

Relationship Between Disorder of Thyroid Gland and the levels of T₃, T₄ and TSH Hormones

العلاقة بين خلل الغدة الدرقية ومستويات الهرمونات T₃, T₄, TSH

Rehab J Mohamed/ Department of Chemistry / College of Education/
University of Kerbala

Abstract:

This study included , thirty patients of hyperthyroidism and twenty eight patients of hypothyroidism. Thirty healthy individuals were taken as control group. The mean of age for patients of hyperthyroidism is 36.13 ± 6.72 years, the mean of age for patients with hypothyroidism is 39.63 ± 8.14 years, and the mean of for control group is 33.40 ± 9.82 years. Blood samples obtained from AL-Hussian hospital in Kerbala city. The sera obtained from the blood for determine the effect of thyroid's diseases on the levels of thyroxine hormone (T₃), triiodothyronine (T₄) and thyroid stimulating hormone (TSH). The results of the present research showed significant increase in T₃ and T₄ concentration, significant decrease in TSH concentration in patients with hyperthyroidism when compared with control group , also this research showed significant decrease in T₃ and T₄ concentrations, significant decrease in TSH concentration in patients of hypothyroidism when compared to those of the control group.

الخلاصة:

اشتملت الدراسة على 30 مريض يعانون من زيادة في نشاط الغدة الدرقية وثمانية وعشرون مريض يعانون من انخفاض في نشاط الغدة الدرقية . ثلاثون شخص من الاصحاء اخذو كمجموعة سيطرة , كان معدل عمر المرضى المصابين بفرط نشاط الغدة الدرقية هو 36.13 ± 6.72 سنة معدل عمر المرضى المصابين بانخفاض نشاط الغدة الدرقية هو 39.63 ± 8.14 سنة , معدل عمر مجموعة السيطرة كان 33.40 ± 9.82 سنة, جمعت العينات من مستشفى الحسين في مدينة كربلاء , العينات جمعت لإيجاد تأثير امراض الغدة الدرقية على مستويات الهرمونات الثايروكسين T₃, ثلاثي ايدوثايرونين T₄ والهرمون المحفز للغدة الدرقية TSH. نتائج البحث اظهرت زياده معنوية ملحوظة في تركيز كل من الهرمونات T₃, T₄ وانخفاض معنوي ملحوظ في TSH لدى المرضى المصابين بزيادة نشاط الغدة الدرقية مقارنة بمجموعة السيطرة, وكذلك اظهرت النتائج انخفاض معنوي ملحوظ في تركيز كل من الهرمونات T₃, T₄ وارتفاع معنوي ملحوظ في TSH لدى المرضى المصابين بانخفاض نشاط الغدة الدرقية مقارنة بمجموعة السيطرة .

Introduction:

Thyroid gland is the largest endocrine gland in the body, highly vascular containing of right and left lobes linked by a thin band of connective tissue called isthmus. It is soft, reddish brown, weighting 18-60 gm. It is placed directly below the larynx on each side and anterior to the trachea [1] . Thyroid gland secrets two principle iodinated hormones called tetraiodothyronine or thyroxine (T₄) and triiodothyronine (T₃) which are accountable for the optimal growth development, function and maintenance of body tissues [2]. T₄ is the major secretory product of the thyroid gland, with a daily production rate of 80-100 µg. T₄ is produced only by the thyroid gland. In contrast, only 20% of the daily production rate of T₃ is derived from thyroid secretion and 80% from peripheral T₄ conversion. The everyday production rate of T₃ is 30-40µg [3]. Thyroid hormones contain 59 % and 65% (of T₃ and T₄ respectively) of iodine as an essential part of the molecule [4], so biosynthesis of active hormones needs an adequate amount of this element. This wants efficient iodide pump that allows thyroid cells to take up and concentrate iodide from food [5], The most common presented clinical features of thyroid disease are the result of: Hypothyroidism, due to deficient thyroid hormone secretion. Hyperthyroidism, due to excessive

thyroid hormone secretion. Hyperthyroidism is a disorder that occurs when the thyroid gland makes more thyroid hormone than the body needs. It is sometimes called thyrotoxicosis, the technical term for too much thyroid hormone in the blood. About one percent of the United State population has hyperthyroidism. Women are much more likely to develop hyperthyroidism than men [6]. Rarely, hyperthyroidism is caused by a pituitary adenoma, which is a noncancerous tumor of the pituitary gland. In this case, hyperthyroidism is due to too much TSH. The signs and symptoms of hyperthyroidism are attributable to the effects of excess thyroid hormone in the circulation. The severity of signs and symptoms may be related to the duration of the illness, the magnitude of the hormone excess, and the age of the patient. Hypothyroidism is caused by suboptimal circulating concentration of thyroid hormones. It becomes more prevalent with age, affecting about 6 percent of people over 60 years, It is more common in women. Hypothyroidism is classified into primary and secondary disorders [7]. The most common type is the primary hypothyroidism. However the secondary hypothyroidism is accounted to be rare among cases of the disease [8]. There are various causes of primary hypothyroidism, but autoimmune disease (Hashimoto's thyroiditis) and thyroid failure or surgical treatment of thyrotoxicosis account for over 90% of cases in those parts of the world which are not significantly iodine-deficient [9].

Material and methods:

Patients and control:

Study samples were obtained from AL Hussian Hospital in Kerbala city. Thirty patients of hyperthyroidism and twenty eight hypothyroidism patients were enrolled in addition to thirty were healthy individuals enrolled as a control group. The mean of age for patients of hyperthyroidism is 36.13 ± 6.72 years, the mean of age for patients of hypothyroidism is 39.63 ± 8.14 years, and the mean of for control group is 31.40 ± 9.82 years.

Specimen collection:

The group of patients who are obtained randomly consisted of thirty females and 28 males. Patients and control group were neither smoking nor suffering from a disease other than hypothyroidism or hyperthyroidism. A questionnaire was designed to obtain the information of patients and control subjects. It contained the name, age, sex, address, weight, height, occupation, socioeconomic status, presence of other diseases, complications of hypothyroidism or hyperthyroidism, and habits like smoking. Collection of Samples Disposable syringes and needles were used for blood collection.

Determination of TSH, T₃ and T₄:

Blood samples VIDAS® T₃, T₄ and TSH is an automated quantitative test for use on the VIDAS® instruments for the quantitative measurement of total triiodothyronine (T₃) and Thyroxine (T₄), and for the immunoenzymatic determination of thyroid-stimulating hormone in human serum using the enzyme linked fluorescent assay technique (ELFA).

Statistical analysis:

The results were expressed as mean \pm SD and analyzed statistically. The differences between the results of patients and control were assessed by student's t test; significant variation was considered when the P value was less than 0.05. The linear regression analysis was applied to evaluate the relationships of the changes of the biochemical parameters, in relevance to various factors related to the study.

Results:

The results of this study were viewed the levels of the T3, T4 and TSH measurements in the patients of hyperthyroidism revealed significant elevation of the concentrations of T3 ($p=0.05$), T4 ($p=0.028$), while there was significant decreased in TSH levels ($p=0.044$) in patients when compared with control group, but The results of patients of hypothyroidism demonstrated the levels of the T3, T4 were significant decreased ($p=0.040$), (0.029) of the concentrations, while there was significant increase in TSH levels ($p=0.046$) in patients when compared with control group these results illustrated in the following tables and figures:

Table (1): Concentrations of hormones in patients of hyperthyroidism and control group.

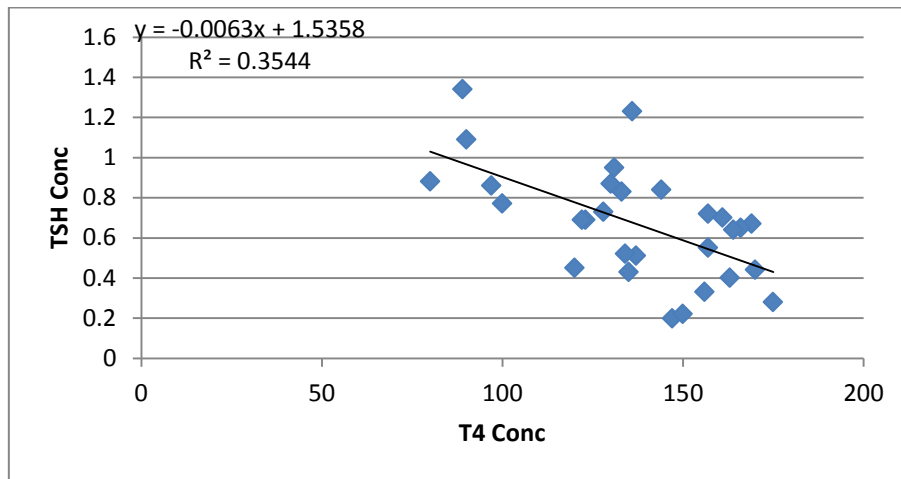
Parameter	Subject	Mean \pm SD	P value
T3 (nM)	Patients	2.42 \pm 5.47	0.05
	Control	1.90 \pm 0.36	
T4 (nM)	Patients	173.48 \pm 94.24	0.028
	Control	88.33 \pm 13.51	
TSH (mU/ml)	Patients	0.53 \pm 1.00	0.044
	Control	1.80 \pm 1.06	

T3: thyroxine hormone , T4: triiodothyronine, TSH: thyroid stimulating hormone
P value was less than 0.05

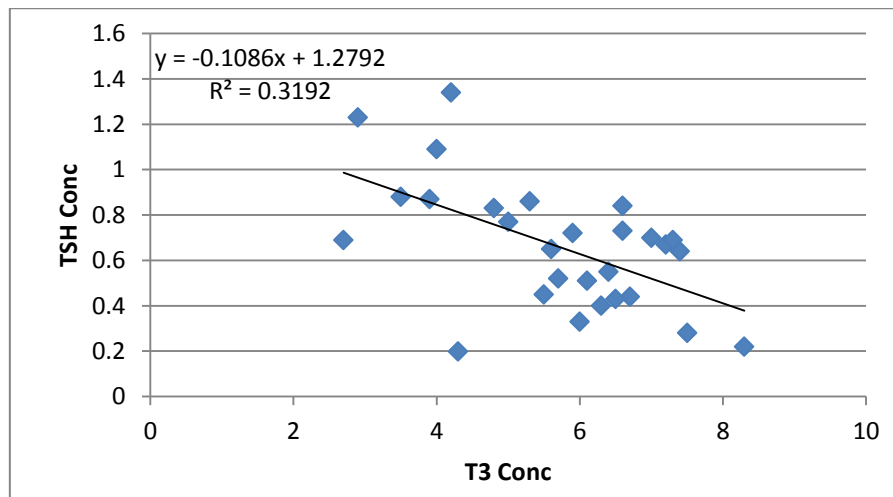
Table (2): Concentrations of hormones in patients of hypothyroidism and control group.

Parameter	Subject	Mean \pm SD	P value
T3 (nM)	Patients	0.87 \pm 4.35	0.048
	Control	1.90 \pm 0.36	
T4 (nM)	Patients	50. \pm 18.33	0.029
	Control	88.33 \pm 13.51	
TSH (mU/ml)	Patients	2.77 \pm 1.24	0.046
	Control	1.80 \pm 1.06	

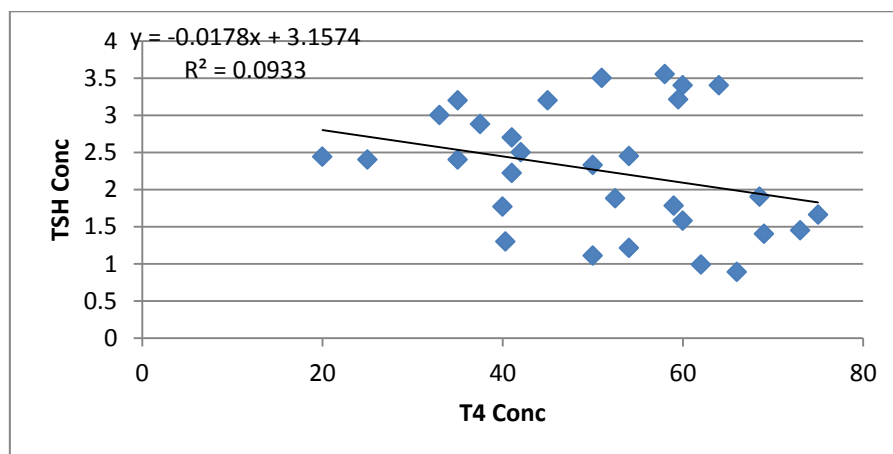
T3: thyroxine hormone , T4: triiodothyronine, TSH: thyroid stimulating hormone
P value was less than 0.05



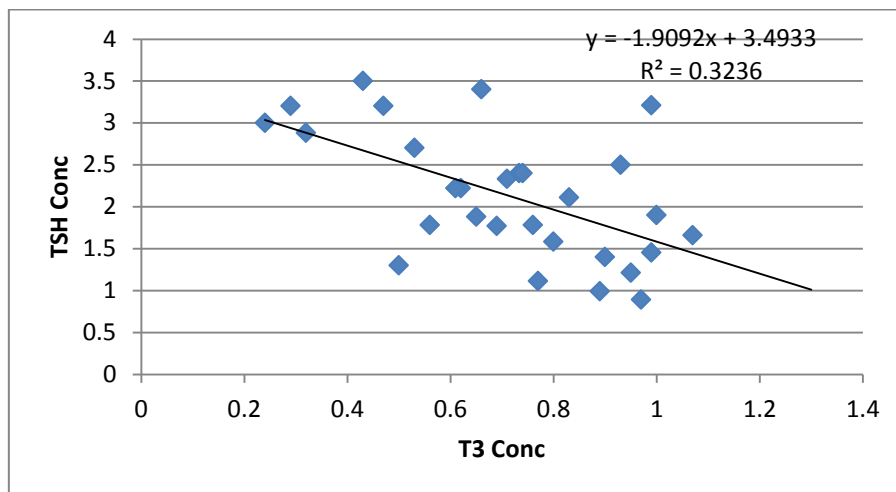
(fig 1): Correlation between T4 hormone concentration and TSH hormone concentration in patients of hyperthyroidism.



(fig 2): Correlation between T3 hormone concentration and TSH hormone concentration in patients of hyperthyroidism.



(fig 3): Correlation between T4 hormone concentration and TSH hormone concentration in patients of hypothyroidism.



(fig 4): Correlation between T3 hormone concentration and TSH hormone concentration in patients of hypothyroidism.

Discussion:

In this study it was investigated of the relation between disorder of thyroid gland with varies of thyroid's hormones, there are two types of dysfunction of thyroid gland were hyperthyroidism and hypothyroidism in every one of it the levels of hormones were varied these results in tables 1 and 2 it may be explained by the tests to measure TSH, T4, T3 tests to evaluate thyroid function include the following: TSH tests The best way to initially test thyroid function is to measure the TSH level in a blood sample. A high TSH level indicates that the thyroid gland is failing because of a problem that is directly affecting the thyroid (primary hypothyroidism). The opposite situation, in which the TSH level is low, usually indicates that the person has an overactive thyroid that is producing too much thyroid hormone (hyperthyroidism). Occasionally, a low TSH may result from an abnormality in the pituitary gland, which prevents it from making enough TSH to stimulate the thyroid (secondary hypothyroidism). In most healthy individuals, a normal TSH value means that the thyroid is functioning normally [10]. Not all high values for T4 and T3, and not all suppressed TSH levels, are associated with hyperthyroidism. Estrogen administration or pregnancy raises the thyroxine-binding globulin level and results in high total T4 and T3 levels but normal free T4 and T3 estimates and a normal result on sensitive TSH assay. Thyroid hyperthyroxinemia may also be attributable to other abnormal binding proteins, including albumin and prealbumin. Similarly, thyroid hormone resistance states can cause increased serum T4 levels without hyperthyroidism. Administration of corticosteroids, severe illness, and pituitary dysfunction can be associated with a suppressed TSH level in the absence of hyperthyroidism [11]. Subclinical hyperthyroidism may result from endogenous overproduction of thyroid hormone; it also may be exogenous as a result of intentional administration of thyroid hormone to suppress thyroid malignancy, or unintentional extreme hormone therapy in patients with hypothyroidism. Common causes of endogenous subclinical hyperthyroidism include Graves' disease, autonomous functioning thyroid adenoma, and toxic multinodular goiter. Transient TSH suppression may occur during subacute, painless, or postpartum thyroiditis [12]. There is an opposite correlation between population iodine intake and the prevalence of thyroid autonomy (thyroid tissue that functions without TSH), with a higher prevalence in iodine-deficient areas. The prevalence of subclinical hyperthyroidism differs among studies because of differences in defining the TSH level for subclinical hyperthyroidism, age of the study population, and use of thyroid hormone medication. Hyperthyroidism has been reported to be as high as 15 percent in persons older than 70 years in iodine-deficient regions [13]. The condition is most common in patients on thyroid hormone therapy, in whom the prevalence may be as high as 20 percent,5,6 particularly in those taking desiccated thyroid hormone [14]. Subclinical hyperthyroidism should be differentiated from other causes of low TSH levels that are not related to relative thyroid over activity, such as the use of certain drugs (dopamine and glucocorticoids),

nonthyroidal illness (euthyroid sick syndrome), pituitary causes (TSH deficiency), hypothalamic causes (thyrotropin-releasing hormone deficiency), and psychiatric conditions, especially affective disorders. T4 and T3 levels are generally lower in persons with these conditions, whereas patients with subclinical hyperthyroidism may have T4 and T3 levels in the mid to high reference range [15]. In normal individuals, TSH is under negative feedback control by the amount of free thyroid hormone (T4 and T3) in the circulation and positive control by the hypothalamic thyroid-releasing hormone (TRH). Thus in the case of thyroid hormone deficiency (hypothyroidism) the TSH level should be elevated. If the hypothyroid state is due to failure of the pituitary gland (TSH) or the hypothalamus (TRH), the values for TSH may be low, normal or occasionally in the borderline range. Thus a TSH above 15 mg/dl is very good evidence for primary hypothyroidism and a value below 5 mg/dl is very good evidence against primary hypothyroidism. The presence of low Free T4 with a TSH of less than 10 strongly suggests a pituitary or hypothalamic etiology for the hypothyroidism (secondary hypothyroidism) [16]. The TSH alone cannot be used to screen for secondary hypothyroidism and usually requires a measurement of thyroid hormone levels to be adequately interpreted. The most common cause (in more than 70% of people) is overproduction of thyroid hormone by the entire thyroid gland, this condition is also known as Graves' disease, Graves' disease is caused by antibodies in the blood that turn on the thyroid and cause it to grow and secrete too much thyroid hormone. This type of hyperthyroidism tends to run in families and it occurs more often in young women. Little is known about why specific individuals get this disease [17]. Another type of hyperthyroidism is characterized by one or more nodules or lumps in the thyroid that may slowly grow and increase their activity so that the total output of thyroid hormone into the blood is larger than normal. This condition is known as toxic nodular also, people may temporarily have symptoms of hyperthyroidism if they have a state called thyroiditis, this condition is caused by a problem with the immune system or a viral infection that causes the gland to leak stored thyroid hormone [18]. The same symptoms can also be caused by taking too much thyroid hormone in tablet form, These last two forms of excess thyroid hormone are only called thyrotoxicosis, since the thyroid is not overcharged [19]. The best way to initially test thyroid function is to measure the TSH level in a blood sample. A high TSH level indicates that the thyroid gland is failing because of a problem that is directly affecting the thyroid (primary hypothyroidism). The opposite situation, in which the TSH level is low, usually indicates that the person has an overactive thyroid that is producing too much thyroid hormone (hyperthyroidism). Occasionally, a low TSH may result from an abnormality in the pituitary gland, which stops it from making enough TSH to stimulate the thyroid (secondary hypothyroidism) [20]. In most healthy persons, a normal TSH value means that the thyroid is functioning normally. T4 circulates in the blood in two forms: 1) T4 bound to proteins that prevent the T4 from entering the various tissues that need thyroid hormone. 2) Free T4, which does enter the several target tissues to exert its effects. The free T4 fraction is the most important to regulate how the thyroid is functioning, and tests to measure this are called the Free T4 (FT4) and the Free T4 Index (FT4I or FTI). Individuals who have hyperthyroidism will have an elevated FT4 or FTI [21], whereas patients with hypothyroidism will have a low level of FT4 or FTI. Combining the TSH test with the FT4 or FTI accurately determines how the thyroid gland is functioning. The finding of an raised TSH and low FT4 or FTI shows primary hypothyroidism due to disease in the thyroid gland. A low TSH and low FT4 or FTI indicates hypothyroidism due to a problem connecting the pituitary gland. A low TSH with an elevated FT4 or FTI is found in individuals who have hyperthyroidism. T3 tests are often useful to diagnosis hyperthyroidism or to determine the severity of the hyperthyroidism. Patients who are hyperthyroid will have an elevated T3 level [22]. In some individuals with a low TSH, only the T3 is elevated and the FT4 or FTI is normal. T3 testing seldom is helpful in the hypothyroid patient, later it is the last test to become abnormal. Patients can be severely hypothyroid with a high TSH and low FT4 or FTI, but have a normal T3 [23]. In some situations, such as through pregnancy or while taking birth control pills, great levels of total T4 and T3 can exist. This is because the estrogens increase the level of the binding proteins. In these situations, it is better to ask both for TSH and free T4 for thyroid evaluation [24]. Correlation between T3, T4 and TSH in fig 1, 2, 3, 4

illustrated the negative correlation between T₃, T₄ with TSH in hyperthyroidism and hypothyroidism.

Conclusion: Improve relationship between disorder of thyroid gland and the levels of T₃, T₄, TSH hormones.

References :

- 1- Agur AM, Dalley AF. Thyroid. In: Grant's Atlas of Anatomy. 12th ed. Tayer C, Scogna KH editors. Lippencott Williams and Wilkins. USA. PP 768-772. 2009.
- 2- Yen PM, Physiological and molecular basis of thyroid hormone actions. *Physiol. Rev.* 81: 1097-1142. 2001.
- 3- Zhang J, Lazar MA. The mechanism of action of thyroid hormones. *Annu Rev Physio.* 62: 439. 2000.
- 4- Francis SG, Dong BJ. Thyroid and Antithyroid Drugs. In: Katzung BG (ed.) Basic and Clinical Pharmacology. 10th ed. Lange Medical Books / McGraw- Hill Companies, San Francisco, USA: PP 618-630. 2007.
- 5- Roti E, Uberti ED. Iodine excess and hyperthyroidism. *Thyroid.* 11: 493-496. 2001.
- 6- Passath A, Leb G, Goebel R. The evaluation of free thyroid hormones (FT₄ and FT₃) in the routine diagnosis of thyroid function. *Nuklearmedizin.* 24(3): 115-121. 1985.
- 7- Bharaktiya S, Orlander PR, Woodhouse WR, *et al.* Hypothyroidism; Follow-up. *Medicine Endocrinology*;17(12): 1211-23. 2007.
- 8- Goswami UC and Choudhury S. The status of retinoids in women suffering from hyper- and hypothyroidism: interrelationship between vitamin A, beta-carotene and thyroid hormones. *Int J Vitam Nutr Res*; 69(2): 132-5. 1999.
- 9- Lafranchi S. Congenital hypothyroidism: Long term outcome. *Thyroid.* 9: 741-741. 1999.
- 10- Bülow Pedersen I, Knudsen N, Jørgensen T, Perrild H, Ovesen L, Laurberg P. Large differences in incidences of overt hyper- and hypothyroidism associated with a small difference in iodine intake: a prospective comparative register-based population survey. *J Clin Endocrinol Metab.* 87(10):4462-4469. 2002.
- 11- Aghini-Lombardi F, Antonangeli L, Martino E, *et al.* The spectrum of thyroid disorders in an iodine-deficient community: the Pescopagano survey. *J Clin Endocrinol Metab.* 84(2):561-566. 1999.
- 12- Canaris GJ, Manowitz NR, Mayor G, Ridgway EC. The Colorado thyroid disease prevalence study. *Arch Intern Med.* 160(4):526-534.2000.
- 13- Rosario PW. Natural history of subclinical hyperthyroidism in elderly patients with TSH between 0.1 and 0.4 mIU/l: a prospective study. *Clin Endocrinol (Oxf).* 72(5):685-688. 2010.
- 14- Rosario PW. The natural history of subclinical hyperthyroidism in patients below the age of 65 years. *Clin Endocrinol (Oxf).* 68(3):491-492. 2008.
- 15- Woeber KA. Observations concerning the natural history of subclinical hyperthyroidism. *Thyroid.* 15(7):687-691. 2005.
- 16- Pedersen IB, Knudsen N, Jørgensen T, *et al.* Large differences in incidences of overt hyper- and hypothyroidism associated with a small difference in iodine intake: a prospective comparative register-based population survey. *J Clin Endocrinol Metab*; 87(10): 4462-9. 2002.
- 17- Greenlund LJ, Nair KS, Brennan MD. Changes in body composition in women following treatment of overt and subclinical hyperthyroidism. *Endocr Pract.* 14(8):973-978. 2008.
- 18- Boon NA, Colledge NR, Walker BR, *et al,* editors. Davidson's principles & practice of medicine. 20th ed. Churchill Livingstone; 739- 804. 2006.
- 19- Lilly LS. Disorders of the thyroid. In: Kasper DL, Braunwald E, Fauci AS, *et al,* editors. Harrison's manual of medicine. 16th ed. McGraw-Hill medical publishing division; 815-822; 2005.

- 20- Sinclair C, Gilchrist JM, Hennessey JV, *et al.* Muscle carnitine in hypo- and hyperthyroidism. *Muscle Nerve*; 32(3): 357-359. 2005.
- 21- Zulewski H, Müller B, Exer P, *et al.* Estimation of Tissue Hypothyroidism by a New Clinical Score; Evaluation of Patients with Various Grades of Hypothyroidism and Controls. *Journal of Clinical Endocrinology and Metabolism*; 82 (3): 771–776. 1997.
- 22- Sgarbi JA, Matsumura LK, Kasamatsu TS, Ferreira SR, Maciel RM. Subclinical thyroid dysfunctions are independent risk factors for mortality in a 7.5-year follow-up: the Japanese-Brazilian thyroid study. *Eur J Endocrinol.* 162(3):569-577. 2010.
- 23- de Jong FJ, den Heijer T, Visser TJ, *et al.* Thyroid hormones, dementia, and atrophy of the medial temporal lobe. *J Clin Endocrinol Metab.* 91(7):2569-2573. 2006.
- 24- Jeffrey R, Rhoda H, James V, Jeffrey I, Peter A. Clinical Practice Guidelines for Hypothyroidism in Adults Cosponsored by The American Association of Clinical Endocrinologists and The American Thyroid Association. *ATA/AACE Guidelines for Hypothyroidism in Adults, Endocr Pract.* 18(No. 6). 2012.