Original Article

Thyromegaly and iodine nutritional status in a tertiary care hospital in South India

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ABSTRACT

Aim and Objectives: 1. To assess the iodine nutritional status in patients with goiter by measuring urinary iodine excretion. 2. To compare the iodine nutritional status with the thyroid function and correlate with the type of thyroid disease. **Study Design:** Case control study. **Materials and Methods:** Three hundred patients with goiter and one hundred euthyroid healthy non-goitrous volunteers were included in this study. **Results and Conclusions:** All patients had elevated urinary iodine suggesting excess iodine intake and absence of iodine deficiency. Complications known to be associated with excess iodine, viz., benign goiter (35%), iodine-induced hyperthyroidism or thyrotoxicosis (34%), thyroiditis (16%) and cancer of thyroid (15%) have been observed in this study. Therefore, continued supplementation of edible salt fortified with iodine should be monitored carefully, and supplementation programs should be tailored to the particular region.

Key words: Goiter, iodine-induced hyperthyroidism, thyroiditis, thyrotoxicosis, urinary iodine

Introduction

Since the historical times of the nonviolent Salt March to Dandi in 1930, India has come a long way in the area of salt production, now providing for millions of its people, salt fortified with iodine under the universal salt iodization (USI) program.

Iodine is an essential part of thyroid hormones, which participate in the normal mental and physical development and maintenance of homeostasis in humans. They regulate many key biochemical reactions, especially protein synthesis and enzymatic activity. Major target organs are the developing brain, muscle, heart, pituitary and kidney.[1]

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The sources of dietary iodine are water, food and the iodized salt. Iodine deficiency affects an approximate two billion people worldwide and is estimated to be the leading preventable cause of mental retardation. The recommended daily intake of Iodine for different age groups is given in Table 1. Decreased consumption of iodine may result in a spectrum of iodine deficiency disorders (IDD), including stunted physical growth, deafness, squint, abortion, stillbirths, impaired mental abilities, neonatal cretinism and hypothyroidism and its complications. This in turn translates into significant morbidity, decreased quality of life and reduced economic productivity in the community at large.

Table 1: WHO recommendations for iodine intake in different age groups[2]

Age or population group	Iodine intake in micrograms per day (µg/day)
Children 0-5 years	90
Children 6-12 years	120
Adults >12 years	150
Pregnancy	250
Lactation	250

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For assessing the impact of the USI program, and to ensure sustainability, the World Health Organization has recommended the measurement of urinary iodine as the standard method to assess the dietary intake of iodine by the community. Urinary iodine excretion is a good marker of dietary intake of iodine and, therefore, is the index of choice for evaluating the degree of iodine deficiency and of its correction.[3]

Iodine excess

Just as low dietary intake can result in a number of thyroid related problems, so can excess intake. Excess intake has been found to be associated with iodine-induced hyperthyroidism (IIH) and autoimmune thyroiditis, due to the stimulation of proliferation of thyroid follicular cells and thereby increasing the chance of mutations.[4] This is all the more so if iodine deficiency is corrected rapidly and drastically as in endemic areas. IIH has been reported in almost all iodine supplementation programs.[5] The outbreak in Tasmania in the late 1960, resulted in an increase in the incidence of IIH from 24/100,000 to 125/100,000 in a span of 3-4 years due to excess iodine supplementation through salt, bread and milk.[5]

Iodine-induced hyperthyroidism (IIH) can also manifest in the form of goiter. Suzuki *et al.* have reported in their study the occurrence of endemic goiter in a coastal area of Japan due to excess intake of iodine rich seafood.[6]

Thyroid cancer and excess iodine: In animals, the chronic stimulation of the thyroid by TSH is known to produce thyroid neoplasm. Vigneri *et al.* have reported Iodine supplementation to be accompanied by a change in the epidemiological pattern of thyroid cancer with an increased prevalence of papillary cancer discovered at autopsy.[7]

Thyroiditis: Iodization is known to produce destruction of the thyroid follicles resulting in thyroiditis. Animal studies have shown that high iodine intake can initiate and worsen infiltration of the thyroid by lymphocytes. Excess iodine triggers the immune system and alters the immunological status resulting in the production of antibodies that gradually destroys the thyroid glandular tissue.

Post-iodization studies by Indian researchers have also observed the association of iodine excess with the development of goiter, hyperthyroidism and thyroiditis. In the study by Amar K. Chandra and Indrajit Ray, on school children in the age group of 6-15 years, a total goiter rate of 21.63% was observed in the absence of iodine deficiency.[8]

In a similar study among 961 school children in North East India, a total goiter rate of 34.96% was identified even though there was no biochemical iodine deficiency.[9]

Two independent studies from the All India Institute of Medical Sciences, New Delhi, by Kochupillai *et al.*, describe the prevalence of residual goiter and autoimmunity with an excess iodine status. Hashimoto's thyroiditis and focal lymphocytic thyroiditis were reported among goitrous healthy young girls consuming adequate iodine and also among school children respectively. In both the studies, the role of other goitrogens was suggested to be involved or associated with the occurrence of goiter and autoimmunity.[10,11]

In the Kangra Valley of Himachal Pradesh where originally iodine deficiency was found to be the causative factor for endemic goiter by Ramalingaswamy *et al.*, a post-iodization study conducted by Kapil Umesh *et al.* also reported a total goiter rate of 19.8% among 6939 school children despite an adequate iodization.[12] Another recent report by Kapil Umesh, highlights the high goiter prevalence in regions with successful salt iodization program.[13]

Even though the USI program has almost eliminated iodine deficiency from goiter endemic areas, goiter prevalence has not been eliminated. In fact, the occurrence of thyroid related disorders have shown a steady upward trend in the past decade. This is best exemplified in the data from the Department of Endocrine Surgery, of a tertiary care hospital in South India [Figure 1]. The common thyroid disorders observed in this hospital are:

1. Goiter (solitary nodule, multinodular, diffuse) in various physiological states of thyroid dysfunction.
2. Thyroiditis.
3. Cancer of thyroid.

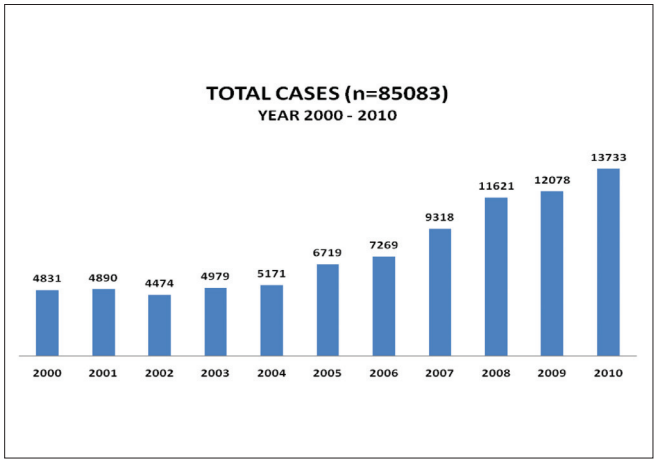

Figure 1: Patient statistics of department of endocrine surgery of a tertiary care hospital in South India

Despite the intake of iodized salt, the increasing occurrence of thyroid disorders has prompted us to investigate the iodine status among these patients and to correlate with the thyroid function.

Aims and objectives

1. To assess the iodine nutritional status in patients with goiter by measuring urinary iodine excretion.
2. To compare the Iodine nutritional status with the thyroid function and correlate with the type of thyroid disease.

Inclusion criteria

Patients with enlargement of thyroid gland were included in the study. All patients were consuming iodized salt as non-iodized salt is not available in the retail market.

Exclusion criteria

Patients with other co-morbid conditions-Tuberculosis patient on anti-TB treatment and patients with multiple endocrine neoplasia were excluded from the study.

Materials and Methods

Type of study: Case-control study

A total of three hundred patients with goiter were included in this study and their urinary iodine excretion and thyroid hormone status were analyzed. One hundred non-goitrous healthy age and sex matched thyroid volunteers were the control group.

All the patients with goiter underwent fine needle aspiration cytology (FNAC) to diagnose the pathology of the goiter. Thyroid hormones (TSH, fT4, fT3 by CLIA method) and urinary iodine[14] were measured in all the patients. If the FNAC report was suggestive of thyroiditis, the antibody titres - antimicrosomal antibodies (TPO) and antithyroglobulin antibodies (ATG) - were also measured (by CLIA method). Similarly those patients, who had toxic level of thyroxin, underwent Tc99 scan and uptake of thyroid for further confirmation.

Results

The mean age of the patients was 40.14 years and there were 38 numbers of males and 262 number of females. The following types of goiter, based on anatomical classification, were identified among the 300 patients:

Solitary thyroid nodule	46
Multinodular goiter	216
Diffuse goiter	34
Ectopic thyroid	4

Control group

The control group was all in euthyroid state without any thyroid glandular enlargement. The mean urinary iodine excretion was 160.95 μg/L, suggesting adequate dietary intake of iodine. This value also falls within the median urinary excretion of 100-200 μg/L.

Based on the thyroid hormone profile, FNAC report and antibody titres, the 300 patients were classified into four groups [Table 2].

Group I (thyroiditis)

The mean urinary iodine excretion for this group of patients was 247.41 μg//L, which is above the median excretion of 100-200 μg/L. This group was further sub-divided into three groups based on the thyroid hormone profile [Table 3]. All patients in the three sub-groups had urinary iodine excretion above the median excretion value.

Group II

Comprises of thyrotoxic patients and the mean UIE was 279.12 μg/L, TSH 0.09 μIU/ml, fT3 12.72 pg/ml and fT4 was 4.9 ng/dl [Table 4].

Group III

Comprising of cancer thyroid (predominantly Pap Ca) had UIE of 272.82 μg/L. This group was also subdivided into three sub-groups based on thyroid hormone profile [Table 4]. The hyperthyroid patients in this group had maximal excretion of iodine in urine.

Group IV (benign goiter)

Comprised of individuals with benign goiter, i.e. without either thyroiditis or thyrotoxicosis [Table 5]. The UIE was

Table 2: Patients with goiter presenting as various disorders of thyroid

	Disorder	No. of patients	Mean UIE (μg/L) Ref range (100-200 μg/L)
Group 1	Thyroiditis	103	247.41
Group 2	Thyrotoxicosis	47	279.12
Group 3	Cancer of thyroid	45	272.82
Group 4	Benign goiter	105	213.53

Table 3: Thyroiditis group

Physiological state	No. of patients	UIE (μg/L) Ref range (100-200)	TSH (μmicro IU/ml) (Ref 0.35-5.5)	fT3 (pg/ml) Ref 2.0-4.4	fT4 (ng/dl) Ref 0.8-2.0
Euthyroid	36	245.44	2.40	3.1	1.5
Hypothyroid	34	228.73	54.89	1.2	0.93
Hyperthyroid	33	268.08	0.01	6.8	3.1

Table 4: Cancer thyroid patients

Physiological state	No. of patients	UIE (µg/L) Ref (100-200)	TSH (µmicro IU/ml) Ref 0.35-5.5)	fT3 (pg/ml) Ref 2.0-4.4	fT4 (ng/dl) Ref 0.8-2.0
Thyroid	34	249.0	2.14	3.2	1.06
Hypothyroid	7	257.42	49.63	1.4	0.62
Hyperthyroid	4	311.25	0.01	9.8	4.4

Table 5: Benign goiter group

	No. of patients	UIE (µg/L) Ref 100-200	TSH (µmicro IU/ml) Ref 0.35-5.5	fT3 (pg/ml) Ref 2.0-4.4	fT4 (ng/dl) Ref 0.8-2.0
Thyroid	91	240.78	1.86	3.0	1.4
Hypothyroid	14	186.28	55.99	1.5	0.8

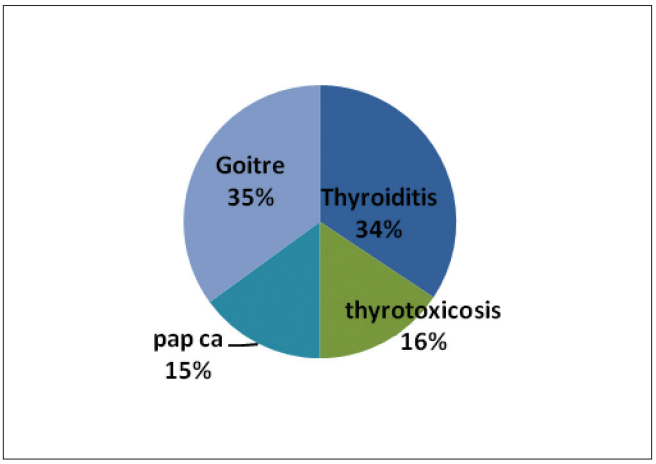

Figure 2: Diagram showing percentage of the various thyroid disorders observed in this study

213.53 µg/L. There were two sub-groups: Thyroid and hypothyroid.

Observation and Discussion

1. One-third of the cases comprise of Thyroiditis and another one-third comprises of benign goiters, the remaining is almost equally distributed between Thyrotoxicosis and cancer Thyroid.
2. Urinary iodine excretion is above the median excretion value (100-200 µg/L) in all the patient groups, suggesting no dietary deficiency. When compared with the control group, there seems to be an excess of urinary iodine excretion suggesting excess intake causing deranged metabolism of the thyroid gland.
3. Maximum UIE is observed in patients with cancer thyroid and thyrotoxicosis, followed by thyroiditis.
4. Of the 105 cases of Group IV (benign goiter), 91 patients (87%) were Thyroid state, while 14 patients (13%) had overt hypothyroidism as observed from the thyroid hormone status.

Increased excretion of iodine in the urine is the common factor among all the patients with thyroid disorders. In this study, the urinary iodine excretion of all the patients is above the median excretion value of 100-200 µg/L. As the urinary excretion reflects the dietary intake, the study population does not have any nutritional deficiency, while on the other hand there appears to be an excess of iodine intake, as is evident from the increased excretion.

All the complications known to be associated with excess iodine, viz., goiter (35%), iodine-induced hyperthyroidism or thyrotoxicosis (34%), thyroiditis (16%) and cancer of thyroid (15%) have been observed in this study.

High iodine intake may trigger and exacerbate autoimmune thyroiditis, increasing the likelihood of overt hypothyroidism.

Two types of antibodies have been documented in thyroiditis-function stimulating/blocking and growth stimulating/blocking. Depending on the type of antibodies produced, the patient may present with either hypothyroidism or hyperthyroidism with or without goiter.

Children are more likely to develop thyroiditis leading to hypothyroidism, requiring lifelong thyroxin replacement, while in adults (above 20 years of age), thyrotoxic goiter is the common presentation, and they require expensive treatment measures involving medical, surgical or radio iodine treatment for control of toxicity apart from investigative procedures. Those undergoing surgery or radio iodine treatment will ultimately develop hypothyroidism, and will need lifelong thyroxin replacement.

Our study population comprises of adults (above 20 years of age) and hence the number of patients with benign goiter and thyrotoxicosis are maximum than Thyroiditis, which is more commonly seen in children.

Papillary carcinoma of thyroid is the predominant form of malignancy in our study which is also reported in studies with excess iodine.

Conclusion

Iodine is adequately available in the coastal regions of our country and Tamil Nadu with a large coastal area, the chances of iodine deficiency is much less. There is no iodine deficiency among the patients, and the USI program has also eliminated the iodine deficiency as reported by many

studies. Iodine excess is the hall mark that is observed among our patients in this study. All the complications known to be associated with excess iodine, viz., goiter (35%), iodine-induced hyperthyroidism or thyrotoxicosis (34%), thyroiditis (16%) and cancer of thyroid (15%) have been observed in this study [Figure 2].

Therefore, continued supplementation of edible salt fortified with iodine should be monitored carefully, and supplementation programs should be tailored to the particular region.

Chronic exposure to excess iodine, which may ultimately create a generation of thyroid cripples in South India should be prevented by careful monitoring and regular follow-up of iodine supplementation. Uniodised salt should also be available in the market so that patients with thyroiditis, thyrotoxicosis and cancer of thyroid can be treated effectively.

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