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Epidemiological Study of T4, T3 and TSH Mean Concentrations in Four Iranian Populations

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Abstract

T4 and T3, two major hormones of thyroid gland, are responsible for regulation of "basal metabolism" in the body. Thyroid function is regulated primarily by variation in the pituitary TSH. In this study, about four hundred individuals were considered from four Iranian populations. They were selected randomly in their cities; Shiraz, Mashhad, Rasht, and Ilam. Essential family information was asked to achieve native belonging of each person to related population. Blood specimens were collected, by separating serums, freezed serums were transferred immediately to Tehran for hormone assay. Assay of T4 and T3 concentrations was carried out by "RIA-magnetic" kits and of TSH by "IRMA-magnetic" kits. Analysis of variance has been taken into account among days of sampling in each city to calculate mean concentrations for T4, T3 and TSH. Analysis of association between age and hormones concentrations in each population was done by the regression and the correlation tests. Significant differences were detected at T4 mean concentration in each of these populations (P=0.0001). Differences for T3 mean concentration were observed only between Shiraz and Mashhad (P=0.021); and Shiraz and Rasht (P=0.003). By increasing age of individuals, there were also a negative correlation at mean concentrations of T4 and T3 in Ilam (P=0.022), and Mashhad (P=0.016) respectively. According to these data, and specificity of environmental and genetic factors to each popualtions, specific "normal reference" of T4 and T3 homones should be considred for each of these populations. Correlation study of mean concentrations of these hormones and genetic variations of some critical genes such as thyroid peroxidase (TPO) and iodothyronine deiodinase can open new window of epidimiology among Iranian popualltions.

Keywords: *T4, T3, TSH, Quantitative traits, Epidemiology, Iran*

Introduction

Thyroid realysing hormone (TRH) is secreted by the hypothalamus and stimulates the production of TSH, a polypeptide, from the anterior pituitary, TSH then raises production and release of thyroxine (T4) and triiodothyronine (T3) from the thyroid. These then exert a negative feedback mechanism on TSH production. T4 is 5x less active than T3 and is the main hormone produced by the thyroid` (1). T3 is mainly produced by peripheral conversion of T4. T3 and T4 are largely protein bound in the plasma, mainly to thyroxine-binding globulin. Only the unbound portion is active. T3 and T4 both act via nuclear receptors to increase cell metabolism.

By means of its regulatory system, thyroid gland bring about appropriate adjustment in its secretion when occur changes in the external and internal environment (2). As different populations can have special basal metabolism, due to various climatic conditions and various

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genetic make-ups, variation in the mean concentrations of T4, T3 and TSH will be obvious (3). Adaptation of thyroid gland- with increased secretion in cold climate and decreased secretion in hot climate- contributes to differences in basal metabolic rate (BMR) of people living in arctic regions with BMRs 10 to 20 per cent higher than those of persons living in tropical regions (3).

In determining a range in that T4, T3 and TSH concentrations are optimal for a person who refers to a physician, ethnical and geographical properties of related population should be considered. Otherwise, choosing an unrelated "normal ranges" may conclude to false diagnosis. So, we directed a plan in which each city of Shiraz, Mashhad, Rasht, and Ilam had about one hundred native individuals who participated in calculating T4, T3 and TSH mean concentrations.

At this epidemiological study we could depict biological polymorphism of these four populations in term of a biological quantitative trait (4). In genetics, these traits are known as "Quantitative traits" (5). Despite qualitative traits that inherit usually by one gene, quantitative traits in their inheritance have polygenic nature. Quantitative traits are of high importance in the population genetic (4, 5); because most of characteristics present in the biological populations and cause derivation of one population from the others, belong to these polygenic traits (5). Genetic analyses of these traits in the populations are carried out by statistical parameters such as variance, mean and standard deviation (4-6). Distribution of T4, T3 and TSH concentrations in the populations shows normal distribution curve (6). This continuous variation can be fluctuated by variation in the living condition and genetic profile (7). The goal of this study was to determine whether the mean plasma concentrations of T4, T3 and TSH were different among populations of four different cities of Shiraz, Mashhad, Rasht, and Ilam.

Materials and Methods

Shiraz, Mashhad, Rasht and Ilam are located in four geographical directions of Iran
(Fig. 1). By attending in each of these cities, individuals who were native residence of the related city were selected. A pretest for thyroid dysfunction was done by filling a questionnaire, taking evidences of hyperthyroidism and hypothyroidism and other thyroid diseases, and clinical examination by local physicain to recruiting only healthy individuals, in terms of thyroid gland function. Randomly selected individuals participated in blood sampling. Serums were kept at-20° C until assay of hormones. All samples were collected in the spring season, from April to June; Shiraz on the April, Mashhad and Rasht on the May and Ilam on the June. Serum concentrations of T4, T3 and TSH were assayed by RIA (radioimmunoassay) and IRMA (immunoradiometricassay) techniques (8); T4 and T3 by RIA-magnetic kits and TSH by IRMA-magnetic kits.

For data analysis, SPSS statistical software was used. Mean of concentrations were calculated by ANOVA-Oneway"and "LSD" tests. Adjustment for sex and age was done by "Independent T-Test" and ANOVA, respectively. Associations between increase of the age and the changes of hormons concentrations were analyzed by the correlation and regression tests (6). Essential geographical information of each city, such as temperature, humidity and altitude were received by correspondence with the related meteorological organization.

Results

The highest T4 mean concentration was in the Shiraz and the lowest in the Rasht (P= 0.0001) (Table 1). There was a similar observation in the T3 mean concentration; the highest value was in Shiraz and the lowest one in Rasht (P= 0.02) (Table 3). There was not any significant difference between mean concentrations of TSH among four popualtions. Significant correlations were found between age and changes

of hormones concentrations in some populations. Negative correlation was seen between T4 concentrations and age in Ilam (*P*= 0.022) (r=-0.3); and between T3 concentrations and age in Mashhad (*P*= 0.016) (r= -0.35) (Table 2). Mean concentrations of T4, T3, and TSH between men and women of any of these populations were not significant (Table 3).

Fig.1: Iran map and location of the four cities sampled

Table 1: T4, T3, and TSH mean concentrations in the four Iranian populations

Means	Shiraz	Mashhad	Rasht	Ilam	*P*
T4 (nmol/L)	137.02 ± 0.14	121.8 ± 0.31	117.24 ± 0.8	119.92 ± 0.3	0.0001*
T3 (nmol/L)	2.92 ± 0.09	2.44 ± 0.12	2.25 ± 0.15	2.59 ± 0.13	0.020**
TSH (mu/L)	1.11 ± 0.11	1.38 ± 0.12	1.41 ± 0.12	1.29 ± .09	0.239

*P=0.0001 between Shiraz and Mashhad, Shiraz and Rasht, Shiraz and Ilam, Mashhad and Rasht; P= 0013 between Mashhad and Ilam; and P=0002 between Rasht and Ilam
**P=0.021 between Shiraz and Mashhad; P=0003 between Shiraz and Rasht

Table 2: Correlation between T4, T3 and TSH mean concentrations with age increment

	Shiraz		Mashhad		Rasht		Ilam	
	r	**p**	**r**	**p**	**r**	**p**	**r**	**p**
T4	-0.128	0.382	0.04	0.763	-0.14	0.342	-0.3	0.022*
T3	0.93	0.503	-0.35	0.016*	-0.122	0.454	-0.099	0.611
TSH	- 0.186	0.206	-0.028	0.859	-0.095	0.558	-0.064	0.672

*Significant levels (<0.05)
r =person's coeffieient correlation

Table 3: T4, T3 and TSH mean concentrations in men (M) and women (W) of the four populations*

	Shiraz		Mashhad		Rasht		Ilam	
Means	**W**	**M**	**W**	**M**	**W**	**M**	**W**	**M**
T4	163.16	129.33	127.31	118.25	119.89	113.72	119.53	113.85
T3	2.91	2.57	2.51	2.38	2.09	2.42	2.73	2.46
TSH	1.14	1.50	1.39	1.13	1.52	1.22	1.23	1.47

*p was not Significant (<0.05) for any mean between men and women of the fout population

Discussion

Thyroid hormones concentrations are being influenced by many external and internal factors such as temperature, humidity, nutrition and altitude (2, 3). Various studies have shown increment of thyroid function at the higher altitude (9); as there is a notable discrepancy between altitude of Shiraz (1488m) and that of Rasht (-20m). Seasonal changes can influence on thyroid hormones variation (3, 10). Some studies have shown that T3 and TSH have decrease from March to June (10). Regarding that Rasht and Ilam have been concluded in the iodine-deficient cities in Iran (11) and iodine deficiency could be resulted in preferential secretion of T3 to T4 (12), so there are some external factors can explain the highest mean concentration of T4 in Shiraz and the lowest means in Rasht and Ilam.

Although role of environmental properties in the mean differences of hormones concentrations, in the four populations, are obvious (3); partly these differences are due to heritable properties (7). As thyroid hormones variations are continuous (quantitative) traits, role of many genes, which participate in hormone biosynthesis, transport and metabolism can not be ignored. As in the genetic diseases of thyroid-not necessarily heritable-(13,14) some defects occur on the molecular level of genes as deiodinase, abnormal-iodinated proteins, and thyroid peroxidase (TPO), then quality of those gene activation can influence on the intensity of thyroid hormones production (2). In addition, activation of 5'-monoiodinase enzyme, structural variants of thyroid binding globulin (TBG) and albumin may affect on the mean concentrations (15).

In view of a negative correlation between increment of age and concentrations of T4 and T3 in Ilam and Mashhad, respectvely, age-related thyroid dysfunction is also common (16). Autoimmunity and an expression of age-associated diseases rather than a consequence of aging process mainly cause these abnormalities (16). Normal aging is accompanied by a slight

decrease in TSH release and gradual age-dependent decline in T3 concentrations without changes in T4 levels (16).

These data along with specificity of environmental and genetic factors to each popualtions, confirm valuability of specific "normal reference" of T4 and T3 hormones for each of these populations. By means of population-specific normal references for T4, T3 and TSH and any other metabolite, we have in hand a valuable criterion to comparise populations in terms of quantitative traits.

Genotype-phenotype correlation study between genetic variations of any genes responsible for biosynthesis of thyroid hormones and thyroid regulation, such as thyroid peroxidase (TPO) and iodothyronine deiodinase with T4, T3, and TSH mean concentrations can open new window of epidimiology among Iranian popualltions.

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