Urinary iodine concentrations and thyroid function in adult Zimbabweans during a period of transition in iodine status[1–3]

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ABSTRACT

Background: In 1993 the compulsory iodization of salt was introduced in Zimbabwe, a country that was previously an area of severe iodine deficiency.

Objective: The objective of this study was to document urinary iodine excretion and biochemical thyroid function in seemingly healthy, community-dwelling adults after the introduction of iodization.

Design: A multistage, random sampling method was used in rural and urban settings to identify households from which the senior household member (aged >35 y) was recruited (alternating male and female recruits). Demographic data were collected for each subject and urinary and venous blood samples were taken. Urinary iodine excretion and serum thyroid hormone status (thyrotropin and total thyroxin) were evaluated according to age, sex, and area of residence.

Results: A total of 736 adults were recruited (253 men; mean age: 64 y). Urinary iodine concentrations were high [median (first and third quartiles): 4.41 (2.84, 6.78) μmol/L, or 560 (360, 860) μg/L] and were significantly higher in rural areas than in urban areas [4.73 (3.07, 7.14) μmol/L, or 600 (390, 906) μg/L, compared with 3.47 (2.05, 4.73) μmol/L, or 440 (260, 600) μg/L; $P < 0.001$]. Urinary iodine excretion declined significantly with increasing age ($r = -0.29$, $P < 0.001$). Serum thyroid status suggested that the prevalence of biochemical hyperthyroidism in the study was 3%, with 13 of 415 cases in rural and 3 of 149 cases in urban subjects.

Conclusion: This study reaffirms the need to continuously monitor iodine replacement programs to ensure efficacy. *Am J Clin Nutr* 1999;70:888–91.

INTRODUCTION

Iodine deficiency is endemic in Zimbabwe, particularly in the northeastern sector of the country. A goiter survey conducted by the Department of Nutrition of the Ministry of Health and Child Welfare in 1988 showed that northeastern Mashonaland and most of Manicaland had goiter prevalences ranging from 10% to 70%. The survey covered the whole country and areas with a prevalence >50% were classified as severe iodine deficiency areas. In addition to goiter, other major effects of iodine deficiency, including cretinism and hypothyroidism (1–3), have been observed and documented in Zimbabwe (4, 5). A survey in 1991 of children aged 9–16 y in Chiweshe showed that 35% had thyrotropin concentrations >5.0 mIU/L and 10% had low serum thyroxine concentrations (<60 nmol/L), confirming the presence of hypothyroidism in the area (5). Low thyrotropin concentrations (<0.2 mIU/L) were not reported, which is consistent with the observation that, historically, hyperthyroidism is rare in Zimbabwe (6).

In keeping with guidelines of the International Council for Control of Iodine Deficiency Disorders, the Zimbabwean government introduced the compulsory iodization of all salt for human consumption in 1993 to prevent complications of iodine deficiency. The effectiveness of this policy is reflected by an increase in urinary iodine excretion. For example, between 1990 and 1993 (the first year of the salt iodization program), mean urinary iodine excretion increased from 0.50 to 2.21 μmol/L (64 to 281μg/L) and from 0.22 to 3.04 μmol/L (28 to 386 μg/L) in the areas of Centenary and Chimanimani, respectively (unpublished observations by a government analyst laboratory supported by the Ministry of Health and Child Welfare of Zimbabwe, 1995).

An increase in thyrotoxicosis was reported in several countries after the introduction of the iodization programs (7, 8). A nonrepresentative study of thyroid hormone results (thyrotropin, free thyroxine, and free triiodothyronine) in the regional endocrinology laboratory at Parirenyatwa Hospital, which serves an area of 8.5 million persons (≈80% of the Zimbabwean population), suggested a shift toward lower incidences of a hypothyroid constellation and a 3-fold higher hyperthyroid pattern beginning in 1993 (9). There was also an increase in the number

of clinical cases of thyrotoxicosis at Parirenyatwa Hospital during the same period (10).

To date, however, no data are available on the thyroid function of seemingly healthy individuals living in rural and urban communities after the introduction of the salt iodization program in Zimbabwe. The aim of this study was to evaluate *1*) urinary iodine excretion as an indicator of iodine intake and *2*) the biochemical thyroid status of adults, especially older adults (who theoretically would be more disposed to adverse consequences), living in an area of previous iodine deficiency.

SUBJECTS AND METHODS

Subjects

The geographic characteristics of the study population and the sampling method used were described in detail previously (11). In summary, 736 subjects aged ≥35 y were recruited from a rural district and from 2 urban, high-density residential areas by using a multistage sampling design. The rural sample was recruited from Uzumba Maramba Pfungwe, an area 1400 m above sea level and ≈250 km northeast of Harare, the capital of Zimbabwe. The urban sample was obtained from Bindura and Marondera, commercial centers for rich agricultural areas lying 1600 m above sea level and ≈80 km from Harare. Briefly, in randomly selected village development units (administrative centers of 60–100 households) of the rural area, alternate households were visited at least twice to recruit the most senior household member of the appropriate sex aged >35 y. The sex of the target subject was alternated in a predetermined manner; pregnant women were excluded from the study. If the target subject was not available or declined, the researchers moved to the next household. For the urban sample, a random sample of streets was selected. Starting from a predetermined point, alternate households were visited from which the senior household member was recruited according to the same criteria used for the rural sample. The study was approved by the Zimbabwe Medical Research Council.

Demographic data and sample collection

Data were collected between October 1994 and March 1995. Only one subject was recruited per household. Selected subjects were visited in their homes by specially trained research nurses who completed a questionnaire of demographic information. As much as possible, men and women were selected alternately to keep the sex ratio equal. All subjects had fasted for ≥12 h before blood samples were taken. Venous blood samples were collected between 0700 and 0900 from each subject. Each subject was also asked to collect a sample of their first morning urine. All samples were kept on ice while being transported to the laboratory. Serum was separated by low-speed centrifugation ($2000 \times g$) for 5 min at room temperature with a GS-15 centrifuge (Beckman Instruments, Fullerton, CA). Urine samples were collected into vessels kept at 4°C. Serum and urine samples were stored at −20°C until analyzed.

Measurement of urinary iodine and serum thyroid hormones

Urinary iodine was measured by using the Dunn method (12), with the modifications described by May et al (13). All reagents were of analytic grade and were obtained from BDH Chemicals (Johannesburg, South Africa). Quality control of the assay was performed by using 3 urine control pools supplied by the Program Against Micronutrient Malnutrition Laboratory (Centers for Disease Control and Prevention, Atlanta).

To assess thyroid function, thyrotropin and total thyroxine were measured by using matched reagents obtained from the North East Thames Regional Immunoassay Unit (St Bartholomew's Hospital, London). The detection limit of the thyrotropin assay was 0.01 mIU/L. The assays were carried out with an LKB 1261 Multi Gamma Counter (Wallac, Turku, Finland). Assay reproducibility was determined by the use of Amerlite thyroid hormone control sera (lot no. 101; Kodak Clinical Diagnostics Ltd, Amersham, United Kingdom), which was included in every run.

Data handling and statistical methods

Urinary iodine, thyrotropin, and total thyroxine were not normally distributed. Therefore, the results are expressed as medians, with the first and third quartiles in parentheses. Between-group differences were analyzed by the Mann-Whitney *U* test. Results were analyzed with EPI-INFO (version 6.04; Centers for Disease Control and Prevention, Atlanta).

RESULTS

The study population consisted of 736 adults: 253 men (median age: 64 y; range: 31–93 y) and 480 women (median age: 55 y; range: 30–92 y). No subject was taking thyroid medication or iodine supplements other than in their normal salt intake. Of the study group, 510 subjects lived in the rural area and 226 in the urban areas. A total of 624 subjects consented to the collection of urine and blood samples; urinary iodine concentrations were measured in 516 subjects, thyrotropin concentrations in 600, and total thyroxine concentrations in 564.

Values for urinary iodine, total thyroxine, and thyrotropin are given in **Tables 1** and **2**. Urinary iodine excretion was significantly higher in rural subjects than in urban subjects (rural: 4.73 (3.07, 7.14) μmol/L, or 600 (390, 906) μg/L; urban: 3.47 (2.05, 4.73) μmol/L, or 440 (260, 600) μg/L; $P < 0.001$). There was a significant decline in urinary iodine with age ($r = -0.29$, $P < 0.001$) and all subjects with urinary iodine <0.79 μmol/L (<100 μg/L) were aged >65 y. No significant differences in urinary iodine excretion were observed between men and women.

The normal range for thyrotropin was 0.2–5.0 mIU/L and that for total thyroxine was 60–160 nmol/L (for the assay kits used). With use of these values as cutoffs, 46 of 564 subjects (8%) had elevated total thyroxine concentrations (>160 nmol/L). Of these subjects, 10 had total thyroxine concentrations >210 nmol/L and thyrotropin concentrations <0.1 mIU/L, suggesting hyper-

TABLE 1
Summary of concentrations of urinary iodine, total thyroxine, and thyrotropin in all subjects[1]

Urinary iodine	
(μmol/L)	4.41 (2.84, 6.78) [516]
(μg/L)	560 (360, 860) [516]
Total thyroxine (nmol/L)	103 (87, 122) [564]
Thyrotropin (mIU/L)	1.0 (0.6, 1.5) [600]

[1] Median with quartiles 1 and 3 in parentheses; *n* in brackets.

TABLE 2
Concentrations of urinary iodine, total thyroxine, and thyrotropin in subjects aged ≤60 and >60 y[1]

Urinary iodine	
(μmol/L)	
≤60 y	5.36 (3.55, 9.46) [215]
>60 y	3.78 (2.44, 5.67) [301][2]
(μg/L)	
≤60 y	680 (450, 1200) [215]
>60 y	480 (310, 720) [301][2]
Total thyroxine (nmol/L)[3]	
≤60 y	92 (79, 110) [289]
>60 y	111 (97, 136) [274][2]
Thyrotropin (mIU/L)[3]	
≤60 y	1.0 (0.7, 1.5) [287]
>60 y	0.9 (0.6, 1.6) [312]

[1] Median with quartiles 1 and 3 in parentheses; *n* in brackets.
[2] Significantly different from ≤60 y, *P* < 0.001 (Mann-Whitney *U* test).
[3] Not measured in all subjects.

thyroidism. Six subjects had total thyroxine concentrations between 170 and 240 nmol/L with accompanying thyrotropin concentrations of between 0.2 and 0.3 mIU/L, suggesting borderline hyperthyroidism. Therefore, 16 subjects (3%) had definite or probable biochemical hyperthyroidism (**Table 3**). For one subject with thyroxine concentrations >210 nmol/L, the thyrotropin result was missing. Of the subjects with elevated total thyroxine and suppressed thyrotropin, 13 of 415 (3.1%) were from the rural area and 3 of 149 (2.0%) were from the urban areas.

Eleven of 373 women (2.9%) and 5 of 191 men (2.6%) were classified biochemically as possibly having hyperthyroidism. Seven subjects had elevated thyrotropin (>5.0 mIU/L), of which 3 subjects had concentrations >10 mIU/L. Of these 7 subjects, 1 had low total thyroxine and 2 had missing total thyroxine results. Thus, there was 1 definite case of biochemical hypothyroidism and 6 possible or compensated cases of hypothyroidism.

In this study, the sample was skewed in age toward the upper end of middle age. This can be explained by the fact that the most senior household member was recruited. There was no significant difference in the prevalence of thyroid hormone dysfunction between those aged ≤60 y and those aged >60 y, although total thyroxine concentrations were significantly higher in those aged >60 y than in those aged ≤60 y (Table 2) and total thyroxine concentrations increased with age (*r* = 0.28, *P* < 0.001). There was no significant difference in thyrotropin concentrations between the 2 age groups and, in contrast with total thyroxine, thyrotropin concentrations did not vary with age. For all subjects, total thyroxine concentrations were higher

in urban subjects than in rural subjects (median: 106.4 compared with 100.3 nmol/L; *P* < 0.05).

DISCUSSION

The measurement of urinary iodine has been recognized as the most common and most reliable biochemical test for assessing the iodine status of populations (13, 14). The urinary iodine concentrations observed in this study confirmed that the iodization program was effective and was reaching most members of the community, including the elderly and persons living in remote rural areas. The range of urinary iodine values in this study population, however, was higher than those documented previously in other areas of Zimbabwe since the start of the iodization program. Additionally, concentrations in many subjects were higher than desirable. Concentrations in the range of 0.79–1.58 μmol/L (100–200 μg/L) are advised with iodine supplementation programs. Thus, it is possible that the salt in Zimbabwe contains higher iodine concentrations than desired.

The target concentration of iodine in iodized salt in Zimbabwe was 30–90 mg I/kg salt (recommended by the Ministry of Health and Child Welfare, Zimbabwe). At the beginning of the iodization program, between 1990 and 1995, however, iodine concentrations were above these limits. This was due in part to poor quality control of the iodization process. The high concentrations of iodine in the salt may explain the high urinary iodine concentrations recorded in this study. Concentrations of 20–40 mg I/kg salt are considered to be acceptable (15). Therefore, the iodine concentration of the salt in Zimbabwe may require review to reduce the complication of acquired hyperthyroidism.

Subjects in the rural area had significantly higher urinary iodine concentrations than did the urban subjects. This finding is surprising because one would expect the availability of manufactured (iodized) salt to be greater in urban areas and suggests that a dietary source other than iodized salt contributed significantly to dietary iodine intake in the rural area. Possible alternative dietary sources have not yet been identified.

We also noted a trend for urinary iodine to decline with age. A previous study from Denmark showed no variation with age in a younger adult population aged 25–40 y (16). In addition, in an older North American population studied in the third National Health and Nutrition Examination Survey, there was no age-related change in urinary iodine excretion from 30 to 74 y (17). The basis of our own finding remains speculative.

Thyroid hormone testing in Zimbabwe is centralized at 2 regional endocrinology laboratories at Parirenyatwa and Mpilo Hospitals. Thyroid hormone testing for the area under study is performed by the endocrinology laboratory at Parirenyatwa Hospital. A retrospective study of thyroid function tests conducted at this laboratory appears to suggest that as the iodization program was implemented countrywide, biochemical hypothyroidism

TABLE 3
Biochemical evidence of thyroid dysfunction

	Total thyroxine	Thyrotropin	Prevalence
	nmol/L	*mIU/L*	*%*
Possible hyperthyroidism (abnormally high total thyroxine)	>160	<0.1–2.3	8 [45/564]
Borderline hyperthyroidism	>170	0.2–0.3	1 [6/564]
Hyperthyroidism	>210	<0.1	2 [10/564]

decreased and biochemical hyperthyroidism increased among patients suspected of having thyroid disease. Furthermore, a 4-fold increase in clinical cases of thyrotoxicosis was reported after the start of the iodization program in Zimbabwe (10). Our study provides some evidence of undiagnosed hyperthyroidism in the rural and urban populations studied and suggests that hypothyroidism is becoming less of a public health issue. Our findings appear consistent with previous studies carried out after the initiation of other iodization programs (18, 19).

Because this was a cross-sectional study, we do not have equivalent data for adults in this area before the iodization program. We are, however, able to compare our observations with those of community-based studies in other settings (20–22). Our findings of 3% of older adults with borderline and frank biochemical hyperthyroidism and an additional 5% with possible hyperthyroidism (abnormally high total thyroxine concentrations) contrasts with community-based studies conducted in England (20) and North America (21), where ≈2% of a similar population had biochemical hyperthyroidism. In our study, 1.2% of subjects had elevated thyrotropin concentrations. In the community-based studies the proportion varied with sex (female preponderance) and age but ≈7% of subjects were found to have elevated thyrotropin concentrations and therefore possible or definite hypothyroidism (20–22). Although these studies may not be directly comparable with ours because the definitions of hyper- and hypothyroidism may differ, our observations suggest that during the time period studied in Zimbabwe (1994–1995), biochemical hyperthyroidism may have been slightly more common and biochemical hypothyroidism less common than in similar populations in areas of stable iodine repletion.

This study could have been improved by examining each subject clinically to confirm the biochemical data. Because total thyroxine concentrations are affected by serum protein concentrations, analysis of hormone concentrations would have helped to clarify the thyroid status of subjects with results indicating borderline disease and of those with elevated total thyroxine concentrations and thyrotropin concentrations near the low cutoff.

In summary, our study confirms that the iodization program in Zimbabwe is reaching persons in remote areas. As might be expected from previous programs (7), there appeared to be a higher-than-expected rate of undiagnosed biochemical hyperthyroidism. Our finding suggests that during this phase of transition in iodine status, the monitoring program needs to include analysis of iodine concentrations in salt, urinary iodine excretion, and thyroid function.

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