

Excessive iodine intake, water chemicals and endemic goitre in a Sudanese coastal area

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Abstract

Objective: To study the associations between intakes of iodine and water chemicals and the thyroid gland status of schoolchildren living in the coastal city of Port Sudan.

Design: In our previous nationwide study on goitre, it was observed that the prevalence of goitre was high in Port Sudan city despite high urinary iodine excretion. A cross-sectional study including schoolchildren aged 6–12 years was designed. Measurements determined the prevalence of goitre, urinary iodine concentration and thiocyanate secretion in casual urine samples, serum levels of thyroxine, triiodothyronine, thyroid-stimulating hormone and thyroglobulin, as well as the levels of Cl^- , F^- , Ca^{2+} , Mg^{2+} and total hardness of drinking water.

Subjects: Schoolchildren (n 654) aged 6–12 years.

Setting: Port Sudan city is located at the western bank of the Red Sea. The city is surrounded by a mountainous area known as the Red Sea Hills. It is the main sea port in the Sudan, inhabited by ethnically and socio-economically heterogeneous populations.

Results: The prevalence of goitre in Port Sudan was 34.86% while the median urinary iodine concentration was 46.4 $\mu\text{g}/\text{dl}$. Out of thirty-one pupils from Port Sudan, twenty-four (77.42%) were found to have urinary iodine concentration greater than 30 $\mu\text{g}/\text{dl}$ and twelve (38.71%) had different degrees of biochemical hypothyroidism. Excessive concentrations of Cl^- , Ca^{2+} , Mg^{2+} and water hardness (369.2, 116.48, 60.21 and 539.0 mg/l , respectively) were detected in drinking water samples collected from Port Sudan that exceeded levels permitted by the WHO.

Conclusions: The coastal city of Port Sudan is a goitre-endemic area. In contrast to other Sudanese cities in which endemic goitre is related to iodine deficiency, goitre in Port Sudan is associated with iodine excess. Water chemicals seemed to have no effects on thyroid status.

Keywords
Endemic goitre
Iodine excess
Water chemicals
Sudan
Schoolchildren

Iodine is a requirement for, as well as a regulator of, the thyroid gland⁽¹⁾. While iodine deficiency may impair thyroid function, iodine excess has been shown to inhibit thyroid hormone synthesis and release through the Wolff–Chaikoff effect^(2,3). Thus both iodine deficiency and iodine excess might result in thyroid dysfunction via a U-shaped relationship⁽⁴⁾. In addition to direct impairment of thyroid function, excessive iodine intake is also believed to induce some autoimmune diseases⁽³⁾. Excess iodine may exist naturally such as that reported in coastal Hokkaido in Japan. In this coastal area, goitre was found to be endemic among Japanese children due to consumption of seaweed⁽⁵⁾. An association between excess iodine intake, increased serum thyroid-stimulating hormone (TSH) and

thyroid volume was detected in China where drinking water is rich in iodine⁽⁶⁾. Excess iodine consumption can also result from additional supplies of iodine to the daily intake in different forms. Endemic goitre was associated with excessive iodine given to refugees in four African countries in the form of fortified food⁽⁷⁾. Distribution of iodized salt poorly monitored for the iodine concentration resulted in excess iodine intake in Iceland⁽⁸⁾. In addition to alteration in iodine intake, other factors have been suggested to be causative agents or contributors to the development of endemic goitre. Among these are genetic or racial factors⁽⁹⁾, dietary goitrogens and high concentrations of some minerals in drinking water⁽¹⁰⁾. Water has a significant role in body homeostasis and metabolism because of its large consumption and high content of trace elements. It has been reported that chlorine and some other chemicals can form different products when they react with organic matter in

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the upper gastrointestinal tract. These products exert significant antithyroidal effects^(11,12). Several environmental chemicals have structural similarities to the thyroid hormones thyroxine (T_4) and triiodothyronine (T_3). These similarities may lead to interference with thyroid homeostasis through many mechanisms of action at different levels of metabolism of thyroid hormones⁽¹⁰⁾. This may lead to insufficient production of hormones by the thyroid gland. Calcium was found to be goitrogenic in rats on a low-iodine diet⁽¹³⁾.

Excess fluoride was reported as a major cause of endemic goitre in the presence of iodine sufficiency in different parts of South Africa^(14,15). A similar relationship between excess fluoride exposure and goitre has been detected in England as well as in the Punjab region of India⁽¹⁶⁾. A close relationship between goitre prevalence and the fluoride content and hardness of water was reported by Day and Powell-Jackson⁽¹⁷⁾. They reported that the prevalence of goitre in some Himalayan villages was attributable to the content of chemicals in water rather than to differences in iodine intake.

The Sudan is located in the middle of a goitre-endemic area. This area includes Algeria, Burundi, Chad, Central African Republic, Congo, Egypt, Eritrea, Ethiopia, Kenya, Mali, Niger, Rwanda, Tunisia and Uganda⁽¹⁸⁾. The endemicity of goitre varies from 12% in Congo to as high as 65% in Algeria.

The Sudan is like other goitre-endemic areas in which iodine deficiency has been implicated as the main aetiological factor⁽¹⁾. The contribution of other factors, like consumption of pearl millet^(19,20), protein-energy malnutrition and vitamin A deficiency⁽²¹⁾, was noted. In a recent goitre survey, we reported a high prevalence of goitre in eleven Sudanese cities, representing nine states. Goitre prevalence ranged from 12 to 78%⁽²²⁾. Iodine deficiency was widespread in the ten non-coastal cities, with median urinary iodine concentration (UIC) ranging from 2.7 to 9.4 $\mu\text{g}/\text{dl}$. The coastal city of Port Sudan, on the other hand, had an exceptionally high median UIC of 46.4 $\mu\text{g}/\text{dl}$. The goitre prevalence in Port Sudan was 34.9% while the combined prevalence in the other cities was 39.3%. Iodine deficiency could explain the high prevalence of endemic goitre in these ten cities. The intention in the present study was to examine possible associations between UIC, water chemicals and thyroid status in the coastal city of Port Sudan.

Methods

A national cross-sectional study for determination of the status of iodine-deficiency disorders in the Sudan was conducted from June to November 2006⁽²²⁾. The study included schoolchildren aged 6–12 years randomly selected from thirty-three preliminary schools in eleven cities. Each city was first divided into three sectors and

one school was randomly selected from each sector. Sample sizes were calculated using a rapid, population-based, multistage random sampling technique⁽²³⁾. In each school, the first, third and fifth year classrooms were selected to participate in the study.

The total number of schoolchildren enrolled in the study was 6038. Out of those, 654 were from Port Sudan city which is the main sea port of the Sudan, connected to Khartoum via a 1200 km highway and recently with another 800 km road. The city is located in an arid area with very saline water. Food and drinking water are imported into Port Sudan from different areas around.

Measurements

Goitre

Goitre was assessed by the same observer for the pupils (in the selected classrooms) who attended school on the day of the survey. Goitre size was graded according to the criteria recommended by the WHO, UNICEF and the International Council for the Control of Iodine Deficiency Disorders (grade 0, no goitre; grade 1, thyroid palpable but not visible; and grade 2, thyroid visible with neck in normal position)⁽²⁴⁾. The combined prevalence of grade 1 and 2 provided the total prevalence of goitre in the study population.

Laboratory study

Four children from each classroom were selected to participate in the laboratory study using a systematic random sampling technique. The number of pupils in the class was divided by four to determine the sample interval (X) in each class. Using the simple random technique a random digit was selected within the sample interval as starting point. X was then added to the number of the first child to select the second in the sample.

Blood and urine samples were collected from thirty-one pupils from Port Sudan and from 329 pupils from the other Sudanese cities. Pupils were chosen irrespective of gender or the results of thyroid gland palpation. Serum samples were analysed for T_4 , T_3 , TSH and thyroglobulin (Tg) using RIA with reagents obtained from the Department of Isotopes of the China Institute for Atomic Energy in Beijing (the multi-channel gamma counter for measuring ^{125}I was obtained from Stratec Biomedical Systems AG, Birkenfeld, Germany).

Urine samples were used for two purposes: (i) a fresh portion was used to determine the UIC; and (ii) a portion that was kept at -20°C for 5 months was used to measure urinary thiocyanate (USCN). UIC was measured using the modified Sandell–Kothoff reaction⁽²⁵⁾. USCN excretion was measured by the modified method of Aldridge⁽²⁶⁾ described by Michajlovskij and Langer⁽²⁷⁾ (using a photometer from Biosystems SA, Barcelona, Spain).

Blood and urine samples were analysed in the laboratories of the Sudan Atomic Energy Commission (SAEC), Khartoum.

The present study was approved by the review board of the Sudanese Academy of Sciences, and consent was obtained from local health and education authorities and the Department of School Nutrition of the Ministry of Education. Permission for collecting blood and urine samples was obtained verbally from one of the parents of each pupil through school headmasters and parent councils. Pupils who declined to participate were randomly substituted with other pupils from the same classroom.

The study covered an ethnically and socio-economically heterogeneous population of schoolchildren who varied considerably with respect to their sources of drinking water and staple foods. Comparisons of the thyroid parameters between thirty-one pupils from Port Sudan and 329 from the rest of the Sudan were obtained. In addition to the mentioned parameters, thirty-one drinking water samples were collected from the houses of the participating pupils from Port Sudan. The water samples represented three localities where the schools were situated and selected accordingly.

Water samples were analysed for their concentrations of Ca^{2+} , Mg^{2+} , Cl^- and F^- and total hardness (CaCO_3 concentration). Ca^{2+} and Mg^{2+} in water samples was measured using the EDTA titrimetric method⁽²⁸⁾, which involves addition of Eriochrome Black or Calmagite dye to an aqueous solution containing Ca^{2+} and Mg^{2+} at pH 10.0 ± 0.1 after addition of EDTA as chelating titrant. Cl^- was measured using the argentometric method⁽²⁸⁾ that depends on the titration of Cl^- with AgNO_3 using K_2CrO_4 for detection of the end point. The reaction took place in a neutral or slightly alkaline medium. F^- was measured by the SPADNS colorimetric method⁽²⁸⁾ using zirconium-dye lake to form the colourless complex anion $(\text{ZrF}_6)^{2-}$. The analysis of water samples took place at the central laboratory belonging to the laboratories department of the Groundwater & Wadis Directorate in Khartoum (micropipettes (20–100 μl) and repeating syringes for

measuring specific volumes of serum and urine were from obtained Eppendorf GmbH, Hamburg, Germany).

Statistical analysis

Statistical analyses were performed using the statistical software package SPSS version 16.0. The central tendency was described by the arithmetic mean of serum and urine levels. Spearman's correlation coefficient was used to explore the relationship between variables (T_4 , T_3 , TSH, Tg, UIC, USCN and water chemical components). One-way ANOVA was used to explore differences in mean serum T_4 , T_3 , TSH, Tg, UIC and USCN levels between Port Sudan and the other Sudanese cities. The procedure of least significant difference was applied to look for differences among pairs of means. Significance was set at $P < 0.05$.

Results

Table 1 presents the mean UIC, USCN and thyroid parameters (serum levels of T_4 , T_3 , TSH and Tg) of thirty-one children from Port Sudan city in comparison with the combined means of 329 children from the other ten Sudanese cities. The mean UIC in Port Sudan was about five times the combined mean UIC of the other Sudanese cities ($P = 0.001$). Compared with children from the other Sudanese cities, the children in Port Sudan had significantly lower serum T_4 and T_3 levels (both $P = 0.001$) and significantly higher serum TSH level ($P = 0.008$). The mean serum level of Tg of the children in Port Sudan was higher than the combined mean of the children in the other cities; however, the difference between the two means was noticeable but statistically insignificant ($P = 0.052$). The mean USCN in the Port Sudan children was significantly lower than the combined mean of the children in other cities ($P = 0.001$).

Furthermore, the UIC of children in Port Sudan ranged from 10.9 to 73.6 $\mu\text{g/dl}$. Out of thirty-one pupils in this

Table 1 Clinical indicators of thyroid function and iodine status in schoolchildren aged 6–12 years from Port Sudan city compared with other Sudanese cities, June–November 2006

	Group	n	Mean	SD	P value	95% CI	
						Lower	Upper
T_4 (nmol/l)	Sudanese cities	329	105.17	27.42	0.001	12.45	32.74
	Port Sudan	31	82.58	27.93			
T_3 (nmol/l)	Sudanese cities	329	1.97	0.51	0.001	0.24	0.62
	Port Sudan	31	1.54	0.48			
TSH (mIU/l)	Sudanese cities	329	2.11	1.28	0.008	−2.74	−0.46
	Port Sudan	31	3.71	3.10			
Tg (ng/ml)	Sudanese cities	329	37.22	21.86	0.052	−16.93	−0.67
	Port Sudan	31	46.02	23.45			
UIC ($\mu\text{g/dl}$)	Sudanese cities	329	7.01	5.17	0.001	−45.20	−31.36
	Port Sudan	31	45.29	18.83			
USCN (mg/l)	Sudanese cities	329	0.40	0.17	0.001	0.06	0.15
	Port Sudan	31	0.29	0.11			

T_4 , thyroxine; T_3 , triiodothyronine; TSH, thyroid-stimulating hormone; Tg, thyroglobulin; UIC, urinary iodine concentration; USCN, urinary thiocyanate.

Normal total serum levels of T_4 , T_3 , TSH and Tg according to the Sudan Atomic Energy Commission are as follows: T_4 , 60–165 nmol/l; T_3 , 0.8–3.0 nmol/l; TSH, 0.7–5.0 mIU/l; Tg, 4.1–24.0 ng/ml.

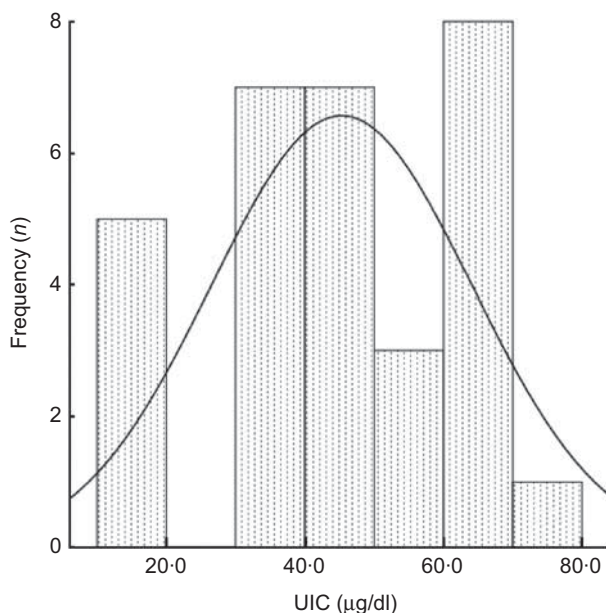


Fig. 1 Distribution of urinary iodine concentration (UIC) among thirty-one schoolchildren aged 6–12 years from Port Sudan city, June–November 2006 (mean UIC = 45.29 (SD 18.82) µg/dl)

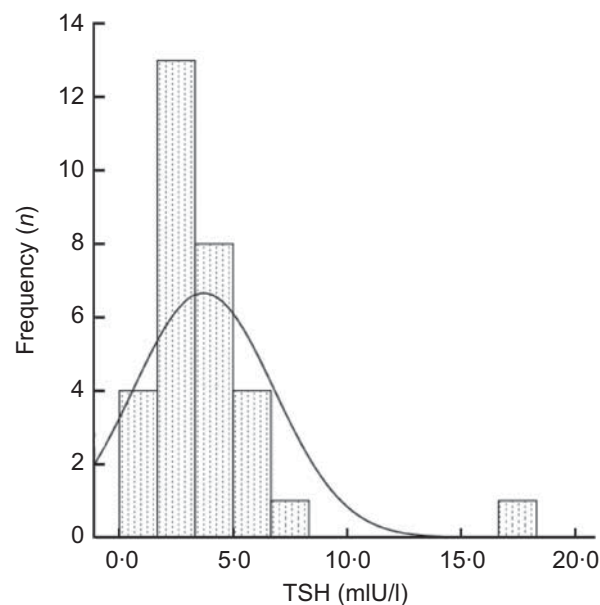


Fig. 3 Distribution of serum thyroid-stimulating hormone (TSH) levels among thirty-one schoolchildren aged 6–12 years from Port Sudan city, June–November 2006 (mean TSH = 3.71 (SD 3.10) mIU/l)

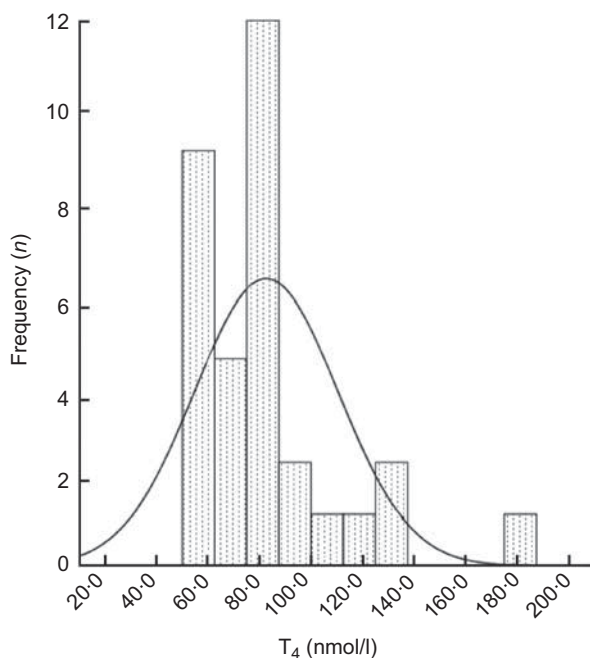


Fig. 2 Distribution of serum thyroxine (T_4) levels among thirty-one schoolchildren aged 6–12 years from Port Sudan city, June–November 2006 (mean T_4 = 82.58 (SD 27.93) nmol/l)

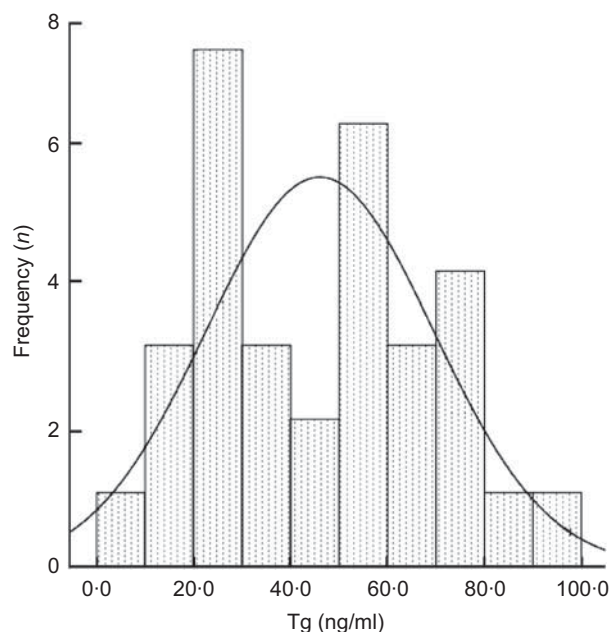


Fig. 4 Distribution of serum thyroglobulin (Tg) levels among thirty-one schoolchildren aged 6–12 years from Port Sudan city, June–November 2006 (mean Tg = 46.02 (SD 23.45) ng/ml)

city, twenty-four (77.42%) were found to have excessive UIC greater than 30 µg/dl, the upper limit of normal UIC estimated by the WHO (Fig. 1). Seven children had serum T_4 lower than the lowest normal T_4 level estimated by the SAEC, which is 60 nmol/l. Only one child had serum T_4 above 165 nmol/l, which is the upper normal T_4 level

estimated by the SAEC (Fig. 2). High serum TSH values were detected in another six children that exceeded the SAEC normal value (0.5–5 mIU/l), as shown in Fig. 3. Moreover, serum Tg concentration was elevated in twenty-five children (80.65%) that exceeded the highest normal value (24 ng/ml) estimated by the SAEC (Fig. 4).

Table 2 Correlation between various clinical indicators of thyroid function, iodine status and water chemicals in a study of thirty-one schoolchildren aged 6–12 years from Port Sudan city, June–November 2006

		T ₄ (nmol/l)	T ₃ (nmol/l)	TSH (mIU/l)	Tg (ng/ml)	UIC (µg/dl)	USCN (mg/l)	Cl ⁻ (mg/l)	Ca ²⁺ (mg/l)	Mg ²⁺ (mg/l)	F ⁻ (mg/l)	Hardness
T ₄ (nmol/l)	<i>r</i> †	1.000	0.203	0.218	0.277	-0.101	0.120	-0.043	-0.157	-0.043	0.157	-0.157
	<i>P</i> value‡		0.273	0.238	0.131	0.589	0.520	0.818	0.398	0.818	0.398	0.398
T ₃ (nmol/l)	<i>r</i>	—	1.000	0.148	0.341	-0.042	-0.020	-0.096	-0.179	-0.096	0.179	-0.179
	<i>P</i> value	—		0.426	0.061	0.823	0.913	0.609	0.335	0.609	0.335	0.335
TSH (mIU/l)	<i>r</i>	—	—	1.000	0.381*	-0.102	-0.194	-0.102	-0.506*	-0.102	0.506*	-0.506*
	<i>P</i> value	—	—		0.034	0.585	0.296	0.586	0.004	0.586	0.004	0.004
Tg (ng/ml)	<i>r</i>	—	—	—	1.000	-0.020	0.042	-0.208	-0.260	-0.208	0.260	-0.260
	<i>P</i> value	—	—	—		0.915	0.823	0.262	0.159	0.262	0.159	0.159
UIC (µg/dl)	<i>r</i>	—	—	—	—	1.000	0.326	-0.405*	0.058	-0.405*	-0.058	0.058
	<i>P</i> value	—	—	—	—		0.074	0.024	0.758	0.024	0.758	0.758
USCN (mg/l)	<i>r</i>	—	—	—	—	—	1.000	-0.021	0.061	-0.021	-0.061	0.061
	<i>P</i> value	—	—	—	—	—		0.910	0.744	0.910	0.744	0.744
Cl ⁻ (mg/l)	<i>r</i>	—	—	—	—	—	—	1.000	0.312	1.000*	-0.312	0.312
	<i>P</i> value	—	—	—	—	—	—		0.087	0.001	0.087	0.087
Ca ²⁺ (mg/l)	<i>r</i>	—	—	—	—	—	—	—	1.000	0.312	-1.000*	1.000*
	<i>P</i> value	—	—	—	—	—	—	—		0.087	0.001	0.001
Mg ²⁺ (mg/l)	<i>r</i>	—	—	—	—	—	—	—	—	1.000	-0.312	0.312
	<i>P</i> value	—	—	—	—	—	—	—	—		0.087	0.087
F ⁻ (mg/l)	<i>r</i>	—	—	—	—	—	—	—	—	—	1.000	-1.000*
	<i>P</i> value	—	—	—	—	—	—	—	—	—		0.001
Hardness	<i>r</i>	—	—	—	—	—	—	—	—	—	—	1.000
	<i>P</i> value	—	—	—	—	—	—	—	—	—	—	—

T₄, thyroxine; T₃, triiodothyronine; TSH, thyroid-stimulating hormone; Tg, thyroglobulin; UIC, urinary iodine concentration; USCN, urinary thiocyanate.

*Correlation is significant at the 0.05 level (two-tailed).

†Spearman's correlation coefficient.

‡Significance on two-tailed test.

Table 2 shows the correlation between various clinical indicators of thyroid function in schoolchildren and the concentration of water chemicals in Port Sudan. It indicates that thyroid hormones (T₃ and T₄) were poorly correlated with the concentration of water chemicals. TSH was significantly correlated with F⁻ concentration ($r=0.506$, $P=0.004$) and inversely correlated with Ca²⁺ concentration ($r=-0.506$, $P=0.004$) and hardness ($r=-0.506$, $P=0.004$). There was also a significant inverse correlation between UIC and the concentration of Cl⁻ ($r=-0.405$, $P=0.024$) and Mg²⁺ ($r=-0.405$, $P=0.024$). Some of the water samples collected from Port Sudan contained excessive concentrations of Cl⁻, Ca²⁺, Mg²⁺ and water hardness (369.2, 116.48, 60.21 and 539.0 mg/l, respectively) exceeding the maximum levels recommended by the WHO^(29,30).

Discussion

The schoolchildren selected from the coastal city of Port Sudan had an excessive iodine intake according to the criteria of the WHO⁽³¹⁾ based on UIC. A couple of factors might have contributed to this excessiveness. Merely being coastal might be associated with the consumption of high amounts of seafood rich in iodine or the inhalation of iodine from the iodine-rich sea environment. Indeed, up to 20 µg of iodine was estimated to be inhaled from such an environment by an adult person every day⁽³²⁾. In addition, the distribution by UNICEF and WHO of food fortified with iodine to the poorest schoolchildren

in the Red Sea State was reported by Hussein *et al.*⁽³³⁾. This could be another factor leading to the excessive urinary iodine excretion among children in this city. A median UIC of 55.5 µg/dl was reported in Hussein *et al.*'s study⁽³³⁾.

It is noteworthy that studies done in the 1980s reported relatively low urinary iodine excretion with lower goitre rates in this city as compared with the recent studies^(22,33). The reason for the high goitre prevalence despite excess iodine intake in the present study needs further evaluation. One possible contributing factor may be the iodine intake as reported previously⁽³³⁾. Dietary goitrogens are unlikely to be involved in the development of goitre in this population since the urinary excretion of thiocyanate was comparatively low.

The high mineral content of the water samples analysed in the present study seems to have no contribution in the goitre aetiology. Indeed, the high concentrations of Cl⁻, Ca²⁺, Mg²⁺ and F⁻, as well as water hardness, were not correlated with serum levels of thyroid hormones T₃ and T₄ in the present children. With the exception of F⁻, all of these chemicals were inversely correlated with the level of serum TSH. This can exclude water chemicals from the list of goitrogens which may interfere with the thyroid function or goitre aetiology in Port Sudan city. The results of the present study thus disagree with previous findings^(11–14) in which increased water chemicals interfered with thyroid hormone production.

It is well known that excessive iodine intake can block thyroid hormone synthesis and release^(34,35). This could

be clearly detected by the reduced serum T_4 and T_3 levels and elevated serum TSH level of the children in this coastal city compared with their peers in the other cities where iodine intake is insufficient. Furthermore, the present findings indicate that excessive intake of iodine may have adverse health impacts on the thyroid gland greater than those induced by the iodine deficiency in the populations of the non-coastal cities. This may indicate also that iodine deficiency can be well tolerated and overcome by the thyroid gland. Normal thyroid hormone concentrations were detected in children living in iodine-deficient Sudanese cities where the median UIC was only $2.7 \mu\text{g}/\text{dl}$ ⁽²⁴⁾. Our findings are in line with what was revealed in a similar study⁽³⁶⁾, i.e. that the thyroid gland can compensate by a number of mechanisms to maintain sufficient thyroid hormone production when iodine supply is limited. The elevated Tg values in Port Sudan compared with the other cities is another indicator for thyroid abnormalities. In a similar cross-sectional study, a negative correlation between Tg and UIC and a positive correlation between Tg, thyroid volume and TSH were reported⁽³⁷⁾. The association between excess UIC and high prevalence of goitre could be extracted from the global scorecard for iodine-deficiency disorders⁽¹⁹⁾; the prevalence of goitre in some African countries surrounding Sudan was 63% in Chad, 36.7% in Eritrea and 36.3% in Tunisia, while their corresponding UIC were 21.3, 16.8 and $16.4 \mu\text{g}/\text{dl}$, respectively. In another endemic goitre study, the association of increased thyroid volume with UIC was detected only among children with UIC greater than $50 \text{ g}/\text{dl}$ ⁽³⁸⁾. Another explanation may arise from the hypothesis that a number of pupils have recently moved with their parents from iodine-deficient areas to the iodine-rich city of Port Sudan and developed iodine-induced hypothyroidism. This hypothesis is in line with previous reports^(4,36) that consumption of a high amount of iodine by a population who is iodine deficient may induce hypothyroidism. It might be of interest to note that excessive iodine intake has been shown to promote the development of autoimmune thyroid disease⁽³⁾ which might cause goitre and/or impair thyroid function⁽²⁾.

Conclusions

Excessive iodine intake is likely a factor in the aetiology of endemic goitre and reduced thyroid activity among schoolchildren in the coastal city of Port Sudan. High mineral content of drinking water and thiocyanate from food consumption were found to have no direct association with thyroid function or size. Measures should be taken to reduce the iodine intake of people living in this city.

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