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# Thyroid Hormone Profile in Rwandan Students

**Jean Bosco Gahutu[1*]**

*[1]Department of Medical Biology, National University of Rwanda, Huye District, Southern Province, Rwanda, P.O. Box 217 Huye, Rwanda.*

***Author's contribution***

*The author designed and carried out the study, performed the statistical analysis and wrote the manuscript.*

***Research Article***

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## ABSTRACT

**Aim:** To illustrate the thyroid hormone profile in young adult students at moderate altitude in Rwanda.
**Study Design:** A population-based cross-sectional study.
**Place and Duration of Study:** The study was conducted among healthy university students living at Butare, Rwanda (altitude: 1,768 m, barometric pressure: 629 mm Hg) in December 2011.
**Methods:** Venous blood was collected in the morning, after overnight fasting. TSH, total T3 and total T4 hormonal assays were performed in the laboratory of Butare University Teaching Hospital by classical sandwich ELISA technique for TSH and competitive ELISA technique for total T4 and total T3.
**Results:** The results of 111 subjects (65 males and 46 females; mean age: 22 years, age range: 18-28 years) are as follows (mean ± SD): total T3: males: 0.9 ± 0.3 ng/mL, females: 1.3 ± 0.3 ng/mL; total T4: males: 6.4 ± 1.1 µg/dL, females: 9.3 ± 2.2 µg/dL; TSH: males: 1.8 ± 1.2 mIU/L, females: 1.9 ± 1.4 mIU/L.
**Conclusion:** The results of our study compare well with findings of other studies, with a slight increase in serum TSH concentration as compared to sea level values. A comprehensive study needs to be done to establish reference intervals.

*Keywords: Thyrotropin; thyroxine; triiodothyronine; altitude.*

**Corresponding author: Email: jgahutu@nur.ac.rw;*

## 1. INTRODUCTION

High altitude induces physiological adaptive changes. An increase in serum T3 and T4 concentration has been observed in high altitude natives and acclimatised lowlanders at 3,500 m [1]. At an altitude of 1,768 m at Butare, Rwanda, we previously reported physiological changes, including a low $PaO_2$ with normal oxygen saturation of haemoglobin [2]. The aim of the present study is to illustrate the profile of thyroid hormones in a healthy young adult population at moderate altitude in Rwanda and evaluate whether moderate altitude has an effect on thyroid hormone concentration.

On the other hand, thyroid hormonal assays are important for the diagnosis and management of thyroid disease. However, laboratory results show intra- and inter-individual variations, depending on the physiological conditions or the environment. The laboratory assays are also source of variation [3]. Reference intervals are necessary for the clinicians to establish the limit between normal and pathologic. They are particularly useful in identifying subclinical thyroid dysfunction. They are also helpful to determine the target for substitution treatment for thyroid diseases. As the normal interval is population-dependent [4], the establishment of local reference intervals is of clinical value. The present study offers a first set of data for the establishment of local reference intervals.

## 2. SUBJECTS AND METHODS

### 2.1 Participants

A population-based cross-sectional study was carried out among students of the National University of Rwanda, in the district of Huye, Southern Province (altitude 1,768 m, latitude: -2.59722, longitude: 29.7389, barometric pressure: 629 mm Hg), in December 2011. The study participants were male and female adults in healthy condition and normal nutritional status on physical examination and without any history of disease in the preceding six months. All study participants had been living in the town for the two months preceding the sampling. There was no history of thyroid disease in the study participants. People under medication, females in the menses period, pregnant or breastfeeding women, and those using hormonal contraception were not included in the study. Smoking was an exclusion factor, considering its effect on thyroid hormone concentration [5]. There was no drug abuse among the study participants. Most of study participants were non-drinkers, some drank alcohol occasionally. Physical examination was carried out to exclude any disease. Height and weight were measured on slightly clothed individuals, without shoes.

### 2.2 Sampling and Sample Storage

The sampling was done in the morning after overnight fasting. The subjects were at complete physical rest for at least 10 minutes before blood sampling. Five mL of venous blood were sampled from the cubital vein in a dry tube without anticoagulant. After clotting at room temperature, the clot was separated from the serum by centrifugation at 3000 rounds per minute during 10 minutes, after which the serum (supernatant) was immediately transferred in another dry tube, stored in the freezer at -20ºC and analysed within one month. Samples were de-frozen at ambient temperature and homogenized before hormonal assays.

## 2.3 Hormonal Assays

TSH, T3 and T4 hormonal assays were performed in the laboratory of Butare University Teaching Hospital by classical sandwich ELISA technique for TSH and competitive ELISA technique for total T4 and total T3, using a Dynex MRX ELISA reader machine and reagent kits from Human diagnostics (Wiesbaden, Germany). Laboratory procedures, including calibration and internal quality control were as per instructions from the manufacturer.

## 2.4 Statistical Analysis

The statistical data analysis was done with the Excel 2007 software for the determination of the mean, the standard deviation and the $2.5^{th}$ and $97.5^{th}$ percentiles and for the distribution charts. Comparison between males and females was done with Student's *t*-test using the statistical package for the social sciences software (SPSS version 16.0). Comparison of our results with findings of studies at sea level was done on Excel using the Student's *t*-test based on mean, standard deviation and sample size.

## 3. RESULTS AND DISCUSSION

After removal of one outlier (whose total T3 concentration was too distant from other data, higher than the mean + 3 SD in the female group) results of 111 subjects (65 males and 46 females) were analysed. The radial pulse was in the normal range of 60-100 beats per minute, the blood pressure was normal (systolic pressure lower than 140 mm Hg and diastolic pressure lower than 90 mm Hg) and the body temperature was in the normal range (36.2-37.5ºC) for all recruited participants. The age of the study participants (mean ± SD) was 22 ± 2 (range: 20-28) years for the male group and 22 ± 1 (range: 18-26) years for the female group. The weight of the study participants was 62.5 ± 6.7 (range: 51-79) kg for the male group and 57.1 ± 7.4 (range: 44-77) kg for the female group. The body mass index of the study participants was 21.2 ± 2.1 (range: 15.7-29.3) kg/m² for the male group and 22.0 ± 2.7 (range: 17.3-27.4) kg/m² for the female group. The results are presented in Table 1 both in conventional units and in SI units. The difference between males and females in the mean total T3 and total T4 is statistically significant ($P$ <.001). Therefore the $2.5^{th}$-$97.5^{th}$ percentile interval for T3 and T4 is presented separately for males and females. The difference between males and females in the mean TSH is not statistically significant ($P$=.70). Therefore a common $2.5^{th}$-$97.5^{th}$ percentile interval valid for males and females is presented.

**Table 1. Hormonal values for the thyroid function**

| Parameter | Unit[1] | Mean ± SD | | $2.5^{th}$-$97.5^{th}$ percentile interval | | *P* |
|---|---|---|---|---|---|---|
| | | Males | Females | Males | Females | |
| Total T3 | (ng/mL) | 0.9 ± 0.3 | 1.3 ± 0.3 | 0.4–1.5 | 0.8–1.7 | <.001 |
| | (nmol/L) | 1.38 ± 0.46 | 2.00 ± 0.46 | 0.61–2.31 | 1.23–2.62 | |
| Total T4 | (µg/dL) | 6.4 ± 1.1 | 9.3 ± 2.2 | 4.6–8.8 | 5.3–13.6 | <.001 |
| | (nmol/L) | 82 ± 14 | 119 ± 28 | 59–113 | 68–175 | |
| TSH | (mIU/L) | 1.8 ± 1.2 | 1.9 ± 1.4 | 0.5–4.7 | | .70 |

*M: Males; F: Females; SD: standard deviation; T3: triiodothyronine; T4: thyroxine; TSH: thyroid-stimulating hormone (thyrotropin)*

*n=65 (males), 46 (females), 111 (males and females)*

[1]*For total T3 and T4, results are shown in conventional units (first row) and in SI units (second row).*

The distribution of values in males and females is shown in Figs. 1-3, for serum total T3, total T4 and TSH respectively.

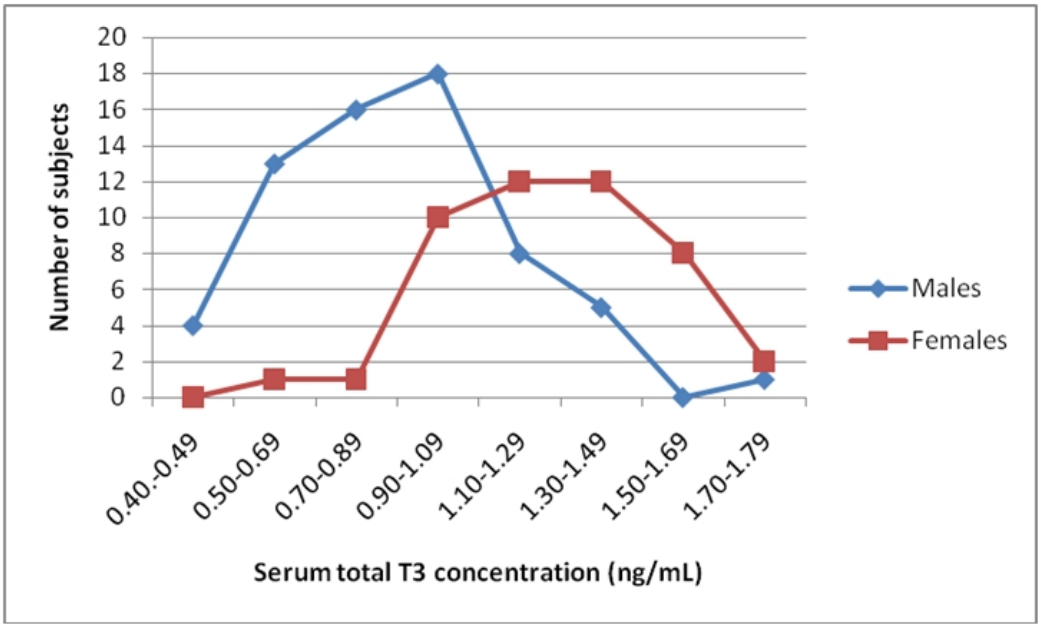


**Fig. 1. Distribution of serum total T3 concentration values in males and females**
*Total T3 values are significantly higher in females than in males.*

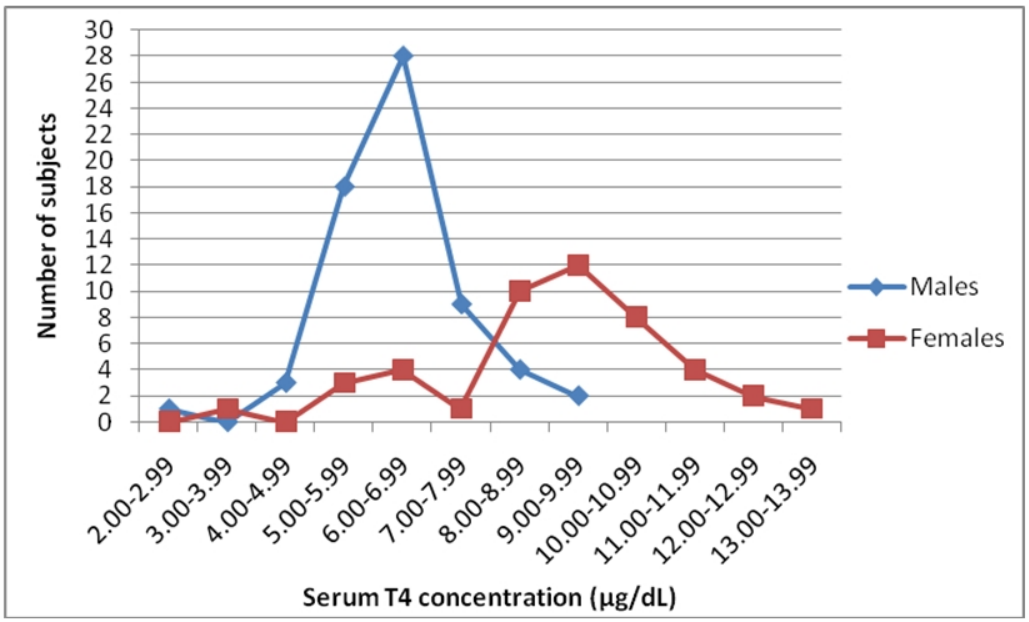


**Fig. 2. Distribution of serum total T4 concentration values in males and females**
*Total T4 values are significantly higher in females than in males.*

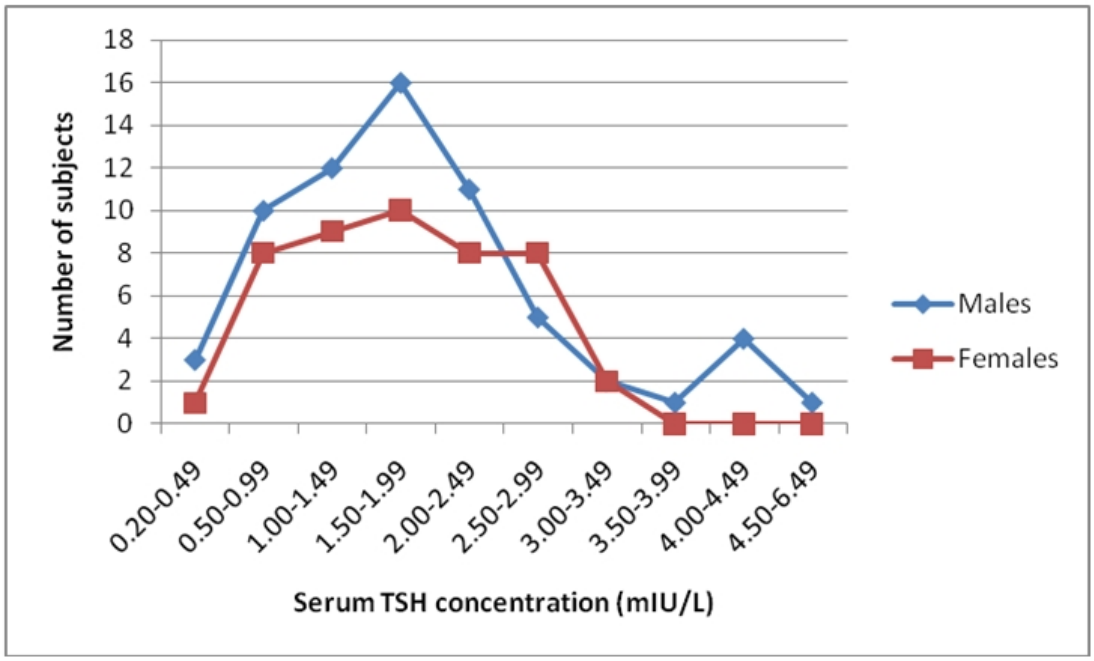


**Fig. 3. Distribution of serum TSH concentration values in males and females**
*There is no statistically significant difference in TSH values between males and females.*

The values of TSH in our study are higher ($P$<.001) than those reported by Surks and Hollowell in the similar age group of 20-29 years at sea level, in which a mean value of 1.59 mIU/L was observed [6]. In a slightly older group (mean age 38 years) at sea level, Andersen et al. found a TSH mean value of 1.27 mIU/L [7], which is significantly lower than our mean ($P$=.02). The higher values of TSH concentration in our study as compared to those reported at sea level by Surks and Hollowell and Andersen et al. in similar age groups could be a result of moderate altitude. However, we previously reported that there is no hypoxemia at the moderate altitude of our study site (1,768 m) [2] and altitude influence on the thyroid function in our study population is expected to be limited. Although in a significantly older group (mean age 58 years), the TSH mean values reported by Jorde and Sundsfjord, 1.95 and 1.86 mIU/L in males and females respectively [5], are comparable to ours. Our mean values for total T3 and total T4 compare well with those reported by Andersen et al. for the mean total T3: 1.64 nmol/L ($P$=.77) and mean total T4: 106 nmol/L ($P$=.26) [7]. Sawhney and Malhotra reported high levels of thyroid hormones at 3,500 m of altitude both in acclimatised low landers and in high altitude natives, with the TSH concentration similar to sea level values. The increase in T3 and T4 is attributed to altitude hypoxic stress [1]. Normoxemia at the altitude of our study site [2] justifies the absence of increase in total T3 and T4 concentration observed at higher altitudes.

Although limited in terms of sample size and representation of all age groups and different socio-economic conditions in the population, the present study offers a first set of data to be completed by further sampling for the establishment of local reference intervals.

The knowledge of thyroid hormone reference intervals is useful for the detection of subclinical cases of hypo- or hyperthyroidism, with the possibility of early and efficient

treatment to avoid progression towards overt disease. However, there are limits in the usefulness of reference intervals for T3, T4 and TSH as there is a high intra- and inter-individual variation, hence the risk of considering as abnormal a normal individual variation [8]. Besides, great intra- and inter-individual variations in thyroid hormone levels lead to wide reference intervals, with the consequence that a pathologic variation in an individual can still be within the population-based normal interval. Own reference interval of the individual determined by several sampling over time has proven to provide narrower intervals, more useful for the diagnosis of subclinical thyroid dysfunction [7,9]. However, the practicability of the method is limited.

The upper limit for TSH in the normal population was re-evaluated in recent studies, based on the fact that a high value could be based on presence of subclinical dysfunction in some study participants and lower values have been proposed based on rigorous inclusion criteria for study participants [4,10]. However, the upper limit of TSH in our study is rather comparable to classically reported limits.

Thyroid ultrasonography is recommended as screening method for reference values studies in currently or previously iodine deficient regions [11], which is not the case for our study area. We did not use thyroid ultrasonography for participant selection in the present study. The measurement of the basal metabolic rate is a useful method to ascertain euthyroidism of the study subjects [12]. However, we did not include it as selection method. Besides, iodine-deficiency hypothyroidism is becoming rare in Rwanda due to the use of iodized table salt.

## 4. CONCLUSION

The results of our study illustrate thyroid hormonal values in a student population at moderate altitude in Rwanda and compare well with findings of other studies. The slightly increased serum TSH concentration as compared to sea level values can be attributed to moderate altitude but the precise mechanism needs to be elucidated. The present study was carried out in young adults. A larger scale study needs to be done to establish reference intervals for the different age groups and socio-economic conditions in the Rwandan population.

## CONSENT

The author declares that written informed consent was obtained from the study participants before enrolment.

## ETHICAL APPROVAL

The research project was approved by the ethics committee of the Faculty of Medicine of the National University of Rwanda.

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## COMPETING INTERESTS

The author has declared that no competing interests exist.

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