Hyperthyroidism: Demography and Clinical Criteria in Al – Nasiriyah City (2022)

Dr. Olfet Jabbar Mekki¹ Dr.Mohammed.K.Yosif² Dr. Saad Khalaf Jaber Alrikabi³ Muntathar Saad Khalaf Alrikabi⁴ Correspondent Author :- Prof. Dr. Ali. Abid Saadoon

Abstract:

Hyperthyroidism is a group of illnesses characterized by excessive thyroid hormone production and secretion by the thyroid gland, resulting in thyrotoxicosis, a hypermetabolic state. Diffuse toxic goiter (Graves disease), toxic multinodular goiter (Plummer disease), and toxic adenoma are the most frequent types of hyperthyroidism. Thyroid hormone levels are high in thyrotoxicosis, with or without increased thyroid hormone production.[1,2] Graves disease is the most frequent kind of hyperthyroidism in the United States, accounting for 60-80% of thyrotoxicosis cases. During a 20year period, the annual incidence of Graves disease was determined to be 0.5 cases per 1000 population, with the peak occurrence in adults aged (20-40) years.[13] Toxic multinodular goiter (which accounts for 15-20% of thyrotoxicosis) is more common in iodine-deficient areas. Most people in the United States have enough iodine, while the incidence of lethal multinodular goiter in the US population is lower than in iodine-deficient are as of the world. Thyrotoxicosisis caused by toxic adenoma in (3-5) percent of patients.

Methods: Descriptive, Cross-sectional study Retrospective study The study took place in Thiqar governate , study begun at 14thof march 2022 and ended at 11thof may 2022. The population of Thiqar about 2 million [20] , The study includes the students and staff from Thiqar university, children younger than 15 and elderly above 70 were excluded. Sample size is 430 given by the supervisor, collected through Google form–based Questionnaires published in the official websites of colleges of Thiqar University.

Analysis : Qualitative data had been analyzed by using SPSS (statistical package for social science), were Reliability, frequency, percentage and chi square had been calculated.

Results: A 430 patients suffer from thyroid disease, were recruited in this study that focus on different aspects of assessment, that include their sociodemography clinical character that scored according to Binned score.

1. Assistant lecturer, Pharmacist, Assistant lecturer, Pharmacist, Al-Ameed University -college of pharmacy.-Holly Karbala, <u>olfet-alhasani@alameed.edu.iq</u>

2. M.B.Ch.B_D.O.Family medicine. Thi_Qar Health Directorate

Plastic surgeon at Al-Nasiriyah teaching hospital, 3, burn and reconstructive unite 5th 4. stage student University of Thi-qar medicine college of Correspondent author: Professor community medicine, PhD. Community physician, college of medicine, university of Thigar, ali.abd.s@utg.edu.ig.

Introduction :

Hyperthyroidism is a group of illnesses characterized by excessive thyroid hormoneproduction and secretion by the thyroid gland, resulting in thyrotoxicosis, a hypermetabolic state. Diffuse toxic goiter (Graves disease), toxic multinodular goiter (Plummer disease), and toxic adenoma are the most frequent types of hyperthyroidism. Thyroid hormone levels are high in thyrotoxicosis, with or withoutincreased thyroid hormone production.[1,2]

Etiology :

Graves disease, toxic multinodular goiter, toxic adenoma, and painless thyroiditis are the most common endogenous causes of hyperthyroidism (Table 1) [3-4]. Graves disease, which is the most frequent cause of hyperthyroidism in the United States[5], is an autoimmune disorder. Female sex and familyhistory risk factors . [5,6] Nodules form over time as clonogenic cells replicate frequently, resulting in somatic activating mutations of TSH receptors. [7] A toxic adenoma is a solitary nodule. In contrast to these three illnesses, painless or temporary (silent) thyroiditis results in the death of thyroid follicles and the release of preformed thyroid hormones into the circulation due to an autoimmune process. [8] It has the same clinical presentation as other reasons. According to scintigraphy, its frequency among patients with thyrotoxicosis was 0.5 percent in a Danish study. [9] Childbirth (postpartum thyroiditis) or the use of medications like lithium, interferon alfa, interleukin-2, and amiodarone can cause painless thyroiditis. [10]

Etiology	Mechanism
Most common causes	
Graves disease	Autoimmune process in which antibodies stimulate the TSH receptor leading to overproduction of thyroid hormones
Painless or transient (silent) thyroiditis	Autoimmune destruction of thyroid tissue leading to a release of preformed thyroid hormones
Toxic adenoma (Plummer disease)	Somatic mutation in TSH receptor or Gs alpha gene in a thyroid nodule
Toxic multinodular golter	Expansion of clonogenic cells with an activating TSH receptor mutation
Less common causes	
Drug-induced thyroiditis	Overproduction of thyroid hormones (amiodarone-induced thyrotoxicosis type 1) or release of preformed thyroid hormones (amiodarone-induced thyrotoxicosis type 2, interferon alfa, interleukin-2, or lithium)
Hyperemesis gravidarum	High level of B-hCG stimulates TSH receptors
Postpartum thyroiditis	Variant of painless thyroiditis with the same mechanism, occurring after delivery
Subacute granulomatous (de Quervain) thyroiditis	Painful inflammation of the thyroid gland caused by viral infection, often with fever, triggering a release of preformed thyroid hormones
Rare causes	
Factitious thyrotoxicosis	Surreptitious ingestion of thyroid hormones
Metastatic follicular thyroid cancer	Metastasis of functional follicular thyroid cancer
Struma ovarii	Ectopic thyroid tissue in ovarian dermoid tumor produces thyroid hormones
Trophoblastic tumor or a germ cell tumor	Tumor produces β-hCG, which stimulates thyroid TSH receptors
TSH-secreting pituitary adenoma	Tumor secreting large quantities of TSH, and not responding to thyroxine and trilodothyronine feedback

Factors increase hyperthyroidism developing risk [11] :

A female.
Over 60 years old.
Previously had thyroid issues.
Have a family history of thyroid issues.
Suffer from certain illnesses, such as type 1 diabetes.
Iodine intake is excessive. This can happen if consume too much
Iodine-rich food or take too much iodine-containing drugs.
Pregnant or have recently given birth to a child.

Symptoms of hyperthyroidism can include[12]: palpitations, nervousness, weight loss increase appetite, diarrhea, visual disturbance, thin hair, sweating, menstruation changes, sensitivity heat, sleep disturbance, bulging of eye, goiter and wasting of muscle.

Epidemiology :

Graves disease is the most frequent kind of hyperthyroidism in the United States, accounting for 60-80% of thyrotoxicosis cases. During a 20-year period, the annualincidence of Graves disease was determined to be 0.5 cases per 1000 population, with the peak occurrence in adults aged 20-40 years. [13]

Toxic multinodular goiter (which accounts for 15-20% of thyrotoxicosis) is more common in iodine-deficient areas. Most people in the United States have enough iodine, while the incidence of lethal multinodular goiter in the US population is lower than in iodine-deficient areas of the world. Thyrotoxicosis is caused by toxic adenoma in 3-5 percent of patients.

Iodine intake affects the incidence of Graves disease and toxic multinodular goiter. The United States had higher cases of Graves disease as well as fewer cases of toxic multinodular goiters than parts of the world with lower iodine intake.

Mortality and Morbidity :

Graves disease"s mean rates of malignancy, toxic adenoma, and toxic multinodular goiter, respectively, were 5.9%, 6.5 %, and 12 %. The mean rates for papillary thyroid cancer, micropapillary carcinoma, and follicular thyroid cancer, respectively, were 3.1 percent, 5.1 percent, and 0.8 percent. [14]

Hyperthyroidism in a study by Kim et al, was found to be as a risk factor for ischemic stroke and myocardial infarction in females, people over 50, and non-obese people, regardless of other cardiovascular risk factors. Hyperthyroidism, on the other hand, was not found to have a substantial impact on mortality from cardiovascular events.[15].

Diagnostic tool and approach screening :

Figure 2 [15,16] shows a diagnostic strategy for patients with hyperthyroidism signs and symptoms. In a patient who has a suspected diagnosis of hyperthyroidism but no indication of pituitary dysfunction, the TSH level is the only initial test that is required. If the TSH level is abnormal, more testing is required. Hyperthyroidism is diagnosed by a TSH level that is undetectable. Antithyroid antibodies are raised in Graves' disease and lymphocytic thyroiditis, but they are usually not required to diagnose the condition [17]. Thyroid-stimulating antibody levels can be used to track the

impact of antithyroid medication treatment in Graves' disease patients [18]. The high uptake of Graves' disease is clearly distinguished from the low uptake of thyroiditis, and the scan also offers additional helpful anatomic information[15].

Table 2:



Preventive control strategy :

The American Thyroid Association (ATA) evaluate that were more than 12% of the US population may have a thyroid issue at some point in their lives. Thyroid disease affects around 20 million Americans, with up to 60% of those affected being unaware of their condition. We've already talked about how the symptoms of this disease arise in people as they get older, which makes it difficult to link them to thesickness [19].

However, this does not make the disease any less dangerous, so must do everything possible to prevent it and reduce your risk of cardiovascular problems that often accompany it[19].

can prevent thyroid illness by doing the following things[19]:

- Quit smoking
- Consume less soy
- During x-rays, request a thyroid collar to protect your thyroid gland from radiation.
- Consider supplementing with selenium.
- □ Regular checks

<u>Aim</u> : to study and assess Hyperthyroidism in Thiqar governorate

<u>Justification</u> :

Hyperthyroidism disease from toxic multinodular goiter and permanent are usually occurs in adults. Later normalization of thyroid function with antithyroid medications, radioactive iodine ablation usually is optional as the absolute therapy. Long-term with high-dose antithyroid medication is not recommended. Toxic multinodular goiters and toxic adenomas possibly will continue to grow slowly in size during antithyroid pharmacotherapy, so quick detection is required.

Methodology :

Type of study : Diagnostic study to assess incidence of hyperthyroidism

Study design : Descriptive , Cross -sectional study

Study patterns : Retrospective study

 $\square \qquad \text{Place \& Time of study : The study took place in Thiqar governate, study begun at 14th of march 2022 and ended at 11th of may 2022.}$

Study Population : The population of Thiqar about 2 million [20], The study includes the students and staff from Thiqar university, children youngerthan 15 and elderly above 70 were excluded.

Sampling and Sample size estimation : Sample size is 430 given by the supervisor , collected through Google form – based Questionnaires published in the official websites of colleges of Thiqar University.

Ethical Consideration : Ethical consent had been attained from the scientific committee of community medicine department / College of Medicine / Thiqar University and also from The Associate scientific Dean of the Same College

, and Finally an written consent was taken from each participant .

Definition of Variables :

Hyperthyroidism (overactive thyroid) occurs when your thyroid gland produces too much of the hormone thyroxine. Hyperthyroidism can accelerate your body's metabolism, causing unintentional weight loss and a rapid or irregular heartbeat.

Statistical Analysis : Qualitative data had been analyzed by using SPSS (statistical package for social science), were Reliability, frequency, percentage and chi square had been calculated.

Epidemiological Analysis :

incidence =

population at risk

Results:

A 430 patients suffer from thyroid disease, were recruited in this study that focus on different aspects of assessment, that include their socio-demography clinical character that scored according to Binned score.

Table 3: Distribution according to the sex					
	Sex	Score	Mean of Score	Score (Binned)	
Male	Ν	171	171	171	
	Mean	14.16	1.6275	1.32	
	Std. Deviation	8.494	.22905	.466	
Female	Ν	259	259	259	
	Mean	16.35	1.5447	1.36	
	Std. Deviation	7.387	.19488	.482	
Total	Ν	430	430	430	
	Mean	15.48	1.5776	1.34	
	Std.Deviation	7.909	.21278	.476	
	ANOVA	8.009	16.154	1.012	
	Р	.005	.000	0.315	

Table 4: Distribution according clinical criteria					
		Score	mean of	Score (Binned)	
			score		
Palpitation	Ν	233	233	233	
yes	Mean	19.46	1.4638	1.53	
	Std. Deviation	6.875	.17938	.500	
No	Ν	197	197	197	
	Mean	10.77	1.7122	1.13	
	Std. Deviation	6.310	.16559	.334	
	ANOVA	183.887	219.495	91.949	
	Р	.0001	.0001	0.0001	
Anxiety yes	Ν	284	284	284	
	Mean	17.94	1.5030	1.46	
	Std. Deviation	7.243	.18910	.499	
No	Ν	146	146	146	
	Mean	10.70	1.7227	1.12	
	Std. Deviation	6.914	.17910	.330	
	ANOVA	99.374	134.845	53.512	
	P	.0001	.0001	0.0001	
Weight	N	179	179	179	
loss	11	1/2	177		
yes					
jes	Mean	18.83	1.4899	1.47	
	Std. Deviation	7.311	.19672	.501	
No	N	251	251	251	
110	Mean	13.09	1.6402	1.25	
	Std. Deviation	7.450	.20176	.434	
	Anova	63.005	59.160	24.407	
	P	0.0001	0.0001	0.0001	
Increase appetite	N	199	199	199	
appente	Mean	18.42	1.5063	1.46	
	Std. Deviation	7.063	.19149	.500	
	N	231	231	231	
	Mean	12.95	1.6391	1.24	
	Std. Deviation	7.733	.21141	.429	
	ANOVA	58.018	45.983	24.075	
	P	0.0001	0.0001	0.0001	
Diarrheal disease yes	N	56	56	56	
5.50	Mean	23.63	1.3443	1.75	
	Std. Deviation	7.747	.19115	.437	
No	N	374	374	374	
	Mean	14.26	1.6126	1.28	
	Std. Deviation	7.187	.19310	.451	
	ANOVA	80.988	94.271	52.491	
	P	0.0001	0.0001	0.0001	
Visual defect	N	197	197	197	
	Mean	18.80	1.4791	1.48	
	1vican	10.00	1,4/71	1.40	

	Std. Deviation	7.388	.19398	.501
	Ν	233	233	233
	Mean	12.67	1.6609	1.23
	Std. Deviation	7.230	.19167	.420
	ANOVA	75.167	94.925	32.900
	Р	0.0001	0.0001	0.0001
Hand	Ν	157	157	157
Wetness and				
Profuse				
Sweating				
Yes				
	Mean	21.28	1.4294	1.65
	Std. Deviation	7.022	.19133	.479
No	Ν	273	273	273
	Mean	12.15	1.6629	1.17
	Std. Deviation	6.309	.17448	.375
	ANOVA	192.175	166.192	133.517
	Р	.000	.000	.000
Hair drop	Ν	309	309	309
	Mean	17.42	1.5122	1.42
	Std. Deviation	7.453	.18961	.494
	Ν	121	121	121
	Mean	10.52	1.7446	1.16
	Std. Deviation	6.820	.17455	.365
	ANOVA	78.156	136.398	27.692
	Р	0.0001	0.0001	0.0001
	Ν	430	430	430
	Mean	15.48	1.5776	1.34
	Std. Deviation	7.909	.21278	.476

Score mean of score (Binned) x sex

• Chi square : there is association between incidence of Hyperthyroidism and female patient more than male (female about 63 % of cases are female while47% are male), also there is an association between incidence of Hyperthyroidism and age group 20 - 29 yrs (73 % of cases of Hyperthyroidism is in this age group).

• Incidence = 7.4 per 100,000 inhabitants



Figure (1):

Table 5: Relationship between types of thyroid diseases and clinical criteria of score

	Euothy	yroid Hyperthyroidism		Total	Chi-square, P value			
Palpitation			Yes	110	123	233	76.042^a	
				39.0%	83.1%	54.2 %	.000	
			No	172	25	197		
				61.0%	16.9%	45.8 %		
Anxiety		Yes	154	130	284	47	7.787 ^a	
· ·			54.6%	87.8%	66.0%			
		No	128	18	146			
			45.4%	12.2%	34.0%			
Weight los	s	Yes	94	85	179		23.198 ^a	
	5	2.00	33.3%	57.4%	41.6%		.000	
		No	188	63	251			
			66.7%	42.6%	58.4%			
Loss of app	etite	Yes	107	92	199	22.899 0.0001		
			37.9%	62.2%	46.3%			
		No	175	56	231			
			62.1%	37.8%	53.7%			
Diarrhea		Yes	14	42	56	46.579		
			5.0%	28.4%	13.0%		0.001	
		No	268	106	374			
			95.0%	71.6%	87.0%			
Sweating		Yes	55	102	157	102,312		
			19.5%	68.9%	36.5%	0.0001		
		No	227	46	273			
			80.5%	31.1%	63.5%			
Sleep disturbanc	P	Yes	128	116	244	43.032		
aloval oulle	-		45.4%	78.4%	56.7%		0.0001	
		No	154	32	186			
		110	54.6%	21.6%	43.3%			
Total		Count	282	148	430			
Ioui		Percentage	100.0%	100.0%	100.0%			
		- creanage	100070					

Discussion :

In this study, the total incidence of hyperthyroidism was 7.4 per 100,000 inhabitants per year in Thiqar governorate, also this study shows that there is association between incidence of Hyperthyroidism and female patients more than male (female about 63 % of cases are female while 47% are male), also there is an association between incidence of Hyperthyroidism and age group 20 - 29 yrs (73 % of cases of Hyperthyroidism is in this age group), The main obstacle in this study was time.

The total incidence in Thiqar governorate is less than that of Sweden which is 27.6/100 000 inhabitants per year [21], and that of Denmark (standardized incidenceratio (SIR) 81.6/100 000 per year) [22]. Although not statistically significant, the month of April had the largest number of patients with hyperthyroidism in this study. This supports prior research that have shown no seasonal fluctuation [23], However, this contradicts other findings of a higher frequency of hyperthyroidism in the spring and summer, which have been linked to increased iodine intake [24, 25] or higher temperatures [26, 27]. Iodine supplementation in an iodine-deficient population has been proven in numerous investigations to increase the number of new cases of hyperthyroidism [28–29].

Iodized salt was first introduced in Iran in 1989, The prevalence rate of overt hyperthyroidism was 0.34 percent one year after 75 percent of the population begantaking iodized salt in a cross-sectional study of 6048 randomly selected patients. Thewriters came to the conclusion that there had been no hyperthyroidism epidemic [30]. Before iodine supplementation, no information on the prevalence of hyperthyroidism was known. Through autoregulation, the typical thyroid can handle a moderate amount of iodine [31]. Extra iodine may cause an increase in thyroid hormone synthesis and IIH in a benign multinodular goiter with autonomous functional nodules. Nontoxic multinodular goiter is common in those who don't getenough iodine [32]. The autonomous thyroid nodules are thought to form as a result of one or more of the compensatory processes for low iodide levels. The production of H2O2, which is up-regulated in thyroid follicular cells during ID, is one possible pathway [33].

Conclusion :

The incidence of hyperthyroidism in Thiqar governorate (7.4 per 100,000 inhabitants per year) is in the lower range compared with earlier international reports. 73 % of cases of Hyperthyroidism is in 20 - 29 yrs age group.We have observed clear geographical differences between male and female about 63 % of cases are female while 47% are male .

References :

1.Blick C, Jialal I. Thyroid, Thyrotoxicosis. 2018 Jan. [QxMD MEDLINE Link]. [Full Text].

2.Doubleday AR, Sippel RS. Hyperthyroidism. *Gland Surg.* 2020 Feb. 9 (1):124-35. [QxMD MEDLINE Link]. [Full Text].

3.Bahn Chair RS, Burch HB, Cooper DS, et al. Hyperthyroidism and other causes of thyrotoxicosis: management guidelines of the American Thy- roid Association and American Association of Clinical Endocrinologists [published corrections appear in *Thyroid*. 2011;21(10):1169, and *Thy- roid*. 2012;22(11):1195]. *Thyroid*. 2011;21(6):593-646.

4.Usui T, Izawa S, Sano T, et al. Clinical and molecular features of a TSH-secreting pituitary microadenoma. *Pituitary*. 2005;8(2):127-134.

5. Vanderpump MP. The epidemiology of thyroid disease. Br Med Bull. 2011;99:39-51.

6.Villanueva R, Greenberg DA, Davies TF, Tomer Y. Sibling recurrence risk in autoimmune thyroid disease. *Thyroid*. 2003;13(8):761-764.

7. Gozu HI, Lublinghoff J, Bircan R, Paschke R. Genetics and phenomics of inherited and sporadic non-autoimmune hyperthyroidism. *Mol Cell Endocrinol*. 2010;322(1-2):125-134.

8.Pearce EN, Farwell AP, Braverman LE. Thyroiditis [published correc- tion appears in *N Engl J Med*. 2003;349(6):620]. *N Engl J Med*. 2003; 348(26):2646-2655.

9.Schwartz F, Bergmann N, Zerahn B, Faber J. Incidence rate of symp- tomatic painless thyroiditis presenting with thyrotoxicosis in Denmark as evaluated by consecutive thyroid scintigraphies. *Scand J Clin Lab Invest*. 2013;73(3):240-244.

10. Sweeney LB, Stewart C, Gaitonde DY. Thyroiditis: an integrated approach. *Am Fam Physician*. 2014;90(6):389-396.

11. https://www.hopkinsmedicine.org/health/conditions-and- diseases/hyperthyroidism

12. https://my.clevelandclinic.org/health/diseases/14129-hyperthyroidism

13. Davies TF, Larsen PR. Thyrotoxicosis. Larsen PR et al, eds. Williams

Textbook of Endocrinology. 10th ed. Philadelphia: Saunders; 2003. 374-421.

14. Varadharajan K, Choudhury N. A systematic review of the incidence of thyroid carcinoma in patients undergoing thyroidectomy forthyrotoxicosis. *Clin Otolaryngol*. 2020 Mar 9. [QxMD MEDLINE Link].

15. Fitzgerald PA. Endocrinology. In: Tierny LM, McPhee SJ, Papadakis MA,eds. Current medical diagnosis and treatment. 44th ed. New York: McGraw-Hill, 2005:1102–10.

16. Taylor RB. The 10-minute diagnosis manual: symptoms and signs in the time-limited encounter. Philadelphia: Lippincott Williams & Wilkins, 2000.

17. American Academy of Clinical Endocrinologists. American Association of Clinical Endocrinologists medical guidelines for clinical practice for the evaluation and treatment of hyperthyroidism and hypothyroidism. *Endocr Pract.* 2002;8:457–69.

18. Harper MB, Mayeaux EJ Jr. Thyroid disease. In: Taylor RB. Family medicine: principles and practice. 6th ed. New York: Springer, 2003:1042–52.

19. <u>https://premierheartandvascular.com/prevent-treat-thyroid-disease-heart- health/</u>

20. <u>http://cosit.gov.iq/ar/?option=com_content&view=article&layout=edit&id=1216</u>

21.Incidence of hyperthyroidism in Sweden Article *in* European Journal of Endocrinology · September 2011 DOI: 10.1530/EJE-11-0548 · Source: PubMed.

22. Carle A, Pedersen IB, Knudsen N, Perrild H, Ovesen L, Rasmussen L & Laurberg P. Epidemiology of subtypes of hyperthyroidism in Denmark – a population-based study. European Journal of Endocrinology 2011 164 801–

809. (doi:10.1530/EJE-10-1155).

23. Brownlie BE & Wells JE. The epidemiology of thyrotoxicosis in New Zealand: incidence and geographical distribution in North Canter- bury, 1983–1985. Clinical Endocrinology 1990 33 249–259. (doi:10.1111/j.1365-2265.1990.tb00489.x).

24. Phillips DI, Barker DJ & Morris JA. Seasonality of thyrotoxicosis. Journal of Epidemiology and Community Health 1985 39 72–74. (doi:10.1136/jech.39.1.72).

25. Buchinger W, Semlitsch G, Pongratz R, Harwalik B & Rainer F.Seasonal variations in the diagnosis of hyperthyroidism. Acta Medica Austriaca 2000 27 51–53. (doi:10.1046/j.1563-2571. 2000.00206.x)

26. Ford HC, Johnson LA, Feek CM & Newton JD. Iodine intake and the seasonal incidence of thyrotoxicosis in New Zealand. Clinical Endocrinology 1991 34 179–181. (doi:10.1111/j.1365-2265. 1991.tb00290.x)

27. Westphal SA. Seasonal variation in the diagnosis of Graves' disease. Clinical Endocrinology 1994 41 27–30. (doi:10.1111/j. 1365- 2265.1994.tb03780.x)

28. Connolly RJ 1971 An increase in thyrotoxicosis in southern Tasmania afteran increase in dietary iodine. Med J Austral 12:1268–1271

29. Sc roeder F 1989 Hyperthyreose manifestation vor und nach alimentarer jod- komplettierung. Verlaufsuntersuchungen in Brandenburg 1983–1988. Z gesa- mte Inn Med 44:229

30. Azizi F, Hedayati M, Rahmani M, Sheikholeslam R, Allahverdian S, Salarkia N 2005 Reappraisal of the risk of iodine-induced hyperthyroidism:an epide- miological population survey. J Endocrinol Invest 28:23–29 31. Roti E, Vagenakis AG 2000 Effect of excess iodide: clinical aspects. In: Braver- man LE, Utiger RD, eds. The thyroid. 8th ed. Philadelphia: Lippincott; 316–329 25

32. Knudsen N, Bu'low I, Jørgensen T, Laurberg P, Ovesen L, Perrild H 2000 Goitre prevalence and thyroid abnormalities at ultrasonography: a compar- ative epidemiological study in two regions with slightly different iodine status. Clin Endocrinol (Oxf) 53:479–485

33. Pisarev MA, Ga^{*}rtner R 2000 Autoregulatory actions of iodine. In: Braverman LE, Utiger RD, eds. The thyroid. 8th ed. Philadelphia: Lippincott; 85–9