

# Urinary Iodine Excretion in Egyptian Females with Nodular Goiter

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## Abstract

**Background:** Iodine is needed for the production of thyroid hormone. The best way to determine iodine deficiency across a large population is to measure the amount of iodine in urine sample.

**The aim of this work:** is to measure the iodine excretion in patients with thyroid nodules in comparison to normal control subjects

**Subjects and methods:** Eighty females were chosen from the outpatient clinic of Diabetes and Endocrine Center in Kasr El Aini hospital, Cairo University, with thyroid disorder. History taking, clinical examination, thyroid ultrasound, thyroid function test, urinary iodine excretion was done to all participants

**Results:** showed that urinary iodine excretion in patients with multinodular and single nodule is significantly lowered than in control subjects

**Conclusion:** Our results showed statistically significant lower urinary iodine excretion (22.6 to 30.6 µg/L) in all patients either with single or multiple nodular goiter with hypothyroidism or euthyroid state. Therefore, iodine deficiency contributes to development of thyroid nodules in Egyptian females.

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## Introduction

Thyroid nodules are common finding in general population their prevalence dramatically increase in areas of iodine deficiency (1). A minimum of approximately 70 µg of iodine is therefore needed to produce thyroid hormones in the thyroid gland each day (2).

In adults, mild-to-moderate iodine deficiency appears to be associated with higher rates of more aggressive subtypes of thyroid cancer, increases risk for diffuse goiter, and increases risk of nontoxic and toxic nodular goiter and associated hyperthyroidism (3).

The prediction of iodine intake is difficult. The standard measure of iodine nutrition in a community or country is the median urinary iodine excretion, expressed in micrograms per liter (4).

Four methods are generally recommended for assessment of iodine nutrition in populations: urinary iodine concentration (UI), the goiter rate, serum TSH, and serum thyroglobulin (5).

Control of iodine deficiency thus a critical and achievable development goal for national governments WHO recommended iodization of all food salt in 1952 started to be applied in 1990 (6).

According to the WHO, a median urinary iodine excretion of 100 to 199  $\mu\text{g/L}$  indicates that the iodine intake is adequate. WHO recommendation for adequate daily iodine intake is 150  $\mu\text{g/d}$  for men and nonpregnant, nonlactating women (7).

Different nutritional and environmental factors are responsible for the pathogenesis of goiter, but iodine deficiency is the most important factor. However, little is known about the natural course of benign thyroid nodules in euthyroid patients over time (8).

This study aims to assess of urinary iodine excretion as standard measure of iodine intake in patients with thyroid nodule-s.

## **Subjects and methods**

Eighty subjects were chosen from the outpatient clinic of Diabetes and Endocrine Center in Kasr El Aini hospital, Cairo University, with thyroid disorder from October 2012 to January 2013.

### **Clinical and laboratory procedures**

All patients and control in this study were submitted to the following;

#### **1-History and Examination:**

Detailed medical history including age, sex, symptoms of thyroid disorder suggestive hyper or hypothyroidism.

Complete physical examination with specific concern to thyroid examination.

#### **2-Laboratory investigation**

- 1- Serum concentrations of thyroid stimulating hormones TSH
- 2- Serum concentrations of free T4
- 3- Serum concentrations of free T3
- 4- Urinary iodine excretion
- 5- Thyroid ultrasound

### **Ultrasonography of the thyroid**

Using an HDL supervision 5000 portable ultrasound machine with a standard 5.0 MHz transducer, Longitudinal and transverse scans were performed allowing the measurement of the thickness, the width, and the length of each lobe.

The US pattern of the thyroid parenchyma is recorded for each scan. Variable size was detected, single from multinodule was differentiated.

### **Urinary iodine:**

A morning urine sample was obtained from each subject in a clean cap and stored at – 20 oC till the time of assay of urinary iodine.

### **Statistical analysis:**

Data were statistically described in terms of mean  $\pm$  standard deviation ( $\pm$ SD). Comparison between the study groups was done using Student *t* test for independent samples in comparing 2 groups and one way analysis of variance (ANOVA) test with posthoc multiple 2-group comparisons when comparing more than 2 groups. Correlation between various variables was done using Pearson moment correlation equation for linear relation. *p* values less than 0.05 was considered statistically significant. All statistical calculations were done using computer programs Microsoft Excel 2007 (Microsoft Corporation, NY, USA) and SPSS (Statistical Package for the Social Science; SPSS Inc., Chicago, IL, USA) version 15 for Microsoft Windows.

## **Results**

### **Demographic Data for studied subjects :**

80 female patients with ages range from 20 to 60 year old. 46 patients with thyroid swelling 20 patients with Single nodule, 40 patients with Multinodular goiter ,Compared to 20 healthy control.

60% of patients were hypothyroidism, 40% of patients were euthyroid.

We divided patients into two groups according to thyroid nodule into (single-multiple) determined by ultrasonography.

**Group I:** 20 patients had single nodule **group II:** 40 patients had multiple nodules of thyroid gland. **Group III:** Control group.

According to thyroid function, all patients of single nodule (group I) were hypothyroidism, while patients of multiple nodular goiter divided into (**group IIa**) 28 patients were hypothyroidism and (**group IIb**) 12 patients were euthyroid.

All hypothyroidism patients were first discovered not on replacement therapy.

Thyroid function of different studied groups shown in table (1).

**Table 1: Thyroid function serum free T<sub>4</sub>, free T<sub>3</sub> and TSH in the studied groups**

	Number of pts	FreeT <sub>4</sub> pmol/l	FreeT <sub>3</sub> pmol/l	TSH mU/l
		Mean± SD	Mean± SD	Mean± SD
Single nodule group I	20	0.9±0.09	1.9 ±0.2	12.2 ±3.7
Multinodular group II a	28	0.9±0.16	1.7±.5	22.8 ± 11.7
Multinodular Group II b	12	1.3 ±.2	3.2 ±.3	1.4 ±.6
Control group III	20	1.2 ± 0.2	3.3 ± 0.3	1.5 ± 0.7

The mean value of urinary iodine excretion in group I is 2.6±4.7 µg/dL it is highly statistically significant lower than in group III (control group) with p value < 0.001.

Also, the group II had highly statistical significant lowered than group III with p value < 0.001.

Even the subgroup of group II, group IIa and group IIb showed lower urinary iodine excretion than group III with p value < 0.001 for each group.

But no statistical significant difference in urinary iodine excretion between group I and group II. Comparison of the laboratory characteristic between the urinary iodine excretion and study groups shown in table (2).

**Table 2: Comparison of the laboratory characteristic between the urinary iodine excretion and study groups**

	Single nodule	Control	Multinodular IIa	Control	Multinodular IIb	control
<b>U. iodine <math>\mu\text{g/dL}</math></b>						
<b>Mean<math>\pm</math>SD</b>	22.6 $\pm$ 4.7	119.2 $\pm$ 7.3	22.9 $\pm$ 5.9	119.2 $\pm$ 7.3	30.6 $\pm$ 2.8	119.2 $\pm$ 7.3
<b>P value</b>	0.000		0.000		0.000	

\*P<0.5 Significant

\*P<0.1 Highly Significant

Correlation between thyroid function and urinary iodine excretion in group IIa multinodular hypothyroid cases which shows negative correlations between TSH and urinary iodine when (shown in Fig. 1).



**Fig. 1: Correlation between urinary Iodine level and thyroid function within multinodular hypothyroid cases.**

Correlation between thyroid function and urinary iodine excretion in group IIB multinodular euthyroid cases which shows no correlations between TSH, free T4, free T3 and urinary iodine (shown in table 3).

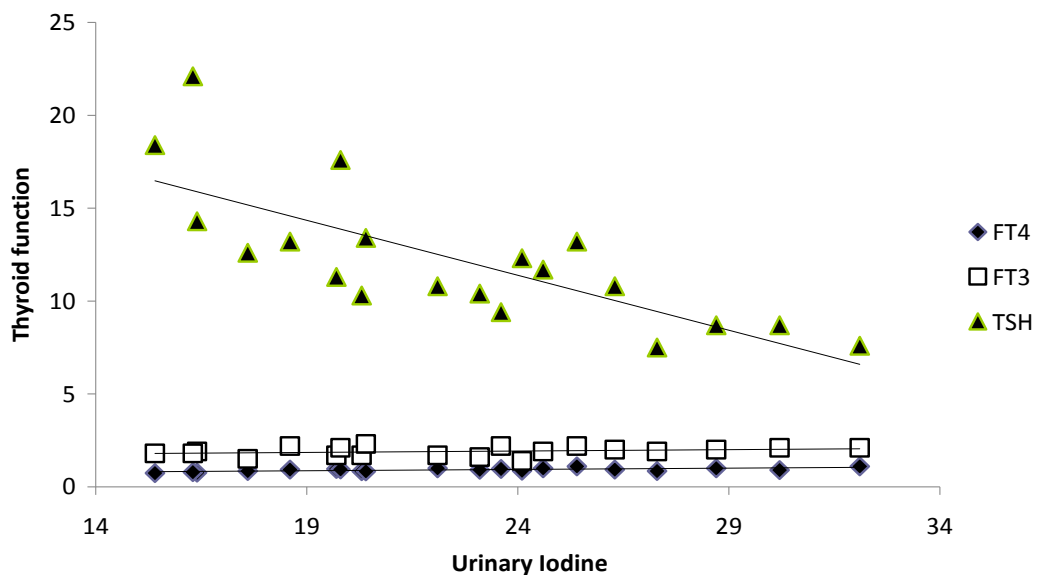
**Table 3: Correlation between thyroid function and urinary iodine excretion in group IIB**

		FT4	FT3	TSH
U.Iodine µg/dL	P	-0.013	0.023	-0.839
	r	0.969	0.942	0.001

Correlation between thyroid function and urinary iodine excretion in group I single nodule cases which shows negative correlations between TSH and urinary iodine and positive correlation between free T4, free T3 and urinary iodine (shown in table 4, Fig. 2).

**Table 4: Correlations between thyroid function, urinary iodine excretion in (group I)**

		FT4	FT3	TSH
U.Iodine µg/dL	P	0.666	0.283	-0.763
	r	0.001	0.226	0.000



**Fig: 2. Correlation between urinary iodine level and thyroid function within single nodule cases**

Our results showed statistically significant lower urinary iodine excretion (22.6 to 30.6 µg/L) in all patients either with single or multiple nodular goiter. Also, in those patients whether hypothyroidism or euthyroid state.

## Discussion

According to the WHO, a median urinary iodine excretion of 100 to 199 µg/L indicates that the iodine intake is adequate. WHO recommendation for adequate daily iodine intake is 150 µg/d for men and nonpregnant, nonlactating women (7).

The prevalence of thyroid nodules in the general population varies according to the method of detection in use. In large population studies, about 5% of subjects have palpable thyroid nodules. The thyroid ultrasonography (US) shows a 13-50% prevalence in the general population (9).

Thyroid nodules are commonly benign. The reported prevalence of nodular thyroid disease depends on the population studied and the methods used to detect nodules. Nodule incidence increases with age, and is increased in women, in people with iodine deficiency, and after radiation exposure (10).

Different nutritional and environmental factors are responsible for the pathogenesis of goiter, but iodine deficiency is the most important factor. However, little is known about the natural course of benign thyroid nodules in euthyroid patients over time (8).

We divided patients into two groups according to number of thyroid nodule. All patients had thyroid nodules determined by ultrasonography. Group I 20 patients had single nodule and group II 40 patients had multiple nodules of thyroid gland. Sub-classification of group II into two groups, according to thyroid function. All patients of single nodule (group I) were hypothyroidism, while patients of multiple nodular goiter divided into (group IIa) 28 patients were hypothyroidism and (group IIb) 12 patients were euthyroid. All hypothyroidism patients were first discovery and without replacement therapy.

Our results showed statistically significant lower urinary iodine excretion (22.6 to 30.6 µg/L) in all patients either with single or multiple nodular goiter. WHO Global Database on Iodine Deficiency, Median urinary iodine (mcg/L) & Moderate deficiency: 20–49 (11)

Also, in those patients whether hypothyroidism or euthyroid state. Severe iodine deficiency results in adverse health outcomes and remains a benchmark for understanding the effects of developmental hypothyroidism iodine deficiency.

In Africa, dietary iodine deficiency is the major determinant of thyroid pathology, resulting in a spectrum of iodine deficiency disorders, including goitres, hypothyroidism and mental retardation (12).

In spite of using iodinated salt dietary assessment of iodine intake is challenging and the large day to day variation makes it difficult to quantify adequate intake. However dietary data can be used to identify the most significant food sources of iodine. This information is useful to design or adapt iodine intervention strategies (13).

Chronic iodine deficiency increases the TSH concentration and produces a thyroid hormone pattern consistent with subclinical hypothyroidism. The subclinical hypothyroidism may be associated with cardiovascular disease risk factors (14) observed that median urinary iodine excretion was 51 mg/L in overt hypothyroidism patients and 84 mg/L in subclinical hypothyroidism. The values were 316 mg/L and 221 mg/L in overt and subclinical hyperthyroidism, respectively. In adult subjects the severe iodine deficiency can be associated with mental disorders due to the direct side effects of hypothyroidism occurred by lack of iodine. The clinical manifestation of iodine deficiency show itself with psychological disorders in adult subjects. The status of iodine within blood can be evaluated through measurement of urinary iodine level and the low urinary concentration is an indicative of hypothyroidism.

The association between iodine status and the prevalence of goiter and thyroid nodules has been well established but the extent to which different iodine intake levels influence the incidence of goiter and thyroid nodules is unclear (15).

In our study, we found that all patients with thyroid nodule-s had significant lowered urinary iodine excretion than healthy controls.

Iodine deficiency is the most important factor in the etiology of nodular goiter. Insulin-like growth factor-I is overexpressed in thyroids in severely iodine deficient areas (16).

Urinary iodine concentration data are extrapolated to iodine intakes, adjusted for intra individual variation then interpreted using the estimated average requirement cut point model.



$$\text{Iodine intake} = \text{UIC}(\mu\text{g}) / 0.92 \times 0.009\text{L} \times \text{Kg} \times 24 \times \text{weight (kg)} \quad (13)$$

The thyroid adapts to low intakes of dietary iodine by marked modification of its activity, triggered by increased secretion of TSH by the pituitary. TSH exerts its action at the transcription level of the NIS(sodium iodine transporter) gene. If iodine intake remains below normal limits the iodine content of the thyroid is depleted, and many individuals develop goiter. Initially, goiters are characterized by diffuse, homogeneous enlargement, but over time, nodules often develop (17). During follicular cell proliferation there is a tendency to mutations leading to multifocal autonomous growth and function. In populations with mild and moderate iodine deficiency, such multifocal autonomous thyroid function is a common cause of hyperthyroidism in elderly people, and the prevalence of thyroid enlargement and nodularity is high (17).

Cakir et.al, 2011, observed that, iodine deficiency was associated with an increase in thyroid nodule volumes. The urinary iodine excretion was  $<50 \mu\text{g/L}$ . An increased level of iodine intake is associated with a decreased thyroid nodule volume. They have emphasized the importance of a critical level of urine iodine excretion that is related with thyroid nodule enlargement. Patients with thyroid nodule volumes related to iodine deficiency can be evaluated and if needed, iodine supplementation can be recommended by an iodine-rich diet (9).

Goiter prevalence and the median urinary iodine concentration in a population usually define endemic iodine deficiency. In addition to goiter prevalence and median urinary concentration, thyroid stimulating hormone (TSH) and thyroxine have been used as iodine deficiency indicators (18).

Both iodine intake levels below and above the recommended interval are associated with an increase in the risk of disease in the population. Optimally, iodine intake of a population should be kept within a relatively narrow interval where iodine deficiency disorders are prevented, but not higher. Monitoring and adjusting of iodine intake in a population is an important part of preventive medicine (17).

## Conclusion

In our study, an iodine deficiency was observed in all studied patients with thyroid nodule-s whether euthyroid or hypothyroidism inspite of using iodized salt. From these results were concluded that reduced urinary iodine excretion in patients is an index of iodine status. In Egyptian females, therefore, iodine deficiency contributes to development of thyroid nodules and hypothyroidism.

## Recommendation

In spite of using iodized salt periodic measurement of population iodine status is of value. The challenge is to choose and apply monitoring indicators that are valid, reliable while keeping minimal cost.

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