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Age and sex specific thyroid hormone profile in euthyroid subjects

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Abstract

Thyroid hormones have pervasive effects on growth and development in the fetus, child, and adolescent regulating calorigenesis and metabolic rate throughout the life. The study was made to investigate the levels of free triiodothyronine (fT3), free thyroxine (fT4) and thyroid stimulating hormone (TSH) of euthyroid subjects. The study included 713 male and 2633 female euthyroid subjects of RIMS, Jharkhand, India during December 2013 to November 2014. It has been found that free triiodothyronine level (p=0.000) varies remarkably among different age group and gender, free thyroxine level (p=0.999) remains almost unaltered throughout all decades of life and TSH level (p=0.000) decreases with age. The levels of free T3, free T4 and TSH have significant effects among gender with age. It is therefore concluded that there should be separate reference range among individuals so that the higher level of hormones in the early decades and the lower level in the older decade cannot be interpreted as abnormal results and under prediction and over prediction of results can be avoided.

Keywords: Thyroid Stimulating Hormone, Euthyroid, free triiodothyronine, free thyroxine.

Introduction

Thyroid gland produces two key metabolic hormones: triiodothyronine and thyroxine. The thyroid hormones play critical role in cell differentiation during development and maintain thermogenic and metabolic homeostasis in the adults. These two hormones are controlled by Thyroid Stimulating Hormone (TSH), produced by anterior pituitary gland and stimulate hormone production of thyroid gland.

The level of serum free T3, free T4 and TSH levels are remarkably different. It has been found that the level of free T3 changes with age from infant to old age. In children and adolescent high level of free T3 is observed. Low levels of free T3 and free T4 have been recorded in neonates and shortly after birth. The level seems to increase markedly, as the concentration is higher in serum of infant (Abuid J et. al. 1973). The serum free T3 level declines in older age. In contrast, the serum free T4 concentration remains almost unaltered in the first and middle decade and shows very minor increment in the older decade which is statistically not significant. Serum TSH level has been found to increase or decrease with age in relation to the iodine intake. Also, the presence of an age related altered set point of the hypothalamic-pituitary-thyroid axis may be involved in the age related modifications of thyroid hormones and thyrotropins. (Mazzoccoli G et. al. 2010). A lot of research has been done earlier by many research workers to estimate the effect of various parameters on the thyroid gland. Blount et. al. 2006 and Shon et. al. 2008, have studied the difference in thyroid function between males and females. Hollowell et al. 2002, have also observed thyroid impact among females. With reference to age, researchers have many finding that is sometimes confounding. Hollowell et al. observed that TSH levels increase with age when iodine intake is sufficient in a population. The reason for T3 level declination in older age can be due to decline in thyroidal T3 secretion, Increase in T3 turnover rate, decline in TBG and decrease in peripheral conversion of T4 to T3

Gender has a vital role in the level of thyroid hormones. In females, the serum T3 and T4 level may raise twice during pregnancy. Women have more economic and family responsibility as compared to men. Illiteracy and poverty additionally has equal effects on thyroid function. Alteration in nutritional status, whether short term or long term has great impact on thyroid status.

The above observation illustrates that both the age and sex have important effect on thyroid hormone function. In view of above, an attempt has been made to study the thyroid hormone profile in the subjects reporting to Rajendra Institute of Medical sciences, Ranchi, Jharkhand, India during December 2013 to November 2014.

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Table 1: Thyroid Function in Males and Females of different Age Group

Gender	Age (years)	Subjects (N)	fT3 (pg/mL)	fT4 (ng/dL)	TSH (uIU/mL)
Males	1-10	36	2.864± 0.533	1.080± 0.178	2.071± 1.079
	11-20	74	2.957± 0.420	1.032± 0.149	2.112± 0.951
	21-30	179	2.867± 0.430	1.046± 0.137	2.003± 0.959
	31-40	145	2.792± 0.427	1.047± 0.142	2.146± 1.044
	41-50	131	2.677± 0.384	1.041± 0.134	1.968± 1.074
	51-60	73	2.770± 0.393	1.033± 0.142	2.059± 1.220
	61-70	62	2.545± 0.348	1.037± 0.158	2.232± 1.281
	71 & above	13	2.319± 0.481	1.110± 0.166	1.764± 0.935
Group Total		713	2.778± 0.144	1.045± 0.144	2.062± 1.061
Females	1-10	28	2.790± 0.572	1.058± 0.154	2.305± 1.162
	11-20	278	2.777± 0.466	1.058± 0.139	2.171± 1.004
	21-30	787	2.686± 0.408	1.036± 0.147	2.287± 1.058
	31-40	702	2.600± 0.424	1.037± 0.141	2.340± 1.081
	41-50	497	2.620± 0.437	1.048± 0.162	2.279± 1.185
	51-60	231	2.574± 0.432	1.057± 0.163	2.189± 1.118
	61-70	84	2.552± 0.421	1.075± 0.163	1.992± 1.169
	71 & above	26	2.500± 0.472	1.113± 0.215	2.024± 1.044
Group Total		2633	2.644± 0.434	1.045± 0.151	2.267± 1.095
Males & Females	1-10	64	2.832± 0.547	1.070± 0.167	2.174± 1.113
	11-20	352	2.815± 0.462	1.053± 0.141	2.159± 0.992
	21-30	966	2.720± 0.418	1.038± 0.145	2.234± 1.046
	31-40	847	2.633± 0.431	1.038± 0.141	2.307± 1.077
	41-50	628	2.632± 0.427	1.046± 0.157	2.214± 1.168
	51-60	304	2.621± 0.431	1.051± 0.159	2.158± 1.143
	61-70	146	2.532± 0.390	1.059± 0.161	2.094± 1.219
	71 & above	39	2.440± 0.477	1.112± 0.198	1.938± 1.004
Group total		3346	2.673± 0.437	1.045± 0.149	2.223± 1.091

Materials and Methods

Patient and Study designs

Secondary analyses have been done that involved the subjects who have visited to Department of Biochemistry, Rajendra Institute of Medical Science during December 2013 to November 2014 for thyroid function test. The candidates were both male and female ranging from age group of 1 day to 95 years. They have undergone thyroid function test. There were 5169 subjects, among them, only 3346 were euthyroid. The subjects suffering from thyroidal illness were excluded from the study. The investigation was done in the Department of Biochemistry and secondary data analysis was done at Biomedical Informatics Centre under Department of Biochemistry, RIMS, Ranchi, India.

Blood Sample Collection

To each participant, tourniquet was applied in the arm and blood was taken from antecubital vein of the patients. Blood was collected in plain vials without any additives. It was allowed to clot for 30 minutes. After clot formation the blood was centrifuged at 3000 rpm for 10 minutes. Serum was separated from cells and collected in a separate aliquot vial and labeled carefully. It was stored at 2-8 ^{0}c in refrigerator and serum concentrations of free T3, free T4 and TSH were assessed on the next day in Abbott i1000 SR by enhanced chemiluminescence method.

Statistics

The data were analysed by using the SPSS software package, version 20.0 (SPSS Inc., Chicago, IL, USA) for windows. The data were expressed as mean ± SD. A student's t-test was used to determine the effect of gender on age. P-value of <0.05 was considered to be statistically significant.

Results and Discussion

The hormonal assay have been analysed by statistical software SPSS version 20.0. The results are given in Tables 1 and 2. Table 1 represents the mean levels of free T3, free T4 and TSH for females and males separately as well as in combined groups.

It has been observed from Table 1, the serum free T3 concentration is found to be higher in males in age group of 11-60 years as compared to females. But in age group of 61-71 years and above the serum concentration of free T3 is more in case of females compared to males. When mean free T3 level in total male group is concerned it is slightly higher 2.778 ± 0.144 against 2.644 ± 0.434 as compared to total female group throughout all decades. There is significant difference among mean free T3 level as compared to age and gender. There is decrease in mean level of serum free T3 level in males in older age group. In case of free T4, the mean free T4 level for female is 1.045 ± 0.151 which is almost equal to that of males 1.045 ± 0.144. No statistical significant difference have been found by age or gender in early and middle decade of life and shows very minor elevation in older age group in the mean level of free T4 that is 1.110 ± 0.166 in males and 1.113 ± 0.215 in females which is also statistically not significant. In case of TSH, in males, the mean TSH level is found to be unaltered among 1- 40 years of age group and decreases in the age group of 41-50 years and 71 & above age group. In females the mean TSH level is found to be slightly lower 1.002 ± 1.169 in age group of 61-70 years as compared to mean TSH level of total females 2.267± 1.095.

From Table 2, it can be observed that the assumption of homogeneity of variance was tested and satisfied via Leven's test (95 % confidence interval). It can be observed that there is significant difference in levels of free T3 among females

Table 2: Description of Independent Sample t-test

Thyroid Hormone Profile			Levene's Test for Equality of Variances		t-test for Equality of Means		
			F	Sig	t	df	Sig. (2-tailed)
free Level	T3	Equal variances assumed	0.067	0.796	-7.297	3344	0.000
		Equal variances not assumed			-7.298	1127.59	0.000
free Level	T4	Equal variances assumed	2.622	0.105	-0.008	3344	0.993
		Equal variances not assumed			-0.008	1169.24	0.993
TSH Level		Equal variances assumed	2.713	0.100	4.470	3344	0.000
		Equal variances not assumed			4.551	1156.02	0.000

(N=2633, M = 2.644, SD = 0.434) and males (N=713, M=2.778, SD=0.144), p= 0.000 and similar results in TSH level among females (N=2633, M=2.267, SD=1.095) and males (N=713, M=2.062, SD=1.061), p= 0.000 have been found. In case of free T4 level among females (N=2633, M = 1.045, SD = 0.151) and males (N=713, M=1.045, SD=0.144), p= 0.993 which is statistically not significant.

Graphs have been plotted to show the significant effect of age and gender among thyroid hormone profile. Blue line denotes level of free T3, red line denotes TSH level and free T4 level is denoted by green line respectively.

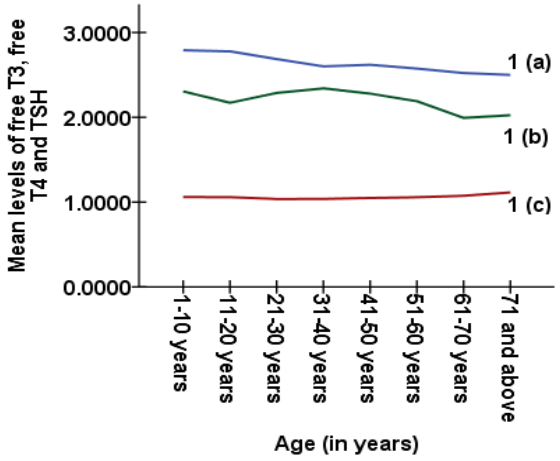

Figure 1: The mean level of free T3, free T4 and TSH is denoted by blue line 1 (a), red line 1 (c) and green line 1 (b) respectively among females.

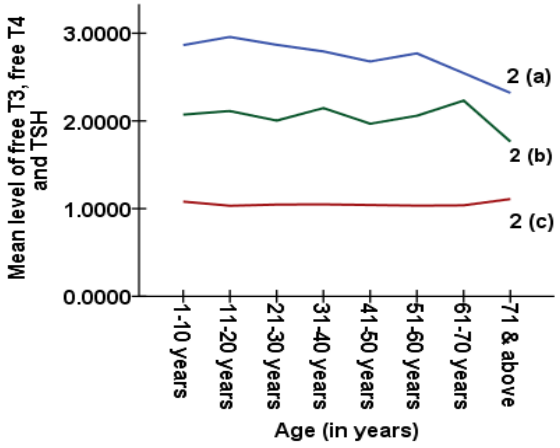

Figure 2: The mean level of free T3, free T4 and TSH is denoted by blue line 2 (a), red line 2 (c) and green line 2 (b) respectively among males.

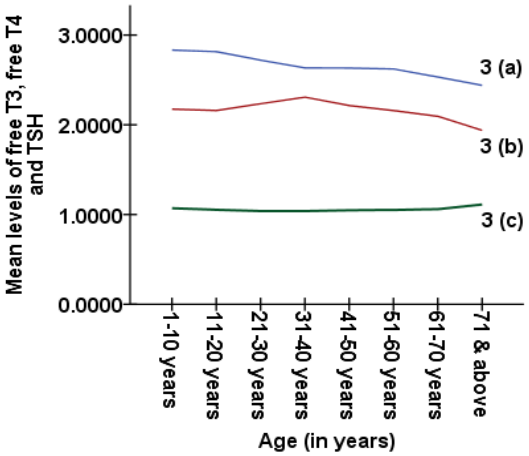

Figure 3: The mean level of free T3, free T4 and TSH is denoted by blue line 3 (a), red line 3 (c) and green line 3 (b) respectively among total population.

Figure 1 (a), 2 (a) and 3 (a) shows the variation of free T3 level among females, males and total population simultaneously. From figure 1 (a), it can be observed that among females, the level of free T3 is highest among age group of 1-20 years, after that is decreases and remains constant up to 60 years and subsequently a declination in free T3 level is observed after the age group of 60 years.

Figure 2 (a) shows the variation among the free T3 level among males. In age group of 1-20 years it is highest, followed by minor increase among age group of 51-60 years and further declination in older age. Figure 3 (a) represents the variation of free T3 level among the total population with age and it follows the same trend as in case of Figure 1 (a). Figure 1 (c), 2 (c) and 3 (c) shows the level of free T4. The level of free T4 does not show any significant changes. The level of TSH among males shows a different trend as compared to females and the population as shown in figure 1 (b), 2 (b) and 3 (c). The level of TSH is slightly higher among 21-40 years and 51-60 years followed by subsequent decrease in the older age. When total population is considered the level of TSH is minorly elevated among 20-40 years followed by declination in level of TSH among the older age group.

The study examines the relationship between thyroid hormone profile, ageing and gender. From the study it can be observed that the number of female subjects is substantially high as compared to males hence gender wise consideration of hormone levels should be taken into account.

There is ambiguity regarding the level of thyroid hormones in various age groups and gender. It has been earlier reported by Abuid et. al. and Montalvo et. al. that serum T3 level are low in newborn children and high in infants. The present study put emphasis on the fact that the serum free T3 level is significantly high in early decades of life, remain unchanged in middle decade and shows subsequent declination in later decades of life. The free T3 level declination in older age may be due to decline in thyroidal free T3 secretion, Increase in free T3 turnover rate and decrease in peripheral conversion of T4 to T3. The increase in the level of free T3 in the early stage may be due to the increased metabolic activity during infancy and childhood.

Free T3 is most active and is secreted by both thyroid glands as well as by the result of de-iodination of T4 in the peripheral tissues. Our finding has been substantiated with the previous studies by research workers Nelson et. al, Delaang and Fisher. However, research workers like Westgreen et. al. found declination in T3 levels only after age 80. Henson et. al. have reported that T3 level decreases with age in both sexes. Samollow and Fathzadeh did not observe any significant change in T3 levels among the gender.

Mean serum free T4 levels shows slight variation among both the gender in different decades of life but the difference is statistically not significant (P=0.6993). Our studies elucidate that the level of free T4 do not vary with age. It might be due to decreased thyroid hormone clearance by liver with advancing age. Surks and Boucai et al., Bremner AP et. al., and Samollow et. al. have also reported that serum T4 levels do not vary with age. However Sawin et. al. observed incomprehensible low levels of thyroxine in the elderly and Razzak et. al. observed higher levels of serum T4 in females as compared to males before age 60 and a decline thereafter. They have also suggested this may be due to the fact that in females after age 60, there is decline in estrogen dependent TBG concentrations.

Many studies are oblique in revealing that TSH levels remain either stable during aging or go up or down. In the present investigation, it has been found that there were significant changes in serum TSH. NHANESIII survey showed that serum TSH level in males were found to have stable level of TSH over 40-50 years of age and were slightly higher thereafter. In contrast to the results of NHANES III, our result shows normal reference range for TSH is decreased in elderly as compared to younger age group. Our result is supported by Laurberg et al., Sawin et al, Mitchell and Simon who have reported that the level of TSH decreases with age. This might be due to increased pituitary sensitivity to circulating thyroid hormones. Undeniably a blunted response to TRH has been demonstrated in elderly subjects. TSH secretion by the pituitary gland has been shown to decrease in advancing age. Yoshida et. al. reported age related decrease in TSH level among males. The results are also comprehensible with Lipson et. al. reporting decrease in TSH level in elderly Research workers like Jseke and Thorner, have reported unexplained higher Serum TSH level in older age. Our results show that Serum free T3 levels gradually decline in older age and serum free T4 levels shows no significant variation with age and serum TSH decreases in the elderly people.

Conclusions

The levels of free T3, free T4 and TSH have significant effects among gender with age. It is therefore concluded that there should be separate age and gender specific reference range among individuals so that the higher level of thyroid hormones in the early decades and the lower level in the elderly may not be interpreted as abnormal results and therefore under prediction and over prediction of results can be avoided.

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