

Thyroid Hormone levels in Highlanders- A Comparison Between Residents of Two Altitudes in Nepal

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ABSTRACT

Background

The endocrine changes related to altitude adaptation in human have attracted physiologists around the globe for long. A number of high altitude studies to detect the physiological changes have been performed now and then. But, the study to see the hormonal changes to compare populations residing at different high altitudes is a scarce. Hence, we have performed a study in native populations of different high altitude comparing changes in thyroid hormones in western Nepal. The Jharkot population included in this study is at altitude of 3760m and Jomsom population at 2800m height from sea bed.

Objective

The study is to compare changes in thyroid hormones at two different high altitude natives.

Methods

To compare thyroid status between high altitude natives at two different altitudes a cross sectional study is performed by random sampling method. The blood sample was collected in a vacutainer from fifty eight individuals after obtaining the informed consent of participants. The blood collected from antecubital vein was centrifuged in an hour and the serum obtained was used for biochemical analysis of free triiodothyronine, free thyroxine and thyroid stimulating hormone.

Results

Mean free thyroxine (fT_4) of Jharkot population is significantly larger ($p = 0.001$) than Jomsom population. Mean thyroid stimulating hormone (TSH) with $p = 0.597$, does not indicate the difference between this two population. There is no significant difference between mean free triiodothyronine (fT_3) of Jharkot and Jomsom population ($p = 0.345$).

Conclusion

The rise in free thyroid hormone at high altitude is not dependent on the thyroid stimulating hormone released from anterior pituitary. The rise in free thyroxine is found at higher altitude and no difference in fT_3 level is detected in population studied at high altitudes.

KEY WORDS

Free triiodothyronine, free thyroxine, TSH, high altitude, t-test

INTRODUCTION

The rise in the plasma T_4 requires activation of hypothalamo-pituitary-thyroid axis in healthy individuals but, the elevation of T_4 independent of TSH has been reported at high altitude.¹⁻³

An intact hypothalamic-pituitary-thyroid axis is well established by 12-16 weeks of gestation. Production of T_3 and T_4 in the thyroid gland is stimulated by thyrotrophin (thyroid-stimulating hormone, TSH), a glycoprotein released from the thyrotroph cells of the anterior pituitary in response to the hypothalamic tripeptide, thyrotrophin-releasing hormone. Thyroid hormone regulates metabolic processes in most organs and is different from many hormones for its stability in response to environmental signals.⁴

Field studies at moderate or high altitude have shown conflicting results regarding level of thyroid hormones which can be due to difficulty in standardization of field studies.⁵ Many factors such as wind, temperature, radiation and others, may affect certain endocrine parameters, but they cannot be individually quantified. Since, thyroid hormone is related to mental development and cognition and psychic stress is known to influence the hypothalamo-pituitary-thyroid/adrenal axis, the fluctuation in thyroid hormone seen at high altitude has been attempted to explain with respect to psychological performance in few studies conducted in the past.⁶⁻⁸

High altitude residence is known to modify body biochemistry and hormone status.⁹

In this study we have attempted to compare the thyroid hormones status in high altitude natives residing at two different altitudes from sea bed.

METHODS

The study was conducted from 15th Nov – 15th Dec of 2010. The population studied was from two different altitudes at 2800 m and 3760 m of Mustang district of western Nepal. The lower altitude natives (2800 m) belonged to Jomsom and the higher altitude (3760 m) were residents of Jharkot. The volunteers subjected to study were fifty eight in number, of which thirty three were from Jomsom and twenty five were natives of Jharkot. Fifty eight subjects aged between 12-75 years, participated voluntarily in the study.

The subjects included in the study were selected randomly from the native population who visited health post for their regular health examination. Healthy volunteers were included in the study after obtaining the history and general clinical examination Individuals on medications and patients suffering from chronic diseases like hypertension, diabetes and pulmonary diseases were excluded from the study.

The sample blood was drawn from the antecubital vein in the vacutainer by the aseptic technique after the written consent from all participants. The 3 ml blood collected from each individual was centrifuged and serum was stored for the analysis of thyroid hormones and thyroid stimulating hormone.

Thyroid hormones level at different altitudes of two different populations was compared using t-test. Data were entered on MS Excel and SPSS version 16 was used to analyze them.

RESULT

The status of thyroid hormones in these high altitude populations was significantly different.

Though sample size in Jomsom population is thirty three, the result for TSH of a subject was not available after biochemical analysis; therefore, thirty two subjects were studied. As in table 1, there is no significant difference between mean (ft_3) of Jharkot and Jomsom population ($p = 0.345$). There is significant difference between mean value of ft_4 between two population- Jomsom and Jharkot ($p = 0.002$) as depicted in table 2. Mean ft_4 of Jharkot population is significantly larger than Jomsom population ($p = 0.001$) but mean thyroid stimulating hormone (TSH) does not differ significantly between two population ($p = 0.597$), shown in table 3.

Table 1. ft_3 comparison between Jomsom and Jharkot population.

| Group Statistics | | | | | |
|------------------|------------|----|--------|----------------|-----------------|
| V | Study Area | N | Mean | Std. Deviation | Std. Error Mean |
| | Jomsom | 33 | 2.3721 | .84301 | .14675 |
| | Jharkot | 25 | 2.5624 | .61456 | .12291 |

There is no significant difference between mean ft_3 value of Jomsom and Jharkot population ($p = 0.345$).

Table 2. ft_4 comparison between Jomsom and Jharkot population.

| Group Statistics | | | | | |
|------------------|------------|----|--------|----------------|-----------------|
| Value | Study Area | N | Mean | Std. Deviation | Std. Error Mean |
| | Jomsom | 33 | 1.3191 | .24002 | .04178 |
| | Jharkot | 25 | 1.5476 | .26932 | .05386 |

There is significant difference between mean ft_4 value of Jomsom and Jharkot population ($p = 0.002$) and mean ft_4 of Jharkot population is significantly larger than Jomsom population ($p = 0.001$).

The normal range of $ft_4 = 0.8 - 2.0$ ng/dl, $ft_3 = 1.4 - 4.2$ pg/ml and TSH = $0.39 - 6.16$ μ U/ml. ft_3 , ft_4 and TSH was measured by ELISA technique (ELISCAN, RFCL, India). Normally, in the healthy adult free T_3 found in the blood is converted from free T_4 at peripheral tissues like liver and kidney.

Table 3. TSH comparison between Jomsom and Jharkot population.

| Value | Study Area | Group Statistics | | | |
|-------|------------|------------------|--------|----------------|-----------------|
| | | N | Mean | Std. Deviation | Std. Error Mean |
| | Jomsom | 32 | 2.8656 | 2.92090 | .51635 |
| | Jharkot | 25 | 2.4672 | 2.65959 | .53192 |

There is no significant difference of mean TSH value between Jomsom and Jharkot population ($p = 0.597$).

DISCUSSION

Thyroid hormone synthesis and secretion by the thyroid gland follows a negative feedback mechanism to keep the normal concentration of plasma T_3 and T_4 . Both of these hormones are bound to plasma proteins albumin and globulin respectively. However, more T_4 is bound to plasma protein than T_3 . The free forms of these two hormones diffuse through cell membrane.

The active form of thyroid hormone is T_3 and is derived from T_4 intracellular after T_4 diffuse into the cell. The rise in the plasma thyroid hormones at high altitude without the rise in TSH has been reported.¹⁰ However, considering the classic feedback mechanism operating physiologically, rise in the thyroid hormones require a thyroid stimulating hormone action over the thyroid gland.¹¹

In the recent study, the finding of rise in free T_4 without a rise in TSH at higher altitude compared to lower high altitude is consistent with previous studies.^{2,3,5,12} However the decrease in free T_3 has been reported with the rise in free T_4 at high altitude.² The total plasma T_4 level is higher than total plasma T_3 as the secretion of thyroxine is greater than triiodothyronine by thyroid gland. The estimation of total thyroid hormones can be misleading because acquired and congenital variations in the concentrations of binding proteins exist between individuals, and it is the free thyroid hormones in plasma that are physiologically active and that feedback to inhibit pituitary secretion of TSH.¹³ Therefore, to observe the change in free thyroid hormones we have analysed fT_3 and fT_4 in our study. Here, the rise in fT_4 without rise in TSH at higher altitude could be an indication of lesser binding of T_4 to thyroxine binding globulin so as to provide conversion of more fT_4 to fT_3 . However, a study in an expedition to climb Mt. McKinley, AK has shown less fT_3 conversion from fT_4 due to cortisol rise in the plasma.¹⁴ The cortisol rise can be due to stress in those who attempt expedition, where as the local natives at high altitude may not have rise in cortisol, hence does not impair the conversion to fT_3 from fT_4 .

Further, stable mean thyroid stimulating hormone (TSH) in both altitude populations signifies the independent rise of serum fT_3 and fT_4 . The rise in thyroid hormone levels independent of pituitary secretion of thyrotropin has been reported and favors the recent finding.^{3,15}

The finding of significantly larger fT_4 in these natives

independent of TSH, rationalizes that TSH estimation in high altitude natives can be useful for pathological diagnosis of hypo or hyperthyroidism in the light of physiologically altered fT_4 . The altered free thyroid hormones can be the adaptive feature of high altitude natives and should be considered clinically while investigating for thyroid pathology.

The study performed to compare the changes in two different altitude natives does not consider the possible changes in parameters like reverse T_3 , thyroxine binding globulin, albumin, transthyretin and cortisol. Total T_3 and total T_4 estimation though ignored in our study, if performed could have been reliable comparator for in depth understanding of fluctuations in binding, and conversion of thyroid hormones.

In order to explore the changes in endocrine system and its effect in metabolism and psychology at high altitude natives, endocrinological parameters related to hypothalamo-hypophysial-target gland axis needs to be further studied in these populations.

CONCLUSION

Higher altitude population has greater fT_4 independent of pituitary secretion of thyrotropin. There is no difference detected in fT_3 level between both the populations studied.

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