



Effect of High Altitude on Thyroid and Thyroid Stimulating Hormones Levels in Taif City

Ayman S Alhazmi^{1*}, Anas Alomey², Hilal Almalki³, Mazen Almeahmadi³, Mohammad Albshri³, Naif Algarni³ and Sultan Almutiri³

¹Associate Professor of Clinical Biochemistry and Molecular Biology, Applied Medical Sciences, Taif University, Saudi Arabia

²Lecturer of Biotechnology and Molecular Biology, Applied Medical Sciences, Taif University, Saudi Arabia

³Laboratory Technician, Ministry of Health, Saudi Arabia

***Corresponding Author:** Ayman S Alhazmi, Associate Professor of Clinical Biochemistry and Molecular Biology, Applied Medical Sciences, Taif University, Saudi Arabia.

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Abstract

Introduction: Thyroid hormones maintains several metabolic functions and induces growth and differentiation. Defect in thyroid hormones levels associated with different metabolic and growth disorders so, its levels strictly regulated. High altitude area may associate with mild hyperthyroidism, so this project was aimed to compare thyroid hormones levels in high altitude area (Taif city) with low altitude area.

Subjects and methods: This project consisted of 420 individuals divided into two groups; high altitude group and low altitude group. For each individual included in this study plasma thyroxine (T4), triiodothyronine (T3) and thyroid stimulating hormone (TSH) were measured.

Results: A significant statistical difference was found in both T4 and T3 levels in people lived-in high-altitude area compared with other lived in low altitude area. Both T3 and T4 were higher in people lived-in high-altitude area compared with another group ($P < 0.05$). The TSH wasn't showed a significant difference between the two groups.

Conclusion: Thyroid hormones levels increase in high altitude area and this elevation may independent on hypothalamic-pituitary thyroid axis.

Keywords: Thyroid Hormones; High Altitude; Thyroid Stimulating Hormone

Introduction

The Thyroid gland is one of the important endocrine glands that plays a vital role in metabolism, growth and tissue differentiation [1]. It produces two hormones; thyroxine (T4) and triiodothyronine (T3) involved in many metabolic processes occur in our bodies. These hormones secreted under the influence of an axis called hypothalamic-anterior pituitary thyroid axis (HPT) [2,3]. Hypothalamus produces a thyrotropin releasing hormone (TRH) that stimulates anterior pituitary to produce thyrotropic hormone or thyroid hormone stimulating hormone (TSH). This TSH is responsible for induction of follicular cells in thyroid gland to produces both T4 and T3. In addition to TSH, some environmental factors such as heat, the degree of altitude and radiation are the other factors participate in thyroid hormones production [4,5]. In high altitude,

hypoxia characterized by low oxygen availability may affect T4 and T3 blood concentrations depending on the degrees of altitude and duration of exposure [6,7]. Chronic exposure to high altitude affects many endocrine hormones including thyroid hormones. Previous studies found that people who habit in high altitude areas had an increase in both T3 and T4. These studies also found that the increase in both T3 and T4 were not accompanied by an increase of TSH. This finding produces an idea that the increase in thyroid hormones in high altitude area was independent on HPT axis [8,9]. Recent studies found that high altitude individuals had elevated T4 without any change in T3 level [10]. Hyperthyroidism occurs due to elevated T4 in exposure to high altitude for long times can be subclinical and if untreated may be developed into severe clinical symptoms. In Saudi Arabia, both west and south

west areas are present in high mountains and can be classified as a high altitude. Taif city is present at 2000 meter above sea level, so it can be classified as high-altitude area. This study was aimed to investigate the effect of hypoxia-induced high-altitude on thyroid hormones levels at Taif city.

Subjects and Methods

This study was done on 420 individuals classified according to the degree of highest, 210 subjects lived at high altitude area represented by Taif city and 156 subjects lived at sea level area represented by Makkah city. The subjects were selected randomly from both Taif and Makkah city between January to June 2018. Fifty-one individuals were rejected because suffering from diabetes, hypertension, liver disease or use medication that may affects thyroid hormones levels. From each subject, a 5 mL venous blood sample was collected under standardized condition after overnight fasting in a plane tube, centrifuged and serum stored at -20C until analysis. Serum free T3, T4 and TSH levels were estimated by automated immunoassay (BIO-RAD automated system).

Statistical analysis

SPSS software version 16 (SPSS Inc., Chicago, IL, USA) was used in the performance of statistical analysis. The t-test was used in comparisons performance. Both comparisons and correlations were considered statistically significant when $P < 0.05$.

Results

This study was done on 400 individuals lived in Makkah as low altitude area and Taif as high-altitude area. The average of both groups was near with means 42.57 in low altitude area and 46.17 in high altitude. Thyroxin level showed a significant difference

	Low altitude group	High altitude group	P value
Age	42.57 ± 5.45	46.17 ± 6.02	0.109
Free thyroxin (pmol/L)	5.23 ± 1.65	16.24 ± 2.69	0.005**
Free triiodothyronine (pmol/L)	1.03 ± 0.02	4.72 ± 0.43	0.016*
Thyroid stimulating hormone (uIU/mL)	2.87 ± 0.03	2.08 ± 0.01	0.169

Table 1: Age, thyroxin, triiodothyronine and thyroid stimulating hormone in high and low altitude groups.

* $P < 0.05$ is considered significant

** $P < 0.01$ is considered significant

between two group with higher level was in high altitude group ($P < 0.01$). the triiodothyronine also showed a significant statistical difference in two group with higher level present in high altitude group ($P < 0.05$). Finally, thyroid stimulating hormone didn't show a statistical difference in this study between both groups.

Discussion

Thyroid hormones involved in several metabolic processes so, it secreted under sensitive axis and some environmental factors. Hyperthyroidism and hypothyroidism occur due to increase and decrease thyroid hormones levels respectively. Both disorders appear with many symptoms ranged from mild to severe depending on how much thyroid hormones levels increased or decreased [11]. The plasma free T4 level is more than the free T3 level, but inside the cell, T3 is more potent than T4 and most cellular T4 is converted into T3. Taif city present at high altitude and it is a one of Saudi Arabia city. Hypoxia is a most environmental factor that may affect different metabolic processes for habitat in this area. Both free T4 and T3 is more accurate than total T4 and T3 because the total level is affected by binding protein including albumin and thyroid binding globulin [12]. Fluctuation results in free T4 and T3 were found in several studies done in a different high-altitude area on different ethics. In Nepal, Nepal and his colleague found that both fT4 and fT3 were higher in high altitude area without any change in TSH [10]. In 2010, Richalet, *et al.* also record high fT4 and fT3 levels in people who stay in Chamonix in France for four days. They suggest that the slight hyperthyroidism is necessary to overcome the effect of hypoxia-induced high altitude. Both fT4 and fT3 is responsible for induction of 2,3-diphosphoglycerate in red blood cells which responsible for the release of oxygen to the tissue [11]. Moreover, they found that fT4 degradation is elevated in the first 3 days with decrease in its clearance. The most previous studies found an increase in both T4 and T3 with unchanged TSH level, so the authors suggest that an increase in thyroid hormones is independent in HPA. One study found elevation in thyroid-binding globulin at high altitude and the authors suggest that the increase in total T4 is due to increase in its transporter [12]. Moreover, they conclude that the increase in fT4 is parallel with an increase in its total level. Another study said that the increase in fT4 is occurring due to cold weather associated with high altitude area [13], but a study done by Sawhney and his colleague found an increase in thyroid hormones at high altitude in warm temperatures [14]. Richalet and his colleague also said that the increase in catecholamine at high altitude may be the factor that influences thyroid hormone elevation [3]. In Saudi Arabia a study done by Alhashem demon-

strated an increase in both T3 and T4 in rats breed in high altitude compared with rats in low altitude [15]. All previous studies mentioned above conclude that increase in both T4 and T3 independent on HPA. Hirooka, *et al.* found that hypoxia suppresses synthesis of TRH in the hypothalamus [16]. Another study found an increase in T4 only with a decrease in T3 in high altitude area [17]. Our study agrees with previous studies that conclude that an increase in both fT4 and fT3 were independent on HPA.

Recommendation and Conclusion

This study didn't focus on iodide consumption and its urinary excretion. In addition, our sample size is small, so a large sample size and estimation of iodine consumption and urinary excretion are recommended. We conclude that, Thyroid hormones levels increased in high altitude area and this elevation is independent on hypothalamic-pituitary thyroid axis.

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