

The Effect of Age on Thyroid and Thyroid Stimulating Hormones Levels in Healthy Iraqi Females

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Abstract

The current study was carried out to investigate the effect of age on the levels of thyroid stimulating hormone (TSH), thyroxine (T_4), triiodothyronine (T_3) and T_3 -Uptake in normal healthy Females. Serum levels of TSH, T_4 , T_3 , and T_3 -Uptake were measured in 79 healthy females aged 20-60 years old. Serum concentrations of TSH, T_4 , T_3 and T_3 -Uptake were estimated by using Vitek Immuno Diagnostic assay System (VIDS). TSH values slightly increase with aging, but without significant changes. Mean T_4 Values for females over age 40 years were significantly lower than younger women. Mean serum T_3 declined with increasing age, but, also without a significant change. Values for T_3 U in females after age 40 years were significantly higher than females under age 40 years. The physiologic reasons for these findings may be due to sex-related changes in binding proteins and alteration in metabolic clearance rates, production, and degradation of these hormones with increasing age.

Key words:-Thyroid stimulating hormone, thyroxine, triiodothyronine, T_3 Uptake, age, healthy females.

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Introduction

Thyroid stimulating hormone, also known as thyrotrophin is an anterior pituitary hormone. Human TSH is a glycoprotein containing 211 amino acids residues, hexamine and sialic acid and is made up of two subunits alpha (α) and beta (β) (1). The α subunit is identical to that of two other pituitary glycoprotein hormone luteinizing hormone (LH) and follicle stimulating hormone (FSH) and human chronic gonadotropin (HCG). The β subunit is unique to TSH and confers its specificity and biological activity. The biological action of TSH occurs through TSH receptors on the surface of the thyroid follicular cell (2) TSH increase T_3 and T_4 biosynthesis (3). Regulation of TSH secretion is affected by two factors at the level of pituitary thyrotrope, the first is hypothalamic TSH-releasing hormone (TRH), a small tri peptide synthesized by hypothalamus which stimulates the secretion and synthesis of TSH (4). The second are T_3 and T_4 which inhibit the TSH secretion by antagonizing the action of TRH (5).

Thyroid hormone secretion is regulated by the hypothalamus –pituitary Thyroid axis. Both active thyroid hormones, thyroxine (T_4) and triiodothyronine (T_3) exert negative feedback upon the hypothalamus and the pituitary (6). T_3 is the active hormone responsible for activation of thyroid hormones-dependent genes. T_4 serves primarily as a prohormone, also named thyroxine (3, 5, 3', 5'-tetraiodothyronine), it is deiodinated in peripheral tissues to form triiodothyronine, which has greater biological activity. 20% of daily production of T_3 being derived from direct secretion by the thyroid and 80% from peripheral T_4 conversion (7). Both T_4 and T_3 hormones are iodine containing amino acids, and their concentrations are 93% and 7% respectively, T_4 is the chief fraction, T_3 present in blood in much smaller quantities and persists for shorter time than does T_4 , But, it is about four times as potent as T_4 (8). T_4 and T_3 are not readily soluble in water, which means they binds to carrier protein that circulates in blood. Thyroxine – binding globulin (TBG) serves as the main transporter of thyroid hormones. This carrier protein permits a more consistent availability of thyroid hormones from which the active, free hormones release for target cell uptake (8). Thyroid hormones are essential for normal growth and development and have many effects on metabolic processes (9).

Primary hypothyroidism or thyroid failure is characterized by an elevation of serum TSH and a reduction in circulating T_3 or T_4 levels. T_3 and T_4 play an important role in regulating major functions in the body, most of cognitive abilities such as concentration, memory, and attention span as well as mood and emotions depend on normal thyroid hormone levels, also thyroid hormones regulates the levels and action of serotonin , noradrenaline , and GABA (gamma- aminobutyric acid) now accepted as the main chemical transmitters implicated in both depression and some anxiety disorders .Maintaining normal serotonin and noradrenaline levels in the brain depends to a great extent on whether the correct amount of T_3 is available . Extensive animal and human research has led scientists to conclude that serotonin levels in the brain decrease if T_3 is not delivered in the right amount .Also a deficit of T_3 in the brain is likely to result in noradrenaline working inefficiently as a chemical transmitter , and noradrenaline deficiency or inefficiency is , in some people, the chemical reason for depression (22) .

The issue of screening normal TSH, T_4 , T_3 and T_3 - uptake is a subject of intense debate among thyroid community (10). The change in these hormones increases with increasing age and is higher in the females population (11).Although there were numerous reports concerning the effect of aging on the thyroid function tests, conflicting data presented about thyroid and thyroid stimulating hormones values in elderly. This study was basically designed to see the levels of these hormones in normal and healthy Iraq females and also to investigate the effect of age on them.

Subjects and Methods

Seventy nine healthy females with an age range of (20- 60) years were involved in this study. None had a history of thyroid disease, goiter, or medication known to alter thyroid function. All were well at the time of examination.

The blood was withdrawn by venipuncture, the amount of blood was not fixed , but usually was in the range (2.5-5)ml. Blood samples were left at room temperature for about half an hour, then the sera were separated by spinning for 25 minutes at 3500 rpm , at room temperature.

Hormonal assay was performed by an instrument called mini VIDOAS (made in France by Bio Mericux Company in 1992, model vidas12).T₄, T₃, TSH and T₃ uptake were measured according to the Enzyme Linked Floursent Assay (ELFA) technique. The assay principles combine an enzyme immunoassay sandwich method with final floursent detection. All the assay steps are performed automatically by the instrument.

An assay kit consists of a plastic pipette shaped device called SPR (Solid Phase Receptacle), the interior of the SPR coated with antibody, antigen or other treatment that capture a target analyses. Each SPR has a corresponding mini VIDAS reagent strip included in the text kit, this single reagent strip has ten wells, the first one is an empty well in which to place the sample. The next eight wells contain reagents or washes; the last well is optical cuvette where the substrate reaction is measured from its strip flouresent reading. Both SPR and reagent strip are coded with matching color dots and assay code.

Results were presented as mean \pm standard deviation (SD). The data were analyzed by analysis of variance (ANOVA) and students t-test using Statistical Package for Social Sciences (SPSS) version 16.Values of p<0.05 was accepted as significant.

Results

The summary of the mean \pm SD for the serum TSH, T₄, T₃ and T₃ uptake concentrations in healthy females aged (20-60) years is demonstrated in table 1. The healthy females were grouped into four groups depending on age: 1) 20-30 years, 2) 31-40 years, 3) 41-50 years,and 4) 51-60 years.

Table (1) The effect of age on the serum concentration of Thyrotropin and Thyroid hormones in healthy Iraq females

Age	(20-30) Years (n=20)	(31-40) Years (n=19)	(41-50) Years (n=21)	(51-60) Years (n=20)	P-value	Sig.
Hormones concentration						
TSH μ IU/mL	197 \pm 2.577	2.3 \pm 0.255	2.9 \pm 0.18	3.02 \pm 0.15	0.103	NS
T ₄ nmole/L	17182 \pm 13.35	108.075 \pm 5.85	100.5 \pm 11.7	86.80 \pm 10.1	0.048*	S
T ₃ nmole/L	1.43 \pm 0.093	1.315 \pm 0.08	1.127 \pm 0.25	1.01 \pm 0.13	0.065	NS
T ₃ -uptake %	27.65 \pm 1.455	28.73 \pm 0.685	28.78 \pm 0.57	30.55 \pm 0.64	0.048**	S

*P<0.05 significantly lower than other age groups.

**P<0.05 significantly higher than other age groups.

The results showed that the TSH concentrations were increased slightly with aging without a significant change ($P > 0.05$) table (1), figure (1).

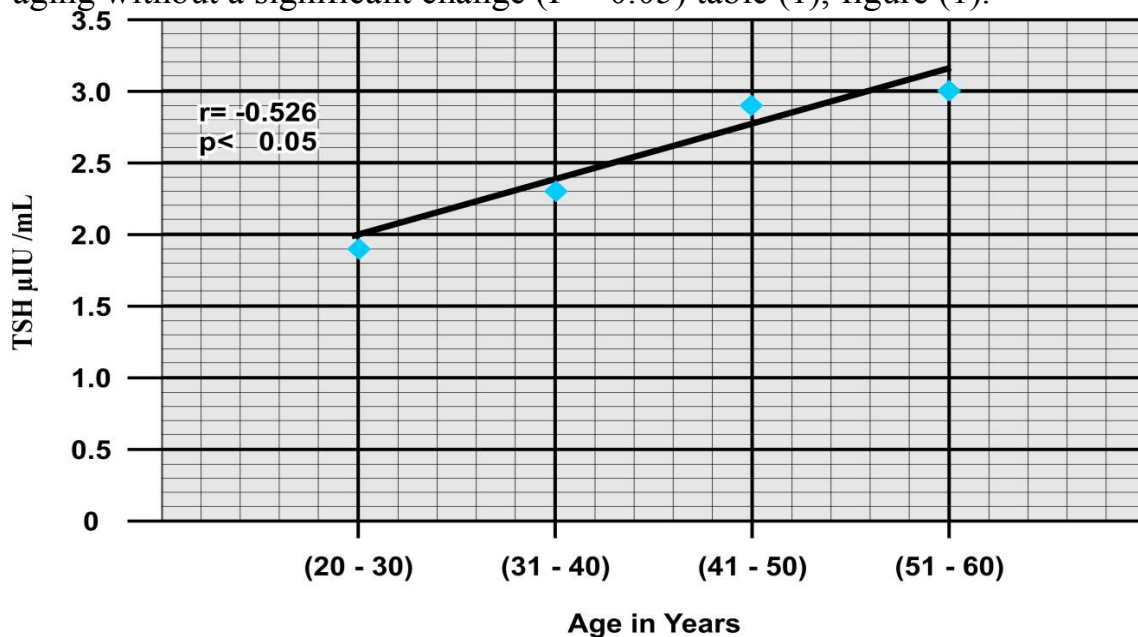


Figure (1): TSH values ($\mu\text{IU} / \text{mL}$) for females aged 20-65 years, show statistically significant positive correlation ($r = 0.526$, $p < 0.05$).

Also the results showed that T_4 concentrations were significantly lower in older females whose age 51 - 60 years old than the other age groups ($P < 0.05$), this is depicted in table (1), figure (2).

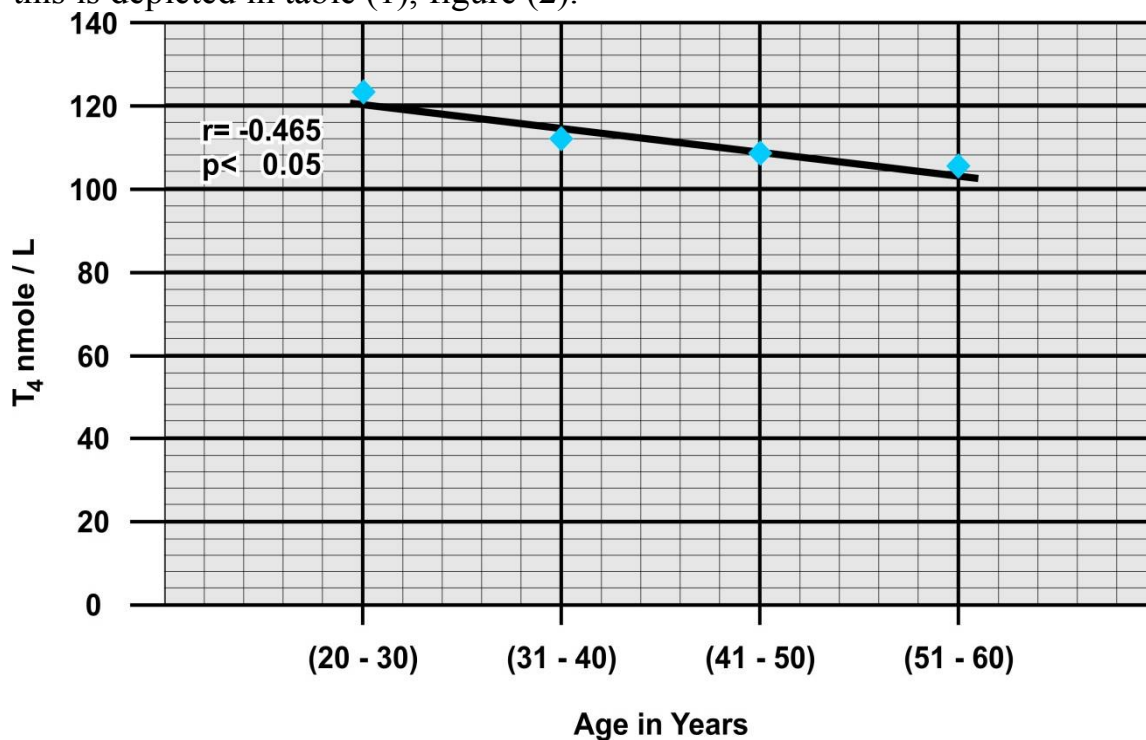


Figure (2): T_4 values (nmole / L) for females aged 20-60 years, show statistically significant positive correlation ($r = 0.465$, $p < 0.05$).

Values for T₃ were found to decrease with age but without significant change (P > 0.05), table (1), figure 3.

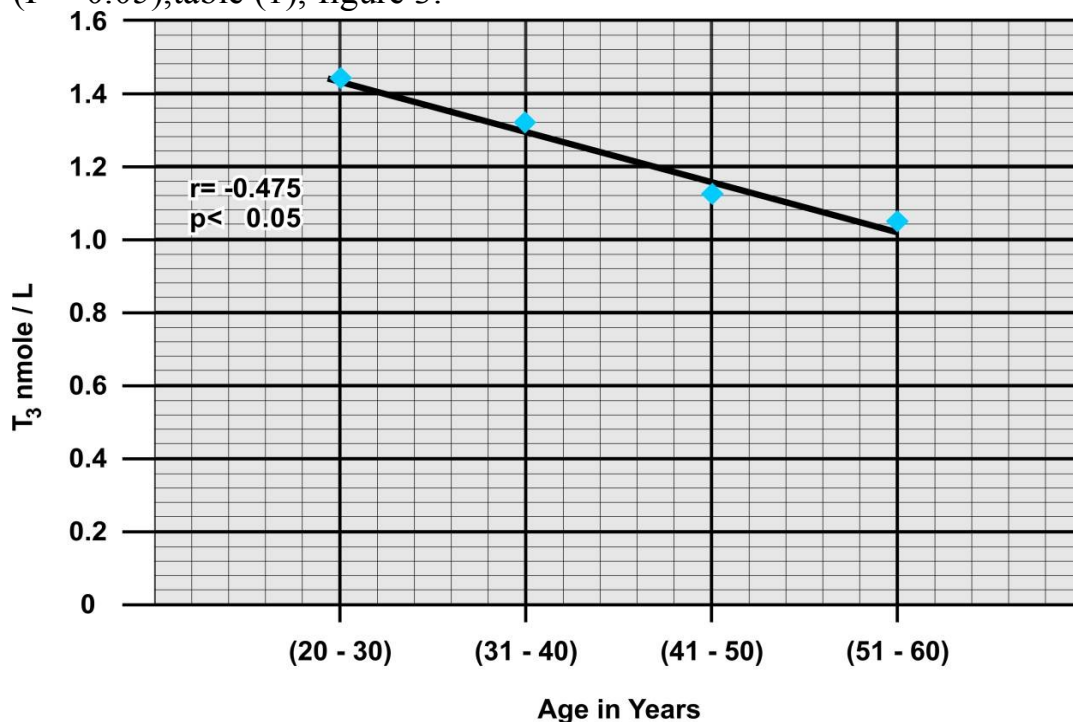


Figure (3): T₃ values (nmole / L) for females aged 20-60 years, show statistically significant negative correlation (r = -0.475 , p<0.05).

Also, serum concentration of T₃ uptake were significantly higher (P>0.05) in females whose age 51 - 60 years than the flames in other age groups, table (1), figure (4).

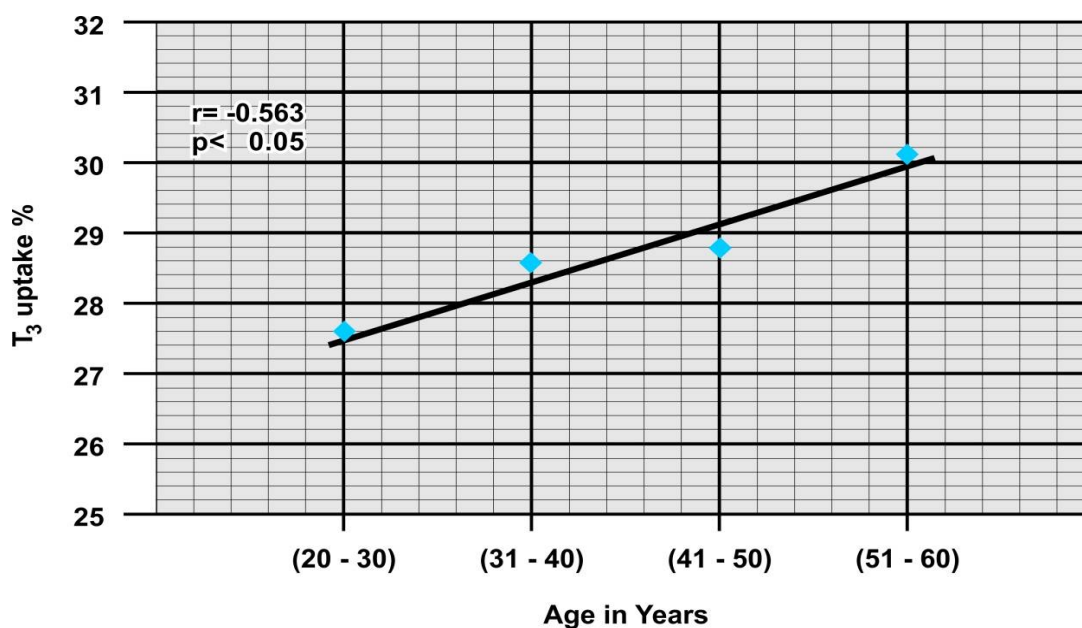


Figure (4): T₃ uptake values (%) for females aged 20-60 years, show statistically significant positive correlation (r = 0.563 , p<0.05).

Discussion

There was no significant difference in serum TSH concentration between all age groups, with a slight increase in TSH concentration with advancing age. Other investigators noted similar findings Jeskeetal (12), found that 20 % of their euthyroid subjects over age 70 had slight increase in TSH. Lauridsen (13) and Vannotti (14) reported unexplained age related TSH increments in both sexes, although values remained within normal limits. It is possible that T₃ level might be mildly lower in older females, resulting higher serum TSH concentration. Both Hesch et al. (15) and Herrmann et al. (16) reported decrement, unrelated to sex, in T₃ in elderly normal subjects and Bermudez et al. (13) noted a decrease in T₃ in a small group of older normal subjects. Another possibility, although not substantiated, is that TSH turnover rates may decrease with age in females. Szabolcs et al. (17) finding of relative hypo responsiveness of TSH to thyrotrophin releasing hormone (TRH) only in older males supports this explanation.

The results showed that mean serum T₄ values in females significantly decline in older females whose age 51-60 years, when compared with the other age groups. This was in good agreement with the results reported by Zahoor et al. (1), who observed unexplained lower T₄ levels (although within normal limits) in the elderly. Finding similar to our data were noted by Hasen et al. (18) in their study of 111 normal subjects. They suggested that the finding in females may have resulted from a decline in estrogen-dependent TBG concentrations after age 50, a theory in a good agreement with our findings (19). Other have reported that T₄ concentrations don't vary with age (20). Triiodothyronine (T₃) level showed a gradual and non-significant decline with age in females. These findings agreed with most previous studies, but the decline in T₃ was not profound as previously reported, Pawlikowski et al. (4) noted variable finding and Westgren et al. (5) found that T₃ decreased in subject only after age 80. The reason for the decline in serum T₃ is unknown. A possible explanation may be decreased thyroidal T₃ production and release. It is also possible that the degradation rate of T₃ is increased in old age McArdle et al. (8) suggested that T₄ disposal and T₄ to T₃ peripheral conversion rates were decreased and it is possible that the lowered T₃ is a result of combination of these factors, also intracellular T₃ concentration in the aged are unknown.

The results for T₃U values correspond well with the thyroxine findings, with T₃U slightly but significantly increased for 51-60 years woman. These results suggest that slight decline in TBG occur in females aged 51-60 years, due most likely to a fall in circulating estrogen. Our results support Braverman's study of sex-related changes in TBG (22), which concluded that premenopausal females had slightly higher TBG Levels than males: and that their T₃U Values

were significantly lower than those of males. In further support of these data, Hansen et al. (9) observed an increase in T₃U in women over age 40 years, from a mean of (27± 4) % to (30.3±3.3) %.

Conclusion

It is concluded from this study that the age of healthy females have appreciable effect on the levels of T₄ and T₃ uptake, while it has a slight and non-significant effect on the levels of TSH and T₃.

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تأثير العمر على هرمونات الدرقية والهرمون المحفز للدرقية في النساء العراقيات

أجريت هذه الدراسة لمعرفة تأثير العمر على مستويات هرمونات الغدة الدرقية والهرمون المحفز للدرقية في النساء العراقيات اللواتي لايعانين من اي مرض في الغدة الدرقية. أظهرت النتائج بأن الهرمون المحفز للدرقية يزداد بإزدياد العمر وان T₄ هرمون الثايروكسين للنساء بعد عمر الاربعين يكون اقل بقيمة ذات دلالة احصائية عن النساء في الفئات العمرية الاقل، وان هرمون الـ T₃ يقل بتقدم العمر كما اظهرت النتائج بأن T₃U في النساء بعد عمر الاربعين يكون اعلى بقيمة ذات دلالة احصائية عن النساء قبل عمر الاربعين.