

## Parameters of thyroid function in the endemic goitre of Akungba and Oke-Agbe villages of Akoko area of southwestern Nigeria

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### Summary

The parameters of thyroid function were determined in Akungba and Oke-Agbe communities of Akoko area, where goiter is endemic and compared to a control population of Erinmo and Ifewara in Ijesha area, both areas being in southwestern Nigeria. The two study areas have similar physical and geological settings. However, while the main carbohydrate source of the control population are yam and/ or breadfruit, the Akoko population derives her carbohydrates mainly from cassava which could lead to increased serum thiocyanate, a goitrogen.

The serum level of tetraiodothyronine ( $T_4$ ) was significantly ( $P < 0.05$ ) higher in Ifewara (11.0) and Erinmo (11.8) compared to Akungba (7.1) and Oke-Agbe (8.8  $\mu\text{g/dL}$ ). The triiodothyronine ( $T_3$ ) was significantly ( $P < 0.05$ ) higher in Ifewara (193) than Erinmo (133) and also significantly ( $P < 0.05$ ) higher in Oke-Agbe (127) compared to Akungba (107 mg /dL). Conversely, thyroid stimulating hormone (TSH) ( $\mu\text{U/mL}$ ) level was significantly ( $P < 0.05$ ) higher than values obtained from Ifewara (4.5) and Erinmo (3.3).  $T_3/T_4$  ratio above 25, indicative of hypothyroidism and endemic goiter, was 14, 7, 4 and 0% from Akungba, Oke-Agbe, Ifewara and Erinmo, respectively. The results of the present study clearly explain the Akoko goiter endemic in the light of modification (s) of thyroid metabolism.

**Keywords:** Goiter, serum,  $T_3$ ,  $T_4$ , TSH, TBG

### Résumé

Les paramètres de la fonction de la thyroïde ont été déterminés dans les communautés Akungba et Oke-Agbe de la région de akoko, où le goitre est considéré endémique comparé aux populations contrôles de Erinmo et Ifewara dans la région d'Ijesha, les 2 régions étant dans la partie sud-ouest du Nigeria. Les 2 régions d'études ont la même apparence physique et géographique. Cependant, lorsque la principale source d'hydrate de carbone (glucides) chez les populations de contrôle est soit l'igname et/ou du pain, les populations de la région d'akoko ont pour principale source de glucide le manioc qui peut aboutir à un taux élevé de thiocyanate (un goitrogène) dans le sérum. Le taux de sérum de la tétraiodothyronine ( $T_4$ ) a été significativement élevé ( $P < 0.05$ ) à Ifewara (11.0) et Erinmo (11.8) comparé à Akungba (7.1) et Oke-Agbe (8.8  $\mu\text{g/dl}$ ). La triiodothyronine ( $T_3$ ) a été significativement ( $P < 0.05$ ) élevée à Ifewara (193) qu'à Erinmo (133) et aussi significativement ( $P < 0.05$ ) élevée à Oke-Agbe (127) comparé à Akungba (107ng/dl). Contrairement, le taux de la Thyroïde Stimulating Hormone (TSH) (en  $\mu\text{U/ml}$ ) a été significativement élevé ( $P < 0.05$ ) à Akungba (10.5) qu'à

celui obtenu à Oke-Agbe (7.6), et les 2 taux ont été significativement élevés comparés aux autres qui ont été significativement ( $P < 0.05$ ) élevés comparés aux valeurs obtenues à Ifewara (14.5) et Erinmo (3.3). Le ratio  $T_3/T_4$  au-dessus de 25 indicatif de l'hyperthyroïdisme et du goitre endémique, a été de 14, 7, 4 et 0% à Akungba, Oke-Agbe, Ifewara et Erinmo respectivement. Les résultats de la présente étude expliquent clairement l'endémie du goitre dans la région de Akoko à la lumière de modification (s) du métabolisme de la thyroïde.

### Introduction

The thyroid gland, situated in front of the neck, produces two major hormones namely, 3,5,3',5' - tetraiodo-L-thyronine ( $T_4$ ) and 3,5,3'-triiodo-L-thyronine ( $T_3$ ). These hormones are particularly important as regulators of differentiation during development, catalysts for the oxidative reactions and regulation of metabolic rates in the body [1].  $T_3$  is the apparent principal thyroid hormone, its circulating prohormone is  $T_4$  [2].

Thyroxine-binding globulin (TBG) is the major serum binding protein for both thyroxine and triiodothyronine, having a binding capacity of about 20  $\mu\text{g}$   $T_4/100$  ml plasma at physiologic pH. TBG, because of its relatively high binding capacity, is therefore the most important determinant in the circulation of total  $T_4$  concentrations.

The diagnosis of primary hypothyroidism is best made by documenting an increase in the concentration of TSH in serum which results from a decrease in thyroid hormone concentrations in the serum [3]. Conversely, an increase in the concentration of thyroid hormones in serum, as occurs in hyperthyroidism, suppresses serum TSH to very low levels [4].

Our earlier study [5] showed that there was a synergistic effect between dietary cyanide low iodine intake and malnutrition in the etiology of goiter and that urinary thiocyanate (SCN) level was significantly higher in the endemic goiter areas of Akungba and Oke-agbe (where protein and iodine ingestion was similarly low) compared to the control populations of Erinmo and Ifewara.

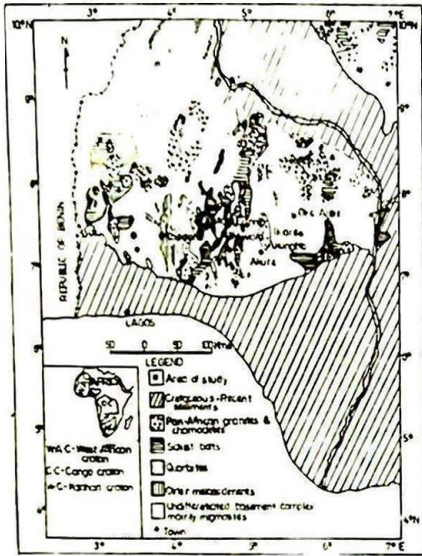
Since the villages of both the test and control populations are situated in southwestern Nigeria with similar geological settings, the present work was designed to compare the thyroid function of the goitrous cassava-eating groups through the levels of their thyroid hormones and associated parameters.

### Materials and methods

Figure 1 shows the study areas under consideration. Akungba (Akoko South) is about 10 kilometers south of Ikare city while Oke-agbe is 12 kilometers to the north. These locations were chosen for this study because a

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detailed survey by Oke *et al.* [6] showed that the goiter prevalence in this area was above 20%. A similar population, Erinmo about 15 kilometers east of Ilesha city, and Ifewara, 18 kilometres to the south, were chosen as the control. The physical and geological settings of the areas are similar; neither area is underlain by sedimentary rocks like shales and coals [7] which have been reported to be the major source of water-borne goitrogen [8]. Though the two populations survive on subsistence farming, the main carbohydrate source (s) of the population are yam/breadfruit, while the Akoko population derives her carbohydrates mainly from cassava, which could lead to increased serum thiocyanate, a goitrogen.



**Fig.1:** Geological settings of the locations studied in southwestern Nigeria.

**Human subjects**

The study focused on young women aged 20 – 45 years. The choice of females was informed by the preponderance

of goiter among females compared to male [6]. Based on oral interviews, neither of the two populations was on any prophylactic program either before or during the study that could affect the pathophysiology of the thyroid. All the subjects gave their oral informed consent prior to the commencement of the study.

**Samples**

Blood samples were randomly obtained from goiter and non-goiter subjects in Akoko (Akungba and Oke-Agbe) and Ilesha (Ifewara and Erinmo) areas. Blood was drawn by venous puncture into sterile tubes with a minimum of stasis. The blood was allowed to clot at room temperature and then centrifuged (manually) for about 10 minutes to separate the serum from the cells. The serum samples were then frozen fresh at - 10° C until analyzed.

**Methods**

Serum thyroid hormones, T<sub>4</sub>, T<sub>3</sub>, and pituitary TSH were quantified by immuno <sup>125</sup> I kits obtained from Pantex, Division of Bio-Analysis Inc., Santa Monica, while TBG was quantified using kits obtained from Nichols Institute Diagnostics, San Juan Capistrano.

**Statistical analysis**

Mean value, standard error of mean (SEM) and new multiple range test were calculated according to zar [9]. Significance levels were calculated and presented at 95% confidence level.

**Results**

A total of serum samples comprising 76, 25, 48, and 54 from Akungba, Oke-Agbe (Akoko), Ifewara and Erinmo (Ilesha), respectively, were analysed. Table I shows a comparison of parameters of thyroid function. The number of samples from Oke-Agbe was small because the villagers misunderstood the objective of the study and all efforts to explain to the chief-in-council and individuals failed.

**Table 1:** Comparison of serum analyses of subjects from Akoko (Akungba and Oke-Agbe) and Ilesha (Ifewara and Erinmo) areas (Mean ± SEM)

Variables	Location			
	Akungba (76*)	Oke-Agbe (25)	Ifewara (48)	Erinmo (154)
T <sub>3</sub> (ng/dL) range	107.04 <sup>a</sup> ± 2.41 (70 – 170)	127.07 <sup>a</sup> ± 6.55 (85 – 280)	192.83 <sup>a</sup> ± 5.34 (110 – 290)	132.76 <sup>a</sup> ± 4.43 (70 – 220)
T <sub>4</sub> (µg/dL) range	7.09 <sup>b</sup> ± 0.33 (1.70 – 15.80)	8.78 <sup>b</sup> ± 0.70 (5.00 – 13.50)	10.99 <sup>a</sup> ± 0.45 (6.30 – 23.50)	11.84 <sup>a</sup> ± 0.77 (8.00 – 38.00)
TSH (µU/ml) range	10.54 <sup>a</sup> ± 0.36 (1.20 – 16.00)	7.59 <sup>b</sup> ± 0.35 (1.25 – 14.00)	4.45 <sup>c</sup> ± 0.26 (1.10 – 8.00)	3.34 <sup>c</sup> ± 0.37 (3.80 – 5.80)
TBG (µg/ml) range	35.26 ± 3.24 (3.10 – 60.05)	31.15 ± 2.60 (20.00 – 55.50)	35.04 ± 1.27 (25.50 – 70.50)	36.70 ± 1.33 (28.00 – 62.50)
T <sub>3</sub> /T <sub>4</sub> (ng/µg) range	18.00 <sup>a</sup> ± 1.43 (5.38 – 76.47)	15.15 <sup>a</sup> ± 1.51 (9.23 – 32.00)	18.43 <sup>a</sup> ± 1.72 (9.23 – 33.54)	12.01 <sup>b</sup> ± 0.51 (3.68 – 17.50)

\*Number of subjects. Means of the same superscript letter along the same row are not significantly (P > 0.05) different

**Table 2:** Coefficients of correlation<sup>a</sup> between goitre incidence<sup>b</sup> and serum analyses of subjects from Akoko (Akungba and Oke Agbe) and Ilesha (Ifewara and Erinmo) areas. Number of cases is 76

Parameter	Akoko				Ilesha			
	Goiter	T <sub>3</sub>	T <sub>4</sub>	T <sub>3</sub> /T <sub>4</sub>	Goiter	T <sub>3</sub>	T <sub>4</sub>	T <sub>3</sub> /T <sub>4</sub>
Goiter	1.00				1.00			
T <sub>3</sub>	-0.02	1.00			-0.02	1.00		
T <sub>4</sub>	-0.16	0.25*	1.00		-0.06	0.12	1.00	
T <sub>3</sub> /T <sub>4</sub>	-0.11	NC	NC	1.00	0.06	NC	NC	1.00

\* Level of significance. \*,  $P < 0.05$ ;

<sup>b</sup> Values were culled from Akindahunsi (1992)

NC: Not calculated

The serum level of  $T_3$  was significantly ( $P < 0.05$ ) higher in Ijesha area compared to the Akoko test locations. Within communities, Oke-Agbe had significantly ( $P < 0.05$ ) higher  $T_3$  level (127) compared to the Akungba which recorded the lowest  $T_3$  level (107 ng/dL) in the study. Ifewara recorded the highest  $T_3$  level (193), significantly ( $P < 0.05$ ) different from the value obtained in Erinmo (133 ng/dL). There was, however, no significant ( $P > 0.05$ ) difference between the  $T_3$  level in Oke-Agbe (test area) and Erinmo (a control area).

The other thyroid hormone considered,  $T_4$  ( $\mu\text{g/dL}$ ), was also significantly ( $P < 0.05$ ) higher in the Ijesha (Erinmo – 11.8; Ifewara – 11.0) than the Akoko area (Akungba – 7.1; Oke-Agbe – 8.8). Though Oke-Agbe recorded a higher  $T_4$  level than Akungba, the difference within communities was not significant ( $P > 0.05$ ).

### Discussion

There has been a lot of variation in the serum  $T_3$  and  $T_4$  contents from goitrous areas of Africa and Europe as reported in the literature. For instance, Lagasse *et al* [10], working in the Ubangi area of Zaire, reported  $T_3$  levels of 136 and 174 ng/dL and  $T_4$  levels of 3.1 and 4.4  $\mu\text{g/dL}$  from Bodiapinga (goiter prevalence of 68%) and Bombaliswe (goiter prevalence of 66%), respectively. Delange *et al* [11], working in Sicily, found  $T_3$  levels of 181, 169, 153 and 145 ng/dL and  $T_4$  levels of 3.5, 3.7, 3.7 and 2.7  $\mu\text{g/dL}$  from Catania, Tronia, Bronie and San Angelo, respectively. Benmiloud *et al* [12], however, reported higher  $T_3$  levels of 240, 235 ng/dL in goitrous Messelmoune and Takana with 166 ng/dL for non-goitrous Algiers while  $T_4$  levels were 5.0, 5.6 and 8.3  $\mu\text{g/dL}$  for these Algerian communities, respectively. Though  $T_3$  levels obtained in this study are comparable to values reported by Lagasse *et al* [10] and Dalenge *et al* [11], they were lower than those reported by Benmiloud *et al* [12]. However,  $T_4$  levels obtained for Ifewara (11.0) and Erinmo (11.8) in this study were generally higher than those quoted above while the values for the goitrous Akungba (7.1) and Oke-Agbe (8.8) compared favourably with the figures quoted for non-goitrous areas by earlier workers.

It had earlier been pointed out that the modification of thyroid metabolism – a feature of goiter endemia – is characterized by decreased serum  $T_4$ , normal  $T_3$  and elevated TSH [13]. Abnormalities in thyroid metabolism induced by cassava ingestion and/or thiocyanate overload are characterized by decreased thyroid iodine reserves, alterations in intrathyroidal hormone production, including MIT/DIT (mono/diiodothyronine) ratio and decreased  $T_4$  synthesis, peripheral distribution of thyroid hormones and increased thyroid size [14]. Though higher in Ijesha than Akoko area,  $T_3$  in Oke-Agbe (127 ng/dL) was not significantly ( $P > 0.05$ ) different from that obtained in a control location – Erinmo (133 ng/dL) whereas  $T_4$  was significantly ( $P < 0.05$ ) lower in both Akungba and Oke-Agbe than Erinmo and Ifewara. This clearly indicates some thyroid abnormalities in the test area as evidenced by the goiter endemia.

The percentage of subjects with a  $T_3/T_4$  (ng/ $\mu\text{g}$ ) ratio greater than 25 (Fig. 2) were 14, 7, 4 and 0 for Akungba, Oke-Agbe, Ifewara and Erinmo, respectively. This clearly explains the Akoko goiter endemia [15].

The TSH levels recorded in this study were 10.54, 7.59, 4.45 and 3.34  $\mu\text{U/ml}$  from Akungba, Oke-Agbe, Ifewara and Erinmo, respectively. This result tends to confirm primary hypothyroidism and goiter endemia in Akungba-Oke Agbe population [12,16]. However, there was no significant ( $P > 0.05$ ) difference in the levels of TBG among the study areas.

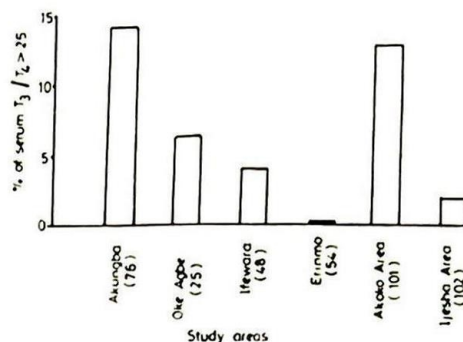


Fig. 2: Comparison of the critical values of  $T_3/T_4$  ratio from Akoko (Akungba and Oke-Agbe) and Ijesha (Ifewara and Erinmo) areas

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