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ORIGINAL ARTICLE

Does Iodine Excess Lead to Hypothyroidism? Evidence from a Case-Control Study in India

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Background. Iodine deficiency disorders have been known to mankind since antiquity and various researchers elucidated the role of iodine in its causation. However, recent evidence shows that the entire control program ignored multi-causality and association of increased iodine intake with hypothyroidism. This study was conducted to assess differences of iodine intake as measured by urinary iodine excretion (UIE) between cases of hypothyroidism and healthy controls.

Methods. A case-control study was conducted with three groups (cases, hospital controls and community controls) in two cities of India. Patients with overt hypothyroidism were cases (n = 150) and were compared with age, sex and socioeconomic status-matched hospital (n = 154) and community (n = 488) controls. Thyroid function tests (T3, T4, TSH) were used as diagnostic and inclusion criteria. TPOAb and UIE estimation were carried out for all study participants.

Results. Mean values of TPOAb and UIE were higher in cases as compared to hospital controls as well as community controls (p <0.05). With a cut off of 34 IU/mL for TPOAb, more cases had an anti-TPO level >34 as compared to hospital controls (p <0.001) as well as community controls (p <0.001); OR, 0.06 (95% CI, 0.03, 0.12) and 0.08 (0.05, 0.12), respectively. For UIE cut-off of 300 μg/L, more cases than hospital controls (p = 0.090) and community controls (p = 0.001) had higher levels; OR, 0.671, (0.422, 1.066) and 0.509, (0.348, 0.744), respectively.

Conclusion. The study has clearly shown that cases of hypothyroidism are associated with excess iodine intake. Cohort studies to generate further evidence and an eco-social epidemiological approach have been suggested as the way forward. © 2015 IMSS. Published by Elsevier Inc.

Key Words: Iodine deficiency disorders, Case-control study, Hypothyroidism, Salt iodization, Autoimmune thyroiditis, Urinary iodine excretion.

Introduction

Goiter and other iodine deficiency disorders (IDDs) have been known for a long time with the existence of endemic goiter in an extensive belt along the southern slopes of the Himalayas, Alps and Andes. The early pioneers in the study of endemic goiter pointed to the complex etiology of goiter and commented on various causative factors (1–3). Later, the role of iodine in the causation of goiter was elucidated by various researchers working in these areas and results of few studies formed the basis of control and prevention activities of goiter (4,5). Worldwide, some countries have resorted to universalization of iodized salt (USI), whereas others have not done so and instead focused on making it available as a choice for the communities. The scientific backbone of universal iodination has been challenged due to weaknesses in the science and politics of the intervention to control IDDs. Few papers have also challenged the research forming the basis of information on the magnitude of the problem and effectiveness of the intervention (6,7). According to available evidence, the issues related to IDDs

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can be classified into four main groups: 1) magnitude of the problem and evidence for multicausality; 2) evidence for benefit of iodized salt; 3) assessment of intervention; and 4) harmful effects of iodine (8).

Recent studies worldwide are clearly pointing out the harmful effects of iodine after prolonged USI. A study in Brazil found that 5 years of excessive iodine intake by the Brazilian population may have increased the prevalence of hypothyroidism in subjects genetically predisposed to autoimmune thyroiditis (AIT) (9). Another study in Denmark has shown that even a cautious iodization of salt was accompanied by a moderate increase in the incidence rate of overt hypothyroidism (10). In Italy, increase in urinary iodine excretion (UIE) was observed 15 years after the introduction of iodine prophylaxis, which was associated with an increase of hypothyroidism (11). In China, studies found that iodine supplementation in a region with previously mildly deficient iodine intake may accelerate development of hypothyroidism and more than adequate levels of iodine intake may increase the prevalence and incidence of AIT and promote the onset of hypothyroidism in subjects with high levels of thyroid autoantibodies (12). Studies conducted post-USI in India have also shown a high prevalence of hypothyroidism and TPOAb antibody positivity (13).

The available studies provide sufficient information for a need to look at evidence about iodine as the sole factor in causality; magnitude of the problem as a major public health problem universally; effectiveness of USI as a measure leading to reduction in goiter and other IDDs by itself; and possible negative impacts on health such as increase in hypohyroidism, hyperthyroidism, and interaction with other minerals like iron. None of the researchers has studied this problem, especially among the higher socioeconomic group: what level of iodine is optimal to avoid the consequences of iodine deficiency while preventing side effects (14). Systematic reviews have shown lack of adequate data on thyroid function, focus on monocausality or ignoring multicausality on finding evidence for that and possible link of increased iodine intake leading to increased hypothyroidism/hyperthyroidism as many researchers have commented on toxicity of iodine. Other harmful effects at smaller dosages have not been adequately studied (8,14).

The present study was conducted to estimate the difference regarding TPOAb antibodies and UIE between cases of hypothyroidism and controls with the aim of generating evidence for recommendations regarding USI.

Materials and Methods

A case-control study was conducted at tertiary health care facilities and nearby areas in Delhi (Metropolis in North India) and Pune (a growing city in Western India) with three groups of study personnel. Group I consisted of cases (patients with overt hypothyroidism in various age groups); Group II comprised of age- and sex-matched hospital controls (those visiting/admitted in hospitals but free from overt or subclinical hypothyroidism in the past as well as in present time); and Group III consisted of community-based controls (healthy individuals without any goiter and overt or subclinical hypothyroidism). Group I and II participants were recruited in the endocrinology outpatient department (OPD) of tertiary health care facilities. Group III participants were selected by random sampling from the community. Both the tertiary care institutions of the Armed Forces receive patients from a well-defined community of serving armed forces personnel and their families. Thus, all cases (hospital as well as community controls) were from the same community and controls had the same probability of being labeled as a case if he/she had the disease. Cases and controls were matched for age, sex and socioeconomic status.

Diagnostic criteria for inclusion in the study as a case were incidental cases (hypothyroid patients) in endocrinology OPD with signs and symptoms of hypothyroidism, elevated TSH levels (>25 mU/L) and decreased T3 and T4 were included in the study as cases. Accrual of incident cases was done over a period of 2 years. Hospital as well as community controls were selected on the basis of lack of any signs and symptoms currently or ever in the past and also a TSH value <5 mU/L. Their accrual was concurrent with that of cases. Any control with abnormal values for T3 and/or T4 was also excluded from the study. Thus, controls were only healthy persons with no history suggestive of any thyroid-related problems in the past and normal values of T3, T4 and TSH. Any control with abnormal value of any of the thyroid hormones was excluded from the study. All those with TSH values between 5 and 25 mU/L were excluded from the study to obviate any confounding. Assay for TSH was done by radioimmunoassay using IRMA-SR 300 Kit from Beckman-Coulter Immunotech (Marseille, France).

UIE and TPOAb estimation was done for all study participants. Urinary iodine is a well-accepted, cost-efficient and easily obtainable indicator for iodine status because the majority of iodine absorbed by the body is excreted in the urine (15). Twenty-four-hour urine collections were used as it is an accepted method for hospital-based studies and results were provided as mean as well as medians (μg/L). Urinary iodine was measured according to the ICCIDD method using ammonium persulfate (Method A) (16). Personnel testing the UIE were trained and certified at the ICCIDD reference center at AIIMS, New Delhi. Assay for TPO Ab was by chemiluminescence assay and kit was from Beckman-Coulter Immunotech Access 2.

Institutional ethical clearance was obtained and the study was approved by the Armed Forces Medical Research Committee. Quality assurance activities were built-in at all levels. Sample size with alpha of 0.05, chance error 5%, power 80% using *t* test method to detect an appropriate