

## Thyroid Hormone Profile for School Children Living in a Severely Goitre Endemic Area in Nigeria.

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### ABSTRACT

One hundred and fifty-four (154) blood samples from Nimbo and Ezzilo were analysed for thyroid hormone profile. These consisted of 98 blood samples from Nimbo (63 males and 35 females) and 56 blood samples from Ezzillo (30 males and 26 females). Thyroid stimulating Hormone (TSH), Thyroxine (T4) and Triiodothyronine (T3) were estimated. In both TSH and T3 the differences observed in the two populations investigated were statistically significant: (TSH: 3.18  $\pm$  1.27 mU/L Vs 1.33  $\pm$  0.43mU/L; P<

0.05). (T3: 2.47  $\pm$  0.79nmol/L Vs 1.74  $\pm$  0.35nmol/L; P<0.05). In both the study and control populations and amongst the various age groupings the observed differences in the calculated mean values of T4 estimations were not statistically significant (P>0.05). The observed difference in the mean values for TSH and T3 were statistically significant (TSH: 3.50  $\pm$  1.49 mU/L Vs. 1.37  $\pm$  0.44mU/L; P<0.05) (T3:2.47  $\pm$  0.81 nmol/L Vs. 1.71  $\pm$  0.34 nmol/L; P<0.05). Amongst the females and age-group matched subjects, a statistically significant difference was observed for TSH and T3 (TSH : 2.90  $\pm$  0.98 mU/L Vs. 1.28  $\pm$  0.44 mU/L; P < 0.05), (T3: 2.47  $\pm$  0.77 Vs. 1.78 nmol/L  $\pm$  0.36 nmol/L; P<0.05). In the female age-group 11 - 15 years, the difference observed in the TSH mean value of both populations was not statistically significant (P> 0.05). In the female subjects, the difference observed in T4 calculated mean values were not statistically significant (132.59  $\pm$  27.57 nmol/L; 129.42  $\pm$  57.05 nmol/L; P>0.05). In both populations under study all the subjects whose blood samples were analysed for thyroid profile were euthyroid. However 63% and 16% respectively of the study and control populations had T3 levels above the normal range while 50% and 42% of the study and control populations had T4 above the normal range. Only one male subject aged 13 years of the study population had TSH above the normal range (6.9mU/L), however, both T4 (112nmol/L) and T3 (1.7nmol/L) were within normal range. Ten and four subjects had TSH values above 5 mU/L and 6 mU/L, respectively amongst the study population. The corresponding T4 and T3 values were normal. In the control group no subject had TSH value up to 5mU/L.

**Keywords:** goiter, thyroid, hormone, profile, tyrosine

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## INTRODUCTION

Over the ages, several efforts had been made to identify the cause and treatment of goitre. Saint Lager in 1867 listed 43 different views on the causes of goitre as expressed by 378 authors. Some of the postulated views included venomous properties of water, it's origin and deficiency or excess of certain venomous mineral, others implicated atmospheric factors such as humidity, temperature and lack of sunshine. Alcoholism, consanguinity in marriage and chemical composition of the air were variously put forward as possible causes of goitre. Faulty nutrition and poverty are the probable cause of goiter [1]. However, Baumann in 1896 identified the presence of iodine in the thyroid gland. From then iodine was considered as a possible treatment for

goiter [2].

The use of iodine in treatment of goitre introduced initially by Coindet in 1820 slowly gained acceptance over the years. [3] However, the present-day practice in the prevention and control of goitre is based on the four years' work (1916-1920) of Marine and Kimball [4], had stated in 1915 that "Simple goitre is the easiest and cheapest of all known diseases to prevent and its control maybe accomplished by available methods as soon as any organised society determines to make effort"<sup>(4)</sup>.

The healthy human adult body contains 15-20 mg of iodine of which 70-80% is in thyridid gland. The gland weighs only 15-25g [5].

Iodine is rapidly absorbed through the guts, via the small intestine as iodide.

The average daily intake is 100-150ug per day. After absorption iodide is effectively removed from the plasma by the thyroid gland and the kidneys. The uptake of iodide by the thyroid cell involves both an active transport process and passive diffusion. The active iodide trapping mechanism of the thyroid with a gradient of 100:1 between the thyroid cell and extra cellular fluid enhances uptake of about 60ug of iodide per day to ensure adequate synthesis and supply of thyroxine. In conditions of iodine deficiency, the trapping gradient increases to 400:1 [5],[6].

Once inside the cell iodide is rapidly oxidized and bound to tyrosine residues of thyroglobulin. The thyroglobulins are the major protein constituents of the thyroid gland. It is a glycoprotein with molecular weight of 660,000 formed on polyribosomes in the endoplasmic reticulum of the follicle cell. Each thyroglobulin molecule has about 1100-1150 tyrosine residues, of which only a fraction are accessible for iodination. The binding of iodine to tyrosine residues (i.e organification) depends on the oxidation of the iodide through a peroxidase -system [5], [6]. The bound iodine forms both mono-iodotyrosine (MIT) and diiodotyrosine (DIT). Under the influence of coupling enzymes, coupling of suitably placed iodotyrosines take place to form tetra iodotyrosine or thyroxine (T4) from two DIT and also tri-iodotyrosine (T3) from one DIT and one MIT. The extrusion of an alanine side chain, accompanies this process. In iodine deficiency DIT is less abundant than MIT and relatively less T4 is formed

than T3 [5],[6].

After production the hormones T4, and T3 are stored in the colloid as iodoproteins. Secretion into the blood is by pinocytosis. This process as every other step in the thyroxine formation is greatly facilitated by thyroid stimulating hormone (TSH) produced by the anterior pituitary gland. The intracellular lysozymes fuses with the droplets and the proteolytic enzymes progressively degrade the thyroglobulin into constituent amino acids releasing T4, and T3 into the cell and then into the blood stream. <sup>(6)</sup>

There are 2 major thyroid hormones, thyroxine and tri-iodothyronine (T4 and T3) although other related substances are also present in blood. [7] In circulation, T4 and T3 are mostly transported in the bound form to plasma protein. T4 is bound mainly and avidly to an alpha globulin thyroxine or thyronine binding globulin (TBG) as well as to T4 binding pre-albumin (TBPA) and to albumin. By virtue of its intense affinity for T4, TBG, is normally the major determinant of overall binding capacity, the other plasma-proteins being less important. Due to the high affinity of the binding of plasma- proteins to T4, only a small proportion of the hormone, approximately 0.03% is free in circulation. Ninety percent of the total circulating thyroid hormone, is made up of T4. However in cases of early thyroid failure, iodine deficiency or increased TSH stimulation, the production of T3 relative to T4, increases due to increased thyroid release of T3, as well as increased efficiency of peripheral production of

T3 from T4 [7]

T3 is less bound by TBPA, and less avidly to TBG, and therefore, the normal proportion of free T3 (0.3%) is about 10 times greater than free T4. T3 has a more rapid onset and offset of action and contributes minimally to the total hormonal iodine concentration in blood. It is responsible for the tissue action of thyroid hormones, and it is also generated peripherally from 5' monodeiodination of T4 (T3 neogenesis); [7]. Expenditure and turn over of essentially all substrates , vitamins and hormones [7]

Mechanisms of action remain uncertain. However, it has been noted

## **MATERIALS AND METHOD**

### **LOCATION OF STUDY AREA**

The research was undertaken at Central Primary School, Nimbo, in Uzo-Uwani Local Government Area of Enugu State.

#### **FACILITIES:**

**Education:** There are 4 primary schools and one Secondary School in Nimbo. The Secondary School is just over 10 years old and is for both boys and girls.

**Water Supply:** There is no pipe borne water or functional bore-hole. Water for drinking and domestic use is usually obtained from poorly protected streams and rivulets that dry up during the dry season, when underground water from poorly protected wells become the main source of water. These are often between 10-20 metres deep and sited within the compound. The presence of a well is a mark of affluence.

**Health:** A poorly staffed and equipped Government Health Centre

exists at Ukpabi village. Most of the health care services are provided by a private clinic at Opana village.  
**Others:** A tarred road constructed about 34 years ago from Nsukka to Ada-rice World Bank irrigation scheme at Adani (25km away) traverse Ukpabi and Opana villages. However, an all-season earth road of about 4 kilometers leads into Nimbo and Owerri villages from Ukpabi. A four day Eke and Orié Markets are located at Nimbo and Opana where mostly farm produce are sold. Salt is preferentially preserved and sold in baked form. Only rice milling and garri grating factories are mechanised industries located in the town. In recent times for the commercial reason of high turnover most of the cassava are grated and fried the same day without enough time for fermentation. None of the villages has electricity supply.

### **STUDY DESIGN**

This is a controlled community based study. Prior to the main study, a preliminary study was carried out to re-establish the prevailing goitre prevalence rates of the previously assessed areas in Enugu State using the palpation method and the WHO grading system [9]. The initial results suggested an increasing trend. The previously known non-endemic areas [10] were noted to have developed high goitre prevalence rates. Further widespread assessment involving cohorts of 50 pupils per school from a minimum of two primary schools (each from a different autonomous community) in each local government

#### **Study Population**

Pupils of the Central Primary School Nimbo, Uzo-Uwani LGA, from primary one to six aged between 6-18 years were studied. Control pupils of similar

#### **Sampling Procedure**

Following the clearance of the Ethical Committee of the University of Nigeria Teaching Hospital, Enugu, consultations were held with the Ministry of Education, Enugu, Uzo-Uwani and Ishielu Local Government officials, Health workers, and the Parents/Teachers Association of the study and Control Primary Schools. The aim, procedure and relevance of the study was fully explained to the relevant officials at each administrative level and their permission obtained. At the school, prior to the commencement of the study, all the pupils were assembled for a health-talk on goitre and other iodine deficiency disorders and the need for supplementation with iodine in their daily diet. The details of the study were explained to them. Pupils had to satisfy the following criteria to

area in Enugu State was done. This was with the view to locating areas that have no goitre endemicity within the same socio-cultural environment as Nimbo town. Udi town which was earlier indicated as the control area (based on the previous goitre rate of 2.6%  $\pm$  0.63%) [10], was found to be inappropriate as the palpable goitre rate in school children was found to be 36%. Consequently Ezillo town was chosen as the alternative control area due to its relatively lower goitre prevalence rate of 19.35% (from the preliminary work) and its agricultural and social economic milieu that is similar to that of Nimbo town.

age and sex from Ezzillo Community Primary School in Ishielu LGA were enlisted.

qualify for inclusion in the study.

- Must have been born in the locality or must have been resident in the locality up to five years consecutively.
- Must be in the age range from six to eighteen years.

The exclusion criteria were:

- Consumption of cough mixture in the preceding six weeks before the study.
- Use of iodine for treatment of external wounds six weeks prior to study.
- Presence of febrile illness on the day of the study (As per collection

of samples for laboratory tests).

### SAMPLING TECHNIQUE

#### Sample Size Determination

To determine the minimum statistically acceptable sample size the formula

$$n = \frac{(1.96)^2 \times P(100-P)}{e^2}$$

where P = Prevalence rate of 38.8%

e = Sampling error of 5% was employed.

#### Sampling

The cluster sampling method was used in which the schools were the clusters. Hence a simple random sampling technique was used to select the Central Primary School out of the four

primary schools in Nimbo. Consequently all the pupils present on the days of the study were examined for goitre.

#### Study Sample Size

The population of pupils at Central Primary School, Nimbo is four hundred and forty-eight. In all, three hundred and ninety-six pupils were examined for goitre: consisting of two hundred and forty-six males (246 males and 150

females) representing 88.4% of the entire study population. Venous blood was collected from ninety eight pupils (representing 24.74%) who gave their informed consent for thyroid hormone profile.

#### Control Sample Size

The school population at Community Primary School Ezzillo is three hundred and seventeen. Of these two hundred and seventy-five pupils were examined for goitre (146 males and 129 females) representing 86.75% of the entire control sample size. Intellectual assessment was performed on one hundred and forty-

four pupils selected by systematic random sampling of every second pupil, representing 52.36% of the control sample size. Venous blood was collected from fifty-six pupils representing 20.36% of the control sample size for thyroid hormone profile.

#### Clinical Assessment

Each pupil was examined for the presence of goitre using the palpation/inspection method. They were requested to drink a mouth full of water while inspecting the anterior aspect of the neck. This was followed with palpation in both the normal and extended positions of the neck. The grading was done according to the

WHO classification [9]. After the examination of the neck, the height and weight of each subject (without footwear's) were measured using a calibrated wall in metres and the HANA bathroom weighing balance (in kilogrammes). The body mass indices (BMI) were subsequently calculated using the formula

$$\frac{(\text{Body Mass in kg}) [11]}{(\text{Height in Metres})^2}$$

Some clinical signs of hypothyroidism were assessed. The intellectual ability

was assessed using the culture free and Nigerian standardized methods of

Raven's Standardized Progressive Matrices (SPM) [12] and Draw A Person Test (DAPT) [13] (appendices ii and iii). The pupils were called into a classroom in groups of 20 each; while 10 were engaged with the SPM test individually (each with a separate booklet) the other 10 were requested to draw a human being the best way they could on the reverse side of the individualized answer sheets. As each pupil completed one test, he/she was

#### LABORATORY TECHNIQUE

The thyroid hormone profiles (TSH, T4 and T3) were analysed on each research at the UNTH radio-immuno-assay research laboratory using a scintillation counter (SD 12, Oakfield Health Care Products, Birmingham, England). All the assays were done with reagents supplied from the North-East Thames Region Immuno-Assay Unit (NETRIA) London at the radio-immuno-assay laboratory of the University of

#### STATISTICAL ANALYSIS

Results were expressed as percentages and mean  $\pm$ SD. Mean values for the two populations with different goitre prevalences were compared.

#### DISCUSSION

One hundred and fifty-four (154) blood samples from Nimbo and Ezzilo were analysed for thyroid hormone profile. These consisted of 98 blood samples from Nimbo (63 males and 35 females) and 56 blood samples from Ezzillo (30 males and 26 females). Thyroid stimulating Hormone (TSH), Thyroxine (T4) and Triiodothyronine (T3) were estimated. Tables 1a, 1b, and 1c show the age-group matched calculated mean values of the estimations of TSH, T4 and T3 respectively from both investigated populations. In both TSH and T3 the differences observed in the two

moved to the other test modality. There was no time limit. Venous blood (2mls) was collected from the cubital vein into a plain bottle and carried in a cold chain box to the Mission Hospital at Adani where the serum was separated by centrifugation and stored in deep freezer. The samples were subsequently transported in a cold chain box to the University of Nigeria Teaching Hospital Enugu for analysis.

Nigeria Teaching Hospital (UNTH) Enugu. The serum concentration of TSH were determined by the sandwich method of immuno-radiometric assay (IRMA). The assay sensitivity was 0.04 mU/L. The serum concentration of T4 and T3 were determined by the double antibody radioimmuno-assay (DA-RIA). The assay sensitivities were 3.103 nmol/L and 0.2051 nmol/L respectively.

Calculations were made with student t test. The difference was considered significant where probability  $P \leq 0.05$ .

populations investigated were statistically significant: (TSH:  $3.18 \pm 1.27$  mU/L Vs  $1.33 \pm 0.43$  mU/L;  $P < 0.05$ ). (T3:  $2.47 \pm 0.79$  nmol/L Vs  $1.74 \pm 0.35$  nmol/L;  $P < 0.05$ ). Tables 6a and 6c also show that for the age-grouping 6-10 years and 11-15 years the observed differences were statistically significant ( $P < 0.05$ ).

In both the study and control populations and amongst the various age groupings the observed differences in the calculated mean values of T4 estimations were not statistically significant ( $P > 0.05$ ) Table 1b.

The male gender and age-group matched calculated mean values of the estimations of TSH, T4 and T3 for both studied populations are shown on Tables 2a, 2b, and 2c. The observed difference in the mean values for TSH and T3 were statistically significant (TSH:  $3.50 \pm 1.49$  mU/L Vs.  $1.37 \pm 0.44$  mU/L;  $P < 0.05$ ) (T3:  $2.47 \pm 0.81$  nmol/L Vs.  $1.71 \pm 0.34$  nmol/L;  $P < 0.05$ ). Tables 7a and 7c also show that for the age-groupings 6-10 years and 11-15 years the observed differences were statistically significant. ( $P < 0.05$ ).

Table 2b shows that there is no statistical significance ( $P > 0.05$ ) in the differences observed for the calculated mean value of T4 estimations in the male subjects of both investigated populations. Amongst the females and age-group matched subjects, a statistically significant difference was observed for TSH and T3 as shown on Tables 3a and 3c (TSH:  $2.90 \pm 0.98$  mU/L Vs.  $1.28 \pm 0.44$  mU/L;  $P < 0.05$ ), (T3:  $2.47 \pm 0.77$  Vs.  $1.78 \pm 0.36$  nmol/L;  $P < 0.05$ ). In the female age-group 11 - 15 years, the difference observed in the TSH mean value of both populations was not statistically significant ( $P > 0.05$ ). In the female subjects (Table 3b), the difference observed in T4 calculated mean values were not statistically significant ( $132.59 \pm 27.57$  nmol/L;  $129.42 \pm 57.05$  nmol/L;  $P > 0.05$ ). In both populations under study all the subjects whose blood samples were analysed for thyroid profile were euthyroid. However 63% and 16% respectively of the study and control populations had T3 levels above the normal range while 50% and 42% of the study and control populations had T4 above the normal range. Only one male subject aged 13 years of the study population had TSH

above the normal range (6.9mU/L), however, both T4 (112nmol/L) and T3 (1.7nmol/L) were within normal range. Other TSH values were within the normal range. Ten and four subjects had TSH values above 5 mU/L and 6 mU/L respectively amongst the study population. The corresponding T4 and T3 values were normal. In the control group no subject had TSH value up to 5mU/L.

Evaluating the thyroid hormone profiles showed that in the study and control populations the mean TSH and T4 values were within the normal range of our Laboratory; the mean T3 value was slightly elevated in the study population, Table 6, 7 and 8,. (normal range TSH 0.3-6.5mU/L; T4 50-138nmol/L; T3 0.5-2.1nmol/L). Though the mean TSH values were within normal range, the study mean value was higher than the control and the difference was statistically significant ( $3.18 \pm 1.27$  mU/L Vs.  $1.33 \pm 0.43$  mU/L;  $P < 0.05$ ). On stratification according to age group and gender, the difference between the study and control population were maintained suggesting that the difference was universal and widespread. The thyroid was obviously more under stress in the study population. The higher TSH mean values that were statistically significant in the study population demonstrates the greater effort of the body system in the more iodine deficient environment to trap more iodine for adequate production of the thyroid hormones. This has been observed in other studies in iodine deficient environments [14] [15] [16]. The higher TSH is consistent with the observed higher prevalence of goitre in the study area. Though the



levels appear surprisingly less than anticipated, similar relatively low TSH had been observed by Isichie [17] who also observed that his findings were in agreement with other workers such as Delange, Ermans and Vis et al, and Chopra and Hershman who had previously worked in endemic areas [17].

The mean T3 values were elevated in the study population and the differences between the estimated values of the study population and that of the control remained significant both on gender and age group stratifications. Previous studies have shown that in an iodine deficient environment, part of the adaptation in thyroid economy includes a relative increase in the production and release of T3 from the thyroid gland [18]. T3 needs less iodine molecule for its production, is less bound to plasma proteins and is the active form of the hormone [18]. In this work, there is a consistent statistically significant difference with the elevation of mean T3 in the study population which is in keeping with the above general view. Sixty-three percent of the T3 estimations from the study population were above the normal range compared to 16% from the control population. Isichie had observed that about 45% of goitre patients in Plateau State of Nigeria had T3 levels above the normal range<sup>(174)</sup>. An increase in transport protein have also been postulated as a possible cause [14]. However, reliance on this parameter only for the diagnosis of thyrotoxicosis in a goitre endemic area is discouraged [14].

The mean T4 value were of normal range but slightly higher in the study male sub-population. However the differences obtained in the total, or stratified data on

gender or age group basis showed no significant difference. Furthermore, a drop in mean T4 value was often observed in upper age group of 11-15 years in study population compared to the increase observed in the control population (Tables 6b, 7b and 8b), a trend which coincides with the period of maximal growth needs of adolescents. This drop in mean T4 level is however in keeping with recent observations that in iodine deficient environments, there is a relative drop in T4 production. Udeozo and Agharanya made similar observation at Obudu [15]. The prime relevance of this, is the dependence of brain T3 on the serum T4 levels as T4 is selectively transported across the blood/brain barrier [19] [20]. The brain is as such afflicted much earlier than other organs with a drop in serum T4 level. This is referred to as cerebral hypothyroidism [20] [21]. It is now believed that this condition stimulates the increased TSH production and is responsible for the mental torpor and general inertia often observed in iodine deficient populations even in the absence of clinical hypothyroidism [20] [21]. However amongst the male sub-population of the study, T4 was elevated and the drop in the age-group 11-15 years was not observed. Ojule [22] and Isichie [14], working in different iodine deficient environments in Nigeria have also observed similar elevations of T4 and T3. Isichie had identified up to 18% of such paradoxical elevations of T4 in his series and had explained that altered binding protein levels often cause false elevation of T4 in goitre endemic areas [14]. In this work, 50% of the test samples of the study population had T4 elevations above normal range compared to 42% observed in the control population.

These elevations of T4 and T3 often on a background of normal TSH observed in goitre endemic areas may be a consequence of improved iodine supply from the current widespread salt iodization programme [23] resulting in increased thyroid hormone production from the already hyperplastic glands. Report of hyperthyroidism or thyrotoxicosis resulting from mass iodization programmes are however rare. Even in the absence of specific iodization programmes, the reduction of goitre

prevalence have been recorded with opening up of previously remote and isolated areas and improvement in it's communication channels with other areas as documented in Switzerland, Italy and Yugoslavia [1]. Though the corresponding thyroid profile of these populations were not available, such improvements pre-supposes an earlier positive change in the thyroid hormone profiles probably due to improved iodine supply from non-specific sources.

**MEAN TSH VALUES ACCORDING TO AGE GROUPS**

Table 1a

AGE GROUP	STUDY ( mU/L)	CONTROL (mU/L)	CRITICAL VALUE	P-VALUE
6 - 10yrs	3.21 $\pm$ 1.13	1.25 $\pm$ 0.39	8.88	<0.05
11 - 15yrs	3.16 $\pm$ 1.36	1.40 $\pm$ 0.47	8.54	<0.05
All ages	3.18 $\pm$ 1.27	1.33 $\pm$ 0.43	12.13	<0.05

**MEAN T4 VALUES ACCORDING TO AGE GROUP**

Table 1b

AGE GROUP	STUDY (nmol/L)	CONTROL (nmol/L)	CRITICAL VALUE	P-VALUE
6 - 10yrs	139.78 $\pm$ 27.32	128 $\pm$ 55.54	1.34	>0.05
11 - 15yrs	127.62 $\pm$ 27.14	130.31 $\pm$ 59.76	0.54	>0.05

AGE GROUP	STUDY (nmol/L)	CONTROL (nmol/L)	CRITICAL VALUE	P-VALUE
All ages	132.59 ± 27.57	129.42 ± 57.05	1.25	>0.05

**MEAN T3 VALUES ACCORDING TO AGE GROUP**

Table 1c

AGE GROUP	STUDY (nmol/L)	CONTROL (nmol/L)	CRITICAL VALUE	P-VALUE
6 - 10yrs	2.43 ± 0.61	1.79 ± 0.37	4.73	<0.05
11 - 15yrs	2.49 ± 0.88	1.70 ± 0.33	5.85	<0.05
All ages	2.47 ± 0.79	1.74 ± 0.35	7.37	<0.05

**MEAN TSH VALUES IN MALES ACCORDING TO AGE GROUP***Table 2a*

AGE GROUP	STUDY ( mU/L)	CONTROL ( mU/L)	CRITICAL VALUE	P-VALUE
6 - 10yrs	3.11 $\pm$ 1.36	1.22 $\pm$ 0.35	4.53	<0.05
11 - 15yrs	3.68 $\pm$ 1.54	1.49 $\pm$ 0.47	6.80	<0.05
All ages	3.50 $\pm$ 1.49	1.37 $\pm$ 0.44	8.35	<0.05

**MEAN T4 VALUES IN MALES ACCORDING TO AGE GROUP***Table 2b*

AGE GROUP	STUDY (nmol/L)	CONTROL (nmol/L)	CRITICAL VALUE	P-VALUE
6 - 10yrs	145.75 $\pm$ 33.96	120 $\pm$ 62.48	1.30	>0.05
11 - 15yrs	146.35 $\pm$ 34.62	131.76 $\pm$ 66.31	0.84	>0.05
All ages	146.16 $\pm$ 33.95	126.67 $\pm$ 63.85	1.51	>0.05

**MEAN T3 VALUES MALES ACCORDING TO AGE GROUP***Table 2c*

AGE GROUP	STUDY (nmol/L)	CONTROL (nmol/L)	CRITICAL VALUE	P-VALUE
6 - 10yrs	2.56 $\pm$ 0.83	1.72 $\pm$ 0.37	3.21	<0.05
11 - 15yrs	2.43 $\pm$ 0.82	1.69 $\pm$ 0.33	4.12	<0.05
All ages	2.47 $\pm$ 0.81	1.71 $\pm$ 0.34	35.95	<0.05

**MEAN TSH VALUES IN FEMALES ACCORDING TO AGE GROUP***Table 3a*

AGE GROUP	STUDY ( mU/L)	CONTROL ( mU/L)	CRITICAL VALUE	P-VALUE
6 - 10yrs	3.27 $\pm$ 0.98	1.24 $\pm$ 0.45	7.50	<0.05
11 - 15yrs	2.64 $\pm$ 0.91	1.31 $\pm$ 0.44	1.16	>0.05
All ages	2.90 $\pm$ 0.98	1.28 $\pm$ 0.44	9.43	<0.05

**MEAN T4 VALUES IN FEMALES ACCORDING TO AGE GROUP***Table 3b*

AGE GROUP	STUDY (nmol/L)	CONTROL (nmol/L)	CRITICAL VALUE	P-VALUE
6 - 10yrs	139.78 $\pm$ 27.33	128 $\pm$ 55.54	0.63	>0.05
11 - 15yrs	127.62 $\pm$ 27.14	130.31 $\pm$ 59.76	-017	>0.05
All ages	132.59 $\pm$ 27.57	129.42 $\pm$ 57.05	0.27	>0.05

**MEAN T3 VALUES IN FEMALES ACCORDING TO AGE GROUP***Table 3c*

AGE GROUP	STUDY (nmol/L)	CONTROL (nmol/L)	CRITICAL VALUE	P-VALUE
6 - 10yrs	2.34 $\pm$ 0.42	1.94 $\pm$ 0.35	2.64	<0.05
11 - 15yrs	2.56 $\pm$ 0.94	1.69 $\pm$ 0.33	4.29	<0.05
All ages	2.47 $\pm$ 0.77	1.78 $\pm$ 0.36	5.02	<0.05

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**CITE AS: Ogbonna Anthony Okechukwu, Ogbonna Obiageli Annastesia, Aniago Magnus, Samuel Ghasi, Nwokike Matthew Onyemaechi, Ugonabo Martin Chukwuka, Ugwuoke Clement Chukwuma, Onyenkwe B., Mgbakor C. Anthony, Mgbakor Miriam Ngozi, <sup>11</sup>Ekpechi O Louis and Mogboh Veronica E. (2023). Thyroid Hormone Profile for School Children Living in a Severely Goitre Endemic Area in Nigeria. IDOSR JOURNAL OF BIOLOGY, CHEMISTRY AND PHARMACY 8 (2) 129-144.**