EFFECT OF RACE, GENDER AND AGE ON THYROID AND THYROID STIMULATING HORMONE LEVELS IN NORTH WEST FRONTIER PROVINCE, PAKISTAN

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Background: Thyroid is one of the ductless endocrine gland, which is located immediately below the larynx on either side of and anterior to the trachea. The principal hormones of thyroid gland are thyroxine (T_4) and triiodothyronine (T_3). The current study was carried out to investigate the impact of race, gender and area on the levels of Thyroxine (T_4), Triiodothyronine (T_3) and Thyroid Stimulating Hormone (TSH) in normal healthy individuals. **Methods:** Serum levels of T_4, T_3 and TSH in 498 normal healthy individuals belonging to different districts of North West Frontier Province, Pakistan, were examined. Serum T_4 and T_3 were analysed by Radio Immuno Assay (RIA) method whereas TSH was estimated by Immunoradiometric assay (IRMA) method. **Results:** Levels of T_4, T_3 and TSH ranged from 53 to 167 ηmol/L, 0.6 to 3.1 ηmol/L and 0.3–4.8 μIU/L respectively. The levels of these hormones show significant change from the reference values that are used in clinical laboratories as well as in Institute of Radiotherapy and Nuclear Medicine (IRNUM), Peshawar, Pakistan. **Conclusion:** It is concluded that the age, gender, race and area, all have an appreciable effect on the levels T_4, T_3 and TSH.

Keywords: Thyroxine, Triiodothyronine, Thyroid Stimulating Hormone, TSH, Thyroid Hormones

INTRODUCTION

Thyroid is one of the ductless endocrine gland, which is located immediately below the larynx on either side of and anterior to the trachea. The normal adult gland has a weight of 25–40 gm.[1] The principal hormones of thyroid gland are Thyroxine (T_4) and Triiodothyronine (T_3) and their concentrations are 93% and 7% respectively. Both T_4 and T_3 hormones are iodine-containing amino acids. T_3 is about four times as potent as T_4, but it is present in the blood in much smaller quantities and persists for shorter time than does T_4. The normal total plasma T_4level is approximately 8 μg/dL (103 ηmol/L), and the plasma T_3 level is 0.15 μg/dL (2.30 ηmol/L). The plasma proteins that bind thyroid hormones (about 1%) are albumin, formerly called Thyroxine-Binding Prealbumin (TBPA) and now called transthyretin, globulin and thyroxine-binding globulin (TBG). Of the three, albumin has the largest capacity to bind T_4 and TBG the smallest.[1,2] Normally, 99.98% of T_4 in plasma is bound; the free T_4 level is only about 2 ηg/dL. The free T_4 in the plasma are physiologically active causing the inhibition of the TSH secretion. The free T_4 in plasma is important in the metabolic control of human body and therefore free T_4 is believed to be a direct indicator of thyroid status in an individual. Free T_3 like free T_4 measurement also reflects the thyroid status of individual accurately.[1–3]

The Thyroid Stimulating Hormone (TSH) also known as thyrotropin is an anterior pituitary hormone. Human TSH is a glycoprotein containing 211 amino acid residues, hexose, hexosamines and sialic acid and is made up of two subunits alpha (α) and beta (β), having molecular weight 28,000 a.m.u. The biological half-life of human TSH is about 60 minutes.[1] The thyroid function is controlled by TSH. The secretion of this tropic hormone is in turn regulated in part by thyrotropin releasing hormone (TRH) form hypothalamus and is subjected to 'negative feed back' control by high circulating levels of thyroid hormones acting on the anterior pituitary and hypothalamus. In normal individuals the range of thyroid hormones and TSH in the blood is as follows:[4–6]

Thyroxine (T_4)	65–156 ηmol/L
Triiodothyronine (T_3)	0.8–2.7 ηmol/L
Thyroid Stimulating Hormone (TSH)	0.5–5.0 μIU/L

In hyperthyroidism T_4 and T_3 levels are elevated and TSH is suppressed due to negative feed back mechanism. Diseases due to hyper function of thyroid hormones are exophthalmic goitre, Grave's disease and thyrotoxicosis. Hyperthyroidism is characterized by nervousness, weight loss, hyperphagia, heat intolerance, soft skin and sweating.[2,3] In Hypothyroidism, the TSH level is raised while T_4 and T_3 are low.[7] Diseases due to hypo function of thyroid are cretinism and myxedema.[2]

Some of the important factors affecting the thyroid hormones level include neonates, in which the T_4 concentration gradually decreases, reaching towards the normal at the end of first year. Serum T_3 remains higher through early adolescences.[8] There appears to be a systemic decrease in the increments of serum TSH in response to TRH in men over 40 years of age. Compared to non-pregnant women, the serum T_3 and T_4 levels may rise to twice in pregnant women. During the first trimester, a decrease of TSH concentration occurs, and the decrease is greater in twin pregnancy.[9] Alteration in nutritional status, whether short term or long term and whether as the result of over feeding or

under feeding or merely a change in substrate mix, affects different aspects of thyroid hormones economy, especially peripheral hormones metabolism.[10]

The study was basically designed to see the level of thyroid and thyroid stimulating hormones in normal and healthy individuals of North West Frontier Province (NWFP), Pakistan and also to investigate the effect of age and gender on T_4, T_3 and TSH.

MATERIAL AND METHODS

Blood samples were obtained from anti-cubital vein of 498 healthy individuals of NWFP, Pakistan. Serum was separated and stored in a freezer at -20 ºC. The individuals had no family or personal history of thyroid disease and were not on any drug, which was feared or suspected to interfere with thyroid hormone assay. They were selected from different districts of NWFP namely Karak, Bannu, Kohat, Hungu and Peshawar districts.

The samples were analysed for T_4, T_3 and TSH levels in Radio Immuno Assay Laboratory (RIA Lab) at the Institute of Radiotherapy and Nuclear Medicine (IRNUM), Peshawar, Pakistan. Serum T_4 and T_3 were analyzed by Radio Immuno Assay (RIA) method using Amerlex-MT_4 and MT_3 RIA kits supplied by Tianjin DEPU (DPC) Biotechnological & Medical Products Inc., China[11–14], whereas serum TSH was estimated by Immunoradiometric assay (IRMA) method using Coat-A-Count TSH IRMA Kit, supplied by Tianjin DEPU (DPC) Biotechnological & Medical Products Inc., China.[15,16] A Gamma Counter Model No. E. Sourcer RIA type SD 12 manufactured by Oakfield, England, UK, was used for determining T_4, T_3 and TSH levels.

RESULTS

In the present study the serum concentrations of T_4, T_3 and TSH were measured in 498 healthy individuals belonging to the area of Karak, Bannu, Kohat, Hungu and Peshawar districts. The Mean±SD for T_4 was 80.75±13.10 ηmol/L with range 53–167 ηmol/L and for T_3 it was found to be 1.81±0.65 ηmol/L with a range of 0.6–3.1 ηmol/L. The normal range for TSH was found to be 0.3–4.8 μIU/L and the Mean±SD for TSH observed was 1.38±0.90 μIU/L.

It was aimed to see the impact of age, gender and climate on the T_4, T_3 and TSH levels. The observed values for T_4, T_3 and TSH reveal that these values deviate from the fixed standard values used in RIA laboratory as the ranges for both T_4 and T_3 have slightly expanded while in case of the TSH it has shrunken. The values of T_4, T_3 and TSH observed were 99.80 ηmol/L, 1.93 ηmol/L and 1.88 μIU/L and are thus different from the current observations.[12]

The normal hormonal levels are different for different genders.[8] The gender impact observed in the current study is shown in (Table-1). Males were found to be 75.50% and females 24.50% respectively. The mean values obtained in case of T_4 and TSH showed very slight difference with elevated level of T_4 in males and TSH in females while the mean values for T_3 were almost the same in both the genders.

The Age-wise distribution of study subjects for the determination of thyroid hormone and TSH levels is shown in Table-2. The study subjects were divided into seven different age groups. It is almost clear from the data that the serum value for T_4 is slightly lower in the first decade of life (63.06±9.60 ηmol/L) than in the second decade (84.93±12.80 ηmol/L). The serum T_4 value increases progressively in the third, fourth and fifth decades of life with a sudden drop in individuals in age groups having age more than 40 years. The T_3 values observed are higher in the first decade of life. The second, third and fourth decades showed a decrease in values of T_3 with an increased value in the fifth and seventh decade of life. The serum TSH value is higher in the first decade of life which decreases up to third decade progressively with an increased value at fourth decade of life.

While comparing the hormonal levels, the study population was classified on the basis of gender into different age groups. The serum thyroid hormones and TSH levels for male of different age groups (Table-3), shows that T_4 values were found a little bit lower in the first decade of life (65.50±15.00 ηmol/L) with the progressive increased values in later decades of life and remain nearly constant.

The values of T_3 were observed higher in the first decade of life while a slight decrease was found in the second decade which remained nearly stable in the later decades of life. It was also observed from (Table-3) that the TSH levels were found higher in the first decade and it remained nearly stable in the later decades of life, slightly with the decreased values from the first decade of life.

In the same way the results of thyroid hormones and TSH level in females of different age groups (Table-4), reveals that serum T_4 values were found lower in the first decade of life which increases in later decades of life and remain nearly the same in rest of life for the population observed. As it is evident from Table-4 that T_3 is slightly higher in the first decade of life, however, which remained nearly constant in later decades, i.e., up to fourth decade of life. In the 5th decade higher T_3 values were observed which latter dropped. In females the serum TSH level showed a higher value in the first and second decades of life, which remained nearly constant in later decades of life with somewhat reduced values.

The results obtained for these hormones in individuals belonging to different areas (Table-5) show a slight difference in T_4 levels. The table also reveals that there was no significant difference observed for T_3 and TSH level.

Table -1: Gender distribution of hormone levels

Gender	T_4 (ηmol/L)	T_3 (ηmol/L)	TSH (µIU/L)
Males (n=376)	83.70±12.50	1.81±0.45	1.35±0.60
Females (n=122)	71.65±15.50	1.80±0.55	1.45±0.65

Values are expressed as Mean±SD

Table-2: Thyroid and TSH level in different age groups (n=498)

Age Groups Years	T_4 (ηmol/L)	T_3 (ηmol/L)	TSH (µIU/L)
1–10 (n=104)	63.06±9.60	1.93±0.55	1.76±0.55
11–20 (n=268)	84.93±12.80	1.83±0.48	1.36±0.52
21–30 (n=106)	85.00±13.00	1.59±0.46	1.05±0.45
31–40 (n=10)	93.30±11.70	1.37±0.38	1.63±0.40
41–50 (n=8)	87 .90±10.90	2.18±0.49	1.00±0.38
51–60 (n=1)	47.00±7.09	1.00±0.55	0.90±0.38
60+ (n=1)	137.0±14.50	3.40±0.65	0.70±0.33

Values are expressed as Mean±SD

Table-3: Thyroid hormones and TSH level in males of different age groups (n=376)

Age Groups Years	T_4 (ηmol/L)	T_3 (ηmol/L)	TSH (µIU/L)
1–10 (n=56)	65.50±15.00	2.05±0.55	1.79±0.45
11–20 (n=217)	87.41±13.00	1.87±0.60	1.32±0.40
21–30 (n=94)	84.61±17.50	1.55±0.65	1.03±0.35
31–40 (n=07)	99.85±16.50	1.83±0.70	1.72±0.35
41–50 (n=02)	91.00±17.50	1.40±0.60	0.40±0.50

Values are expressed as Mean±SD

Table-4: Thyroid hormones and TSH levels in females of different age groups (n=122)

Age Groups Years	T_4 (ηmol/L)	T_3 (ηmol/L)	TSH (µIU/L)
1–10 (n=48)	61.50±14.00	1.97±0.50	1.52±0.50
11–20 (n=51)	74.39±16.50	1.68±0.55	1.51±0.45
21–30 (n=12)	88.08±16.00	1.90±0.50	1.20±0.55
31–40 (n=03)	78.00±17.50	1.86±0.60	1.40±0.65
41–50 (n=06)	86.83±17.00	2.45±0.55	1.20±0.60
51–60 (n=01)	47.00±18.50	1.00±0.65	0.90±0.65

Values are expressed as Mean±SD

Table-5: Different Districts of NWFP and Thyroid Hormones and TSH Levels (n=498)

Districts	%	T_4 (ηmol/L)	T_3 (ηmol/L)	TSH (µIU/L)
Karak (n=209)	41.96	76.42±16.60	1. 80±0.70	1.46±0.85
Bannu (n=98)	19.67	80.76±15.90	1.70±0.65	1.31±0.90
Kohat (n=100)	20.08	81.78±16.50	1.90±0.60	1.31±0.75
Hungu (n=80)	16.06	89.00±17.00	2.05±0.80	1.39±0.55
Peshawar (n=11)	2.20	92.90±14.70	1.20±0.75	1.16±0.65

Values are expressed as Mean±SD

DISCUSSION

The variations in the mean values of the concerned hormones with gender (Table-2) suggests that a small change within the normal range can be seen in serum T_4, in both genders with a slightly higher level in males than females. This observation is in accordance with the previous work, that in males the value of sex hormones increases the circulating level of thyroxine binding globulin (TBG), which directly leads to increase in circulating level of T_4[8]. However, some what contradictory results were reported by others who worked on the effect of age and gender on thyroid function and concluded that level of T_4 was higher in females than males. They further concluded that T_3 and TSH levels are not influenced by gender.[8,17,18]

The present work also examines the effect of age on the levels T_4, T_3 and TSH (Table-2) which show a decreased level of T_4 in the first ten years of life. This is in accordance with the previous works.[8] Similar trends of changes in T_4 levels were also found by other workers.[17] In the first decade, the T_3 level was found to be elevated, which was followed by a drop then it increases in the later decades. This pattern of effect is also in agreement with the findings of previous workers.[17–20]

The effect of age on TSH level was observed to increase in the first decade and then decreased in second and third decades of life. The TSH level remained nearly unaffected beyond the fourth decade of life. This pattern of result is in agreement with the results obtained in the previous study[18,21], while some workers showed a higher TSH level with an increase in age[19,22]. This difference may be due to the fact that the subjects in that study were not screened for any kind of illness that may affect the thyroid function tests. In the present work we selected normal and healthy individuals. Further more a longitudinal study was conducted which might affect the results.[19] Some other researchers also assayed thyroid hormones and TSH and found no changes in TSH level with age.[10]

The level of thyroid hormones and TSH both in males and females of different age groups are depicted in Table-3 and 4. In the first decade, like that found by Razzak[8], the value of T_4 in case of males and females was found lower but it increased in the next decades, which is in accordance with the results obtained by Sack.[23] In the case of males the T_4 value increases progressively. While in the case of females the decreased values were observed in the fourth and sixth decades with an elevated value in the last decade of life. The lower T_4 level in the first decade of life in both the genders and a decreased value in the fourth and sixth decades of life in females may be attributed to the decreased concentration of TBG. In case of females the elevated T_4 value in the last decade of life may be due to the increased concentration of TBG during pre-menopausal period. The higher value of T_4 in the last ten years in females than in males is in accordance with the result obtained by earlier investigators.[17,24] The T_3 values were found higher in the first decade in both genders, which latter on decreased in the second decade and was stable in the remaining age. Such results were obtained by Muslim and Khalil[17], Westgren *et al*[20]. A slight difference was

shown in TSH level of males in different age groups (Table-3). The TSH level was found higher in the first decade of life with a little decrease in the latter decades of life. These results are similar to the previous work of Razzak[8], Muslim and Khalil[17], Franklyn[18], Hoogendoorn *et al*[22]. While in case of females it remained nearly constant in first few decades of life with a little decreased value in the last decades of life (Table-4). The TSH level was found decreased with age.[21,25,26] Our results are in agreement with the previous results. This decrease in hormonal levels may be in direct relation with the increased T_4 level in the respective decades of life.

This study determines the normal levels of hormones in healthy volunteers from different districts of NWFP, province, especially from Karak, Bannu, Kohat, Hungu and Peshawar. The difference in the observed T_4 may be due to the difference in their food habit, race and socio-economic conditions of peoples belonging to the above mentioned areas of the province.

CONCLUSION

It can be concluded from the present study that the age, gender, race and area all have an appreciable effect on the levels T_4, T_3 and TSH.

ACKNOWLEDGEMENT

The cooperation of Dr. Muhammad Ayub, Director IRNUM, Peshawar for providing RIA facilities is highly acknowledged.

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