AB, Smyth PP, et al.** Increased prevalence of thyroglobulin antibodies in Sri Lankan schoolgirls—is iodine the cause? *Eur J Endocrinol.* 2000;143:185-188.
27. **Nohr SB, Jorgensen A, Pedersen KM, Laurberg P.** Postpartum thyroid dysfunction in pregnant thyroid peroxidase antibody-positive women living in an area with mild to moderate iodine deficiency: is iodine supplementation safe? *J Clin Endocrinol Metab.* 2000;85:3191-3198.

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.