Original Article

Assessment of iodine nutritional status in school children concerning autoimmune thyroiditis in Tamil Nadu, India

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ABSTRACT

Objective: To eliminate iodine deficiency disorders (IDD) in children, the Indian government implemented a universal salt iodization program more than 3 decades ago. Recently, it was identified that excess iodine intake could lead to autoimmune thyroiditis in children. We aimed to measure the level of iodine excretion as well as thyroid profiles as an option to identify autoimmune thyroiditis in school-going children. **Materials and Methods:** A total of 111 children between the ages of 6 and 12 years were subjected to a blood test to measure free thyroxine, thyroid-stimulating hormone, anti-thyroglobulin, and anti-thyroperoxidase levels. The children were categorized into control and case groups based on the clinical outcome. Biochemical analysis, thyroid gland assessment, fine-needle aspiration cytology (FNAC), and ultrasound sonography were performed. Urinary iodine excretion (UIE) level was measured by the Sandell-Kolthoff reaction method. **Results:** Approximately 90% of the study population was identified with a higher level of iodine in urine. A positive correlation was observed between the UIE, anti-TPO, and anti-TGO titers among the cases. Out of 61 cases, 21 children showed overt hypothyroidism (34.43%) and the remaining were identified with subclinical thyroid symptoms (65.57%). FNAC confirmed autoimmune thyroiditis in 43 children within the case group. **Conclusion:** Excess iodine intake may trigger thyroid autoimmunity in children. Children who are having higher levels of anti-thyroid antibodies are at risk of developing thyroid dysfunction if they consume more than the required iodine for metabolism. High levels of iodine in the urine of control children indicate that the IDD program in our nation is running successfully.

Key words: Iodine, Autoimmune thyroiditis, Urinary iodine level

Iodine is an inevitable constituent of thyroid hormones and plays an essential role in the functioning of a healthy thyroid [1-3]. Iodine deficiency induces a wide spectrum of iodine deficiency disorders (IDDs) and becomes a major causative problem for brain damage in children [4]. So far, iodization of salt is considered as the main way to eradicate IDDs within a population [2].

The Government of India has implemented National IDD Control Programme (NIDDCP) through Universal Salt Iodization Recommendation from 1962 onward [4,5]. As a result till date, 92% of the Indian population consume iodized salt. It was observed that the pattern of thyroid diseases undergoes definitive beneficial changes when a cohort is supplemented with iodine. On the other hand, many population-based studies from the west observed an increase in juvenile autoimmune thyroiditis (JAT) within a population that has been supplemented with an iodine diet [6]. Autoimmune thyroiditis has a higher prevalence in those societies who are having a higher intake of an iodine-rich diet [7]. So far, there were only a few reports published from the different regions of India, regarding the impact of excessive iodine on thyroid autoimmunity [8,9].

Since the Indian population has diversity in food habits based on geography, we decided to perform a study to analyze iodine intake level by measuring the urine iodine excretion level (UIE) to find the prevalence of autoimmune thyroiditis in children residing at Tamil Nadu coastal areas (Chennai). We also try to find a correlation between the UIE level and thyroid parameters such as free thyroxine (T4), triiodothyronine (T3), thyroid-stimulating

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hormone (TSH), thyroperoxidase, and thyroglobulin antibodies (anti-TPO and anti-TG) among children.

MATERIALS AND METHODS

A case–control study was performed over a period of 3 months. Madras Medical College, Chennai, Tamil Nadu, India, Ethical Review Board approved the study (EC Reg. no. ECR/270/Imt. TN), and written informed consent was obtained from the parents/guardians.

The study included 111 children between the ages of 6 and 12 years. Children attending the Department of Paediatric Endocrinology, Institute of Child Health and Hospital for Children, Egmore, Tamil Nadu, India, with complaints of swelling in the neck, difficulty in swallowing, short stature, obesity, constipation, and poor mental development were grouped together as cases. All were newly reported cases not receiving any treatment for thyroid disorders (n=61 children). Children studying in a school situated near Egmore, Tamil Nadu state, India, were grouped under the control category (n=50 children). Children with proven congenital hypothyroidism, IDD, other endocrine disorders, and having a history of taking iodine-containing medications such as cough suppressants were excluded from the study.

The sample size of the study was calculated as 45 children per group with the formula n=(Zα+Zβ)2 × 2×S2/d2 where, Zα = 1.96 and Zβ = 1.28 with S2 = 79.6 with absolute precision of d2 = 52. However, we collected the data from 61 children under the case group 50 children under the control group. The z-score is the number of standard deviations a given proportion is away from the mean; d is the acceptable standard error of the mean.

Children were subjected to a blood test to measure free T4, TSH, anti-TG, and anti-TPO levels. Free T4 and TSH levels were measured by the enzyme immune assay method [10]. Values 47-128 pM/L for T4 and 0.5–5 μIU/mL for TSH were considered as standard [11]. Electrochemiluminescence assay was performed to measure anti-TG and anti-TPO values. Values above 34 IU/L for anti-TPO and 115 IU/L for anti-TG were considered positive [12]. Body mass index (BMI) was calculated based on the formula – Weight in kilograms/Square of Height in meters.

Assessment of thyroid gland was done and was graded according to goiter classification system proposed by the World Health Organization (WHO). Ultrasound analysis of the thyroid gland was performed for the case group and was categorized as per the Neu's reference criteria [12]. Based on the clinical data obtained from the hospital, the case population was divided into two categories: (a) The children with thyroiditis and (b) with thyromegaly conditions. All the children with goiter underwent fine-needle aspiration cytology (FNAC) analysis. The stained slides were blindly reported by a cytopathologist who had no access to clinical and serological data. The criteria adopted for the diagnosis of autoimmune thyroiditis include the presence of lymphocytic infiltrate, diminished colloid, and minimal to moderate follicular destruction with or without cell change [13].

Urine samples were taken from all the children (5 mL) for the determination of UIE level using the Sandell-Kolthoff reaction. Spot urine samples were collected in a wide-mouthed plastic container with tight screw tops and kept in a refrigerator at 4°C after the addition of one drop of toluene. Urine was digested with ammonium persulfate to get rid of interfering substances. Iodide level was measured based on its catalytic action on the reduction of ceric ammonium sulfate (yellow) to the cerous form (colorless) and the oxidation of arsenite to arsenate [8].

According to the UIE values, children were grouped under severe iodine deficiency (<20 μg/L) moderate iodine deficiency (20–49 μg/L), mild iodine deficiency (50–99 μg/L), adequate iodine store (100–199 μg/L), iodine above the requirement status (200–299 μg/L), and iodine excess which can cause adverse side effects (>300 μg/L) [14]. The epidemiological criteria used to assess the iodine nutrition status were followed as per the WHO, United Nations International Children's Emergency Fund (UNICEF), and the International Council for Control of IDD (ICCIDD) recommendations.

The primary data were analyzed using SPSS statistics software for Windows version 21. Descriptive statistics such as mean and standard deviation were calculated for continuous variables and frequency and percentages were for categorical variables. The difference between the two groups was assessed by the Student's t-test and Mann–Whitney U-test for quantitative data and Chi-square test for qualitative data with 5% α. The relationship between the continuous variables was calculated by Spearman correlation with a significant value of <0.0001.

RESULTS

The study consists of 61 children in the case category and 50 children in the control category. The case group was noted with the presence of more female candidates (n=48) and represents 78.68% of the case population. The baseline demographic and biochemical parameters of the study population are mentioned in Table 1 and the clinical description in Table 2. The division of the study population as per the iodine status is given in Table 3.

Within the case group, 41 children showed excessive UIE values and represent 67.21% of the total case population. Within the case group, the mean UIE value was 495.65 for the autoimmune

Table 1: Description of the study population

Variables	Mean±SD		
	Control (n=50)	Case (n=16)	p value
Age (years)	7.52±0.646	9.46±2.24	
BMI	14.16±2.28	15.99±1.73	
FT4 (pM/L)	1.38±0.13	37.96±32.85	0.0001
TSH (μIU/Ml)	2.50±1.12	33.014±108.23	0.0001
Anti-TPO (1 U/L)	21.09±39.94	332.32±474.14	0.0001
Anti -TGA (1 U/L)	23.68±40.09	179.98±217.39	0.0001
UIE (μg/L)	668.37±231.80	440.07±282.62	0.0001

BMI: Body mass index, FT4: Free thyroxine, TSH: Thyroid-stimulating hormone, TPO Ab: Thyroperoxidase antibody, TG Ab: Thyroglobulin antibody, UIE: Urinary iodine excretion level

Table 2: Clinical description of case population (n=61)

Variables	Category	n	%	Mean±SD	p value
Thyroid function test	Overt	21	34.43	428.32±279.41	0.001
	Subclinical hypothyroidism	40	65.57	446.24±287.63	
Autoimmunothyroiditis	0	18	29.51	307±233.99	0.001
	1	43	70.49	95.61±288.26	
Ultrasonography	Not done	2	3.28		0.001
	Thyroiditis	25	40.98	394.67±266.00	
	Thyromegaly	34	55.74	486.57±294.74	
Fine-needle aspiration cytology	Not done	1	1.64		0.001
	Colloid	36	59.02	356.16±191.28	
	Thyroiditis	24	39.34	576.76±345.29	
Goiter grading	0	2	3.28	193.55±19.16	0.001
	1	7	11.48	429.67±240.49	
	2	52	85.25	450.95±290.91	

Table 3: Median urinary iodine excretion level distribution pattern in control and case

Median urinary iodine excretion in μg/L	Iodine nutritional status	Case group	Control group
<20	Severe iodine deficiency	0	1
20–49	Moderate iodine deficiency	0	0
50–99	Mild iodine deficiency	1	1
100–199	Adequate iodine nutrition	6	1
200–299	Above iodine nutrition	13	1

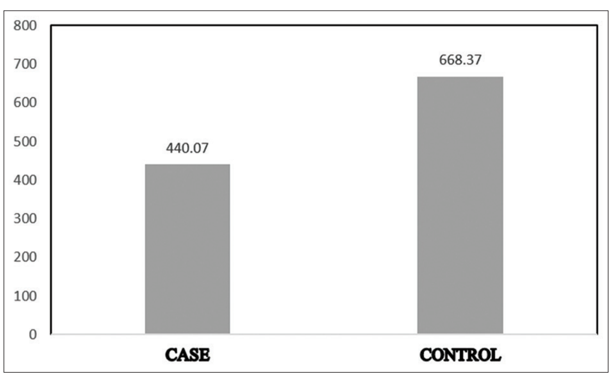

Figure 1: The bar diagram showing comparison between case and control groups for urinary iodine excretion pattern. Cases were having a mean value of 440.07±282.622 (SD) and control group with a mean value of 668.37±231.807 (SD). The significant correlation was 440.07±282.622 (SD) and the control growing showing the mean value of 668.37±231.807 (SD). The significant correlation was p=0.0001

thyroiditis population (n=45) and 307.11 for the hypothyroid population (n=18). Surprisingly, the 46 children from the control group showed excessive UIE levels and represent 90.19% of the control population (Fig. 1).

To understand the connection between UIE level and thyroid clinical parameters such as FT4, TSH, anti-TPO, and anti-TGA titer with respect to autoimmune thyroiditis, a correlation analysis was performed. A positive correlation was observed between UIE and anti-TPO and anti-TGA Ab ($p<0.0001$) levels of the case population. Among the cases, 39 children were noted with higher titer values for anti-TPO and 29 with anti-TGA titer values. However, we have not found any correlation between the UIE level and FT4 and TSH values of the case group.

Autoimmune thyroiditis among the cases was confirmed by correlating the data obtained from FNAC along with anti-thyroid antibody levels. Out of 61 children in the case group, the FNAC method confirmed autoimmune thyroiditis in 43 children (51%). Within the autoimmune thyroiditis category, lymphocytic infiltrations were noted with 22 children and excessive colloid accumulation in 37 children. Among the cases, 21 children showed overt condition with a population strength of 34.43% and the remaining showed subclinical thyroid symptoms which signify the population volume up to 65.57%. Ultrasound evaluation was carried out in 59 children of the case group. Among them, 34 children showed an enlarged thyroid gland and were grouped under thyromegaly condition, whereas, 25 children were grouped under thyroiditis condition because of inflammation. Goiter grading was carried out in the case population on the basis of the WHO-recommended criteria. Among the case population, two children were reported for no goiter condition (1.22%), 7 for Grade 1 goiter (11.48%), and 52 children reported for Grade 2 goiter condition (85.25%). We have also done a comparative study of thyroid parameters between the case and control groups and are given in Table 4. The children in the case group showed significantly higher levels of thyroid parameters than the control ones.

DISCUSSION

In the earlier period, iodine deficiency was more common in India and a reasonable percentage of the population reported growth or mental retardation due to iodine deficiency [8]. After having a successful trial of iodization of salt in Kangra Valley,

Table 4: Comparison of thyroid profile between case and control

Thyroid profiles	Mean±SD			
	Control (n=50)	Case (n=61)	Z factor	p value
TSH	2.50±1.12	33.01±108.23	8.94	0.001
FT4	1.38±0.13	37.96±32.85	6.94	0.0001
Anti-TPO Ab	21.07±39.94	332.32±473.14	6.65	0.0001
Anti-TGA Ab	23.68±40.09	179.98±217.39	6.001	0.0001

FT4: Free thyroxine, TSH: Thyroid-stimulating hormone, anti-TPO Ab: Thyroperoxidase antibody, anti-TG Ab: Thyroglobulin antibody

Himachal Pradesh district, India, has launched a 100% centrally sponsored program called the National Goitre Control program (NIDDCP) in 1992 and recommended for salt iodization program to eliminate IDDs from the nation [15]. Reports say that there is a prevalence of 13% of goiter, 3% of childhood hypothyroidism, and 10% of subclinical hypothyroidism in India even after the implementation of the salt iodization program [5]. Studies from the Southeast Asian countries also showed an increase in the detection of JAT in post-iodization assessment [9,16]. Based on the available knowledge, we designed to conduct a study to assess the iodine nutritional status in schoolchildren from South India, especially from Tamil Nadu, a state which focused more on the eradication of IDD among children through salt iodization program for the past three decades.

From our data, we observed that 79.6% of the study population exhibited higher than the optimal UIE levels. It was noticed that 92% of the children in the case group were reported with higher levels of iodine in their urine excretion. Within the cases, children those who were reported with autoimmune thyroiditis showed higher UIE level than the other children from the same group. This finding agrees with the previous data which concluded that the silent iodine prophylaxis results in the elimination of iodine deficiency but increases the prevalence of autoimmune thyroiditis in children [17]. A significant correlation was found between the UIE, TPO, and TGO antibody titers levels among the case group children. At the same time, we found no correlation between the UIE, TSH, and T4 values of the case group. We also observed female preponderance in the study (2.7:1), especially within the case group. Among the autoimmune thyroiditis population (n=48), females represent 87% of the population (mean age 9.45±2.54 years). These data are in accordance with the earlier report which supported that the sex of the children is a strong determinant factor for the occurrence of autoimmune thyroiditis in children and is highly associated with the female sex [18].

To diagnose autoimmune thyroiditis in children, we have not only considered serological data but also the cytomorphological evaluation, since most of the members of the study population reported higher UIE values. In general, thyroiditis is initially identified by the antibody titer values from the patients. However, the fact is that the expression of thyroid hormones will fluctuate based on the various clinical and non-clinical conditions, whereas, the cytomorphological features persist and will not alter based on the patient's health conditions. In this study, we could identify autoimmune thyroiditis among 43 children (70% of the case population) combining both the cytological and serological data along with UIE levels.

In 2017, Palaniappan *et al*. reported the higher levels of UIE in children with autoimmune thyroiditis from Tamil Nadu state. We also observed the same excretion pattern in our research too [8]. This is in line with the previous studies reported from the Western part of India and also from the Western countries [9,19,20]. Dilip *et al*. showed that nowadays iodine deficiency is no longer reported from any part of India since 80% of the household's salt was adequately iodized [21]. Thus, the data implicate that thyroiditis due to excess iodine intake is more prevalent in those children who are vulnerable to thyroid dysfunction. The presence of excess iodine in the urine of the children who are reported with autoimmune thyroiditis is hypothesized in such a way that this excess excretion of iodine could be due to the inability of the thyroid gland to trap the available iodine efficiently.

Reported data emphasized that children who are having higher levels of anti-thyroid antibodies are at risk of developing thyroid dysfunction if they consume more than the required iodine [22]. The study published by Zimmerman *et al.* showed that iodine deficiency in children could cause autoimmune thyroiditis [23]. Ours is a clinic-based study, hence, a detailed community-based study is also required to know the fact behind the scenario along with the identification of the genetics as well as the environmental factors with more population strength and iodine nutritional status in general.

CONCLUSION

The results of our study uncover an unexpected and complicating issue of high levels of iodine in healthy schoolchildren. We also found high levels of UIE in children reported with autoimmune thyroiditis. We observed a positive correlation between anti-TG and anti-TPO titer with UIE levels in autoimmune thyroiditis children. These data directly indicate that in our nation, IDD programs are executing successfully and the population is sufficiently supported by iodine supplementation mainly through the salt.

AUTHORS' CONTRIBUTIONS

Dr. Divya and Dr. Durai conceptualized and designed the study. Dr. Karamath and Dr. Seenivasan coordinated and supervised FNAC data collection. Dr. Kumaraswamy and Dr. Athmarthan carried out the initial analyses of thyroid profiles data. Dr. Sathya critically reviewed the manuscript for important intellectual content. Dr. Reji analysed the data, wrote, and revised the manuscript.

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