

## **Correlation Between Iodine Status and Dysfunctional Parameters of the Thyroid Gland of Djidja Schoolchildren**

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### **Abstract**

Iodine is reported to be one of the main trace mineral constituting thyroid hormones. The aim of this study was to determine the correlation between urinary iodine concentration status and dysfunctional parameters of the thyroid gland of schoolchildren in central Benin. In our study we selected 108 schoolchildren to whom we performed T3, T4, TSH, iodine and thyroid volume tests. The determination of the morning urinary iodine (iodine) in Djidja schoolchildren gave satisfactory results to 72% thus declaring our study area as a zone of non-iodine dietary deficiency. The hormone assay results are favorable at a rate of 92% and corresponds to hypothyroidism. In fact, TSH

are high in 85% of the study population, T3 are in their case low in 93% of our study population and finally T4 are lower in the 100% of individuals in the study population. But these results are not in agreement with the iodine obtained. Indeed, in the study environment, the population is forced to drink some water rich in fluoride. Fluorine is an iodine antagonist that it can easily substitute, disrupting the production of T3, T4 and TSH hormones. To end, the calculated thyroid echography volumes are for the most part normal volumes with a rate of 45.37 for boys and 35.19 for girls.

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**Keywords:** Iodine, Hormones, Fluorine, Ultrasound volume, Schoolchildren, Benin

## **Introduction**

Iodine is an essential nutrient found in the human body as a key component of the thyroid hormones, thyroxine (T4) and triiodothyronine (T3). So, according to Stangubgy (1992), iodine is a principal trace element constituting thyroid hormones. These thyroid hormones regulate cellular oxidation, energy metabolism, and the basal metabolic rate, and are critically important for neurological growth and development, particularly during gestation and early infancy (Rohner et al., 2014; Skeaff, 2011). It is reported that a low intake in iodine is associated with several negative health effect affecting about 2 million people worldwide and generically named iodine deficiency disorders (Zimmermann et al., 2012). One of the most important iodine disorder is hypothyroidism and goiter (enlarged thyroid gland). This is the result of excessive secretion of thyroid stimulating hormone in response to low levels of circulating T4 resulting in an overactive thyroid gland (Zimmermann and Boelaert, 2015; Rohner et al., 2014; Zimmermann et al., 2008). Those disorder negatively affect the productivity of the one suffering and is known to be one of the most common preventable causes of mental retardation (ICCIDD, 1999; WHO, 2007). This study was undertaken in order to determine the correlation between urinary iodine concentration status and dysfunctional parameters of the thyroid gland of schoolchildren in central Benin.

## **Material and Methods**

### **Study area and Sampling**

Our study was conducted in southern Benin precisely at Djidja (7°20'40" North, 1°56'00" Est) (Figure 1). The study population was composed of children age from 6 to 13 years, born in the municipality and had lived there since birth and attending primary schools (Hanagbo, Dridji, Assegon and Akazounnongon). The study population was the same to those reported in a previous study (Avocefohoun et al., 2017).

## Data collection

A fasting single spot urine sample (~2 mL) was collected from children in the morning from each of the selected students from the 4 primary schools. Children were instructed to void their bladders in the morning before beginning the 24-h urine sample, and spot urine samples were taken from the first morning urine. Once collected, urine samples were transported on ice (4°C) from the schools to the Laboratory and immediately analyzed or stored at -80°C until analysis. Age, sociodemographic and other data were collected using a questionnaire prepared and administered for the study. Urinary iodine concentrations were determined using ammonium persulfate digestion followed by colorimetric analysis based on the Sandell-Kolthoff (Sandell and Kolthoff, 1937) reaction according to a modified microplate method (Ohashi et al., 2000).

Venous blood samples were collected from the same children's and were taken from the cubital veins into vacutainers. The collected blood was allowed to coagulate at room temperature, before the sera were separated by centrifugation and kept at 4°C for 24h or -20°C until analysis.

Serum triiodothyronine (T3) and free thyroxine (FT4) were measured with solid phase time-resolved fluoro-immunoassays (TR-FIA). The reference range for T3 is 4 – 8.3 pmol/L and for FT4 is 10-19.4 pmol/L. TSH was measured with a sandwich TR-FIA and classified as euthyroid ( $0.25 \mu\text{U/l} < \text{TSH} < 5 \mu\text{U/l}$ ), hyperthyroid ( $\text{TSH} < 0.15 \mu\text{U/l}$ ) or hypothyroid ( $\text{TSH} > 7 \mu\text{U/l}$ ).

The thyroid size was determined by ultrasonography. Thus, the longitudinal and transverse scans are performed allowing the measurements of the depth (d), the width (w) and the length (l) of each lobe. The volume (V) of the lobe is calculated by the formula:  $V \text{ (ml)} = 0.479 \times d \times w \times l \text{ (cm)}$ . The thyroid volume is the sum of the volumes of both lobes. The volume of the isthmus is not included.

The body surface area (BSA) is calculated using the formula of Dubois and Dubois (1989):  $\text{BSA (m}^2\text{)} = W^{0.425} \times H^{0.725} \times 71.84 \times 10^{-4}$ . It should be emphasized that by using the ultra-sonographic criteria, a thyroid gland will be called goitrous when its values will be above the 97<sup>th</sup> percentile of the volume found in an iodine replete population used as control.

## Data analysis

The collected data were coded, captured and processed with SPSS 20.0 (Norusis, 2002) for the determination of descriptive statistics in terms of percentage and average. As for the quantitative data, they were subjected to ANOVA using the ANOVA procedure of the SAS 9.2 to assess the gap between girls and boys. Multiple mean comparisons were made with the Student Newman-Keuls test (Dagnelie, 2012). The different correlations of

Person were made with the Minitab 14 software. The results of the different analyzes are presented in the form of tables according to Kisauzi et al. (2012).

## Results

### General condition of the study

The analysis of the surveyed population size (Table 1) and the results of the analysis of the variance and the Student Newan Keuls test (Table 2) shows that the boys dominate the surveyed population with a percentage of 57% but the difference of proportion was not significant in terms of age, height, weight, body surface area and body age ( $p>0.05$ ).

**Table 1.** Number of people surveyed

Modality	Proportion of Population (N)	Samples proportion (N)
Boys	56.74 (320)	57.40 (62)
Girls	43.26 (240)	42.60 (46)
TOTAL	100 (560)	100 (108)

**Table 2.** Analysis of variance performed on the quantitative data

Parameters	Sex		P-value
	Boys	Girls	
Age (years)	9,58± 0,23a	9,28± 0,29a	0,4157
Length (m)	1,30± 0,01a	1,30± 0,02a	0,9924
Weight	25,05± 0,96a	24,15± 1,06a	0,5363
Body surface area	1510,36±0,98a	1509,46±1,08a	0,5419
V R	1587,09± 77,29a	1573,13± 86,94a	0,9052
V L	1523,31±76,37a	1591,21±87,26a	0,5604
V (V L+VR)	3110,40± 143,24a	3164,34±160,73a	0,8036
Iodine	216,45± 30,51a	284,78± 45,14a	0,1959
TSH	7,00± 0,27a	7,04±0,27a	0,9238
T4	3,02±0,18a	3,02±0,24a	0,9879

The averages followed by the same alphabetical letters of the same characters and for the same characteristics are not significantly different ( $p>0.05$ ) according to the Student Newman test -Keuls

### Iodine content determined on subjects and relationship with physical parameters

Table 3 shows the different standards for the iodine rate analyzed on urine.

The analysis of urinary iodine content (UIC) shows that the majority of surveyed students (51%) do not suffer from iodine deficiency (Table 3). Additionally, iodine levels obtained do not vary significantly among age groups. However, people with high body surface area are less iodine deficient compared to others (47%). The Person correlation between iodine levels and physical parameters (age, weight, body surface area) measured on students shows that no significant correlation is obtained between iodine and these

physical parameters ( $p > 0.05$ ). Iodine levels therefore do not depend on sex, body size, and body surface area.

**Table 3.** Iodine content measured on the surveyed students

Categories	Parameters					
	Sex		Age (years)		Body surface area (BSA)	
	Boys	Girls	0<age<10	Age>10	BSA<1500	BSA > 1500
UIC < 20 µg/l (severe deficiency)	13.89 %	4.63 %	08.33 %	10.19%	02.78 %	15.74 %
20 < UIC (µg/l) ≤ 49 (moderate deficiency)	0%	0%	0%	0%	0%	0%
50 < UIC (µg/l) ≤ 99 (slight deficiency)	03.70 %	02.78 %	02.78 %	03.70%	0%	06.48 %
100 < UIC (µg/l) ≤ 300 (No iodine deficiency)	27.78 %	23.15 %	26.85 %	24.07 %	03.70 %	47.22 %
UIC > 300 µg/l (excess of iodine)	09.26 %	12.04 %	07.41 %	13.89 %	0%	21.30%

**Hormone levels determined on students**

Table 4 presents the results of the hormones measured. This table shows that the majority (55%) of the students involved in this study are hypothyroid with a T3 level below 4 pmol/l and a T4 below 10.6 p mol/l. Similarly, subjects with a body surface area greater than 1500 are main part (85%) of this category of hypothyroid.

**Table 4.** Hormone level recorded according the sex, age and body surface area.

Categories	Parameters						
	Sex		Age (years)		Body surface area (BSA)		
	Boys	Girls	0<age<10	Age>10	BSA<1500	BSA > 1500	
TSH	<0.25 µ UI	0%	0%	0%	0%	0%	0%
	0.25-5 µ UI/l	08.33%	06.48%	06.48%	02.85%	0%	12.96%
	>5 µ UI/l	49.08%	36.11%	37.96%	53.71%	06.48%	80.56%
T3	<4 pmol/l	63.89%	29.63%	42.59%	57.41%	06.48%	93.52%
	4-8.3 pmol/l	02.78%	02.78%	0%	0%	0%	0%
	>8.3 pmol/l	0.93%	0%	0%	0%	0%	0%
T4	<10.6 pmol/l	56.48%	43.52%	55.56%	44.45%	6.48%	93.52%
	10.6 -19.4 pmol/l	0%	0%	0%	0%	0%	0%
	>19.4 pmol/l	0%	0%	0%	0%	0%	0%

The thyroid volume values (VT) recorded among the investigated students shows that the majority of the students are in the standards (Table 5). Similarly, students older than 10 years and Body surface area less than 1500 are still present in the standard.

**Table 5.** Presentation of thyroid volume values by sex, age and body surface area

Categories	Parameters
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		Sex		Age (years)		Body surface area (BSA)	
		Boys	Girls	0<age<10	Age>10	BSA<1500	BSA > 1500
Boys	<1.80 ml	06.48%	-	06.48%	0 %	01.85%	04.63v
	1.80 – 4.60 ml	45.37%	-	20.37%	25.00%	0.93%	44.44v
	> 4.60 ml	05.56%	-	0 %	05.56%	04.63%	0.93v
Girls	< 1.99 ml	-	05.56%	05.56%	0%	01.85%	10v
	1.99 – 5.22 ml	-	35.19%	15.74%	19.45%	01.85%	33.33%
	>5.22 ml	-	01.85%	0%	01.85%	0%	01.85%

## Discussion

Our research target 560 schoolchildren (56.74% of boys and 43.26% girls) of the district of Djidja in Central Benin (West Africa). After the first investigation of the visible effect of fluorosis, 108 school children composed of boys (57.40%) and girls (42.60%) were finally retained as study sample. It appears that the boys are in the majority, however, the boy-girl relationship has been maintained in the same proportion as well in the initial population as in the study population. Our observation corroborate those reported by Djossou et al. (2017) in a similar study on the link between fluorosis and sex. However, the difference remains not significant. But considering goiter, the prevalence shows that girls are more affected than boys (Malbossbaf et al., 2013).

The analysis of variances for anthropometric factors and other data such as iodine, T4, T3, TSH and TV shows no significant difference. In addition, the iodine analysis of the urines among our study population shows that 51% of investigated schoolchildren were in the standards (100 - 300 µg/l) recommended by WHO. This proportion include both boys (28% of the total) and girls (23%). It was observed that 21% of the investigated population shows an excess of iodine. Globally, the iodine test in urines is satisfactory at 72% and according to the recommendations of WHO, we can declare that our study area is a zone of non-dietary iodine deficiency. As previously reported in Abomey-Calavi, Southern Benin (Gbaguidi et al., 2013), Djidja in the center of the country is also non-dietary iodine deficiency. In fact, in their study on the status in the district of Abomey-Calavi where 134 schoolchildren were surveyed, the results showed that 92.28% of schoolchildren from 6 to 12 years old had normal iodine rate.

Thought the global status of the area is good, it should be noted that cases of excess iodine are on some schoolchildren in Djidja (21%) do not reassure the health situation of those children. This could occur in a Wolf - Chaikoff effect exposure situation (Wolf and Chaikoff, 1948) that could plunge into thyroid dysfunction states with the support of adverse effects and complications. It was observed a very significant difference in school children with a body surface area greater than 1500 in which the proportion of normal

results was 68% of the investigated population for iodine status. The status is mainly justified by the fact that Djidja is a district where subsistence farming is practiced on a large scale despite the expansion of cotton production. In addition, Djidja is the breadbasket of Zou (a department located in central Benin) with a strong capacity for diversification of foodstuffs. So, according to MPDEPPCAG (2010), food consumption patterns in Benin are mainly determined by agro-ecological zones and the level of urbanization.

These results of iodine are not in adequacy with the TSH, T3 and T4 hormonal results observed. Indeed, in the surveyed population 85% of the schoolchildren displays a TSH level higher than normal (0.25 - 5 UI/l) while the dosage of T3 reveals a positive result with 93% less than 4 pmol/l and the assay of T4 has a positive result with almost 100% less than 10.6 pmol/l. These results allow us to conclude that the schoolchildren surveyed develop hormonal disorders deficiency (hypothyroidism). According to Masson (2014) the thyroid hormones are tri-iodothyronine (T3) and tetra-iodothyronine (T4) secreted from the food hormone and regulated by a pituitary hormone, thyrotropin (TSH), secreted in turn by a gland located on the underside of the brain. Under these conditions the results given by iodine allow to have regular hormonal secretions. Indeed, in a previous work, we studied the prevalence of fluorosis in drinking water consumption by Djidja schoolchildren (Avocefohoum et al., 2017). The analysis of drinking water revealed that these waters are rich in fluoride. In its 2006 report, the National Research Council on National Academies states that fluoride is an endocrine disruptor in the broad sense of normal endocrine function (National Research Council, 2006; Cornet et al., 2010). According to Hetzeil (1983), this impaired function may involve the thyroid gland, parathyroid gland, pineal glands as well as the adrenal glands, the pancreas and the pituitary gland. The consequence is the replacement of the iodine molecules by fluorine. Indeed, fluorine, extremely negative element in the classification of Mendeleev is an antagonist of iodine (Bürge et al., 1984).

Results on thyroid ultrasound volumes show that the majority of school children have normal thyroid echography volume with 45.37% in boys and 35.19% in girls. This is consistent with the result of iodine achieved. But in Japan Fuse et al. (2007) found extreme volumes ranging from 0.8 to 8.5 ml, although conditions are almost identical to iodine or iodine status. This difference may be due to the phenotypical difference among our study population and Japanese. Similarly, in Belgium, Delange et al. (2000) found in their study that the size of the thyroid increased with age and the prevalence of goiter increased from 3.9 in children aged 6 to 11.7 children 12 years old.

## Conclusion

In our study we found that the iodine status observed at Djidja with a 72% appreciation of satisfactory morning iodine results did not agree with the thyroid function test results of the schoolchildren sampled. These school children present the results of T3, T4 and TSH of anyone developing hypothyroidism. This is justified by the substitution of iodine by an antagonistic substance, fluorine. On the other hand, the study of the thyroid echography volume reveals no significant difference. At 80% the thyroid echography volume of schoolchildren as boys is normal, which means that the substitution of fluorine for iodine does not have too much influence on the thyroid morphology.

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