

# THE RELATIONSHIP BETWEEN THE THYROID HORMONES & SOME IMMUNOLOGICAL PARAMETERS AMONG PATIENTS WITH HYPOTHYROIDISM <sup>+</sup>

العلاقة بين هرمونات الغدة الدرقية وبعض المعالم المناعية لدى المرضى قصور الغدة الدرقية

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المستخلص:

نقص إفراز الغده الدرقية هو مصطلح يعني قلة هرمونات الغدة الدرقية T3, T4 وزيادة TSH الهرمون المحفز للغدة الدرقية . الهدف من الدراسة هو تقييم العلاقة بين إفراز هرمونات الغدة الدرقية و تحسس المتممات البروتينية المناعية لدى مرضى نقص إفراز الغدة الدرقية. أجريت هذه الدراسة في المختبرات التعليمية / مدينة الطب للفترة من 2009/10/1 ولغاية 2010/7/1 على 35 مريضاً يعانون من نقص إفراز الغدة الدرقية ، تتراوح أعمارهم بين (30-40) سنة تتضمن العينة 17 ذكراً و 18 أنثى تمت مقارنتهم مع مجموعة من الأصحاء (المجموعة القياسية) من 25 شخص (13 ذكراً و 12 أنثى) تتراوح أعمارهم من (25-35) سنة تم فحصهم سريرياً و تشخيصهم من خلال الفحص الهرموني T3, T4, TSH بطريقة (RIA) وعلاقتها مع البروتينات و المتممات المناعية (IgG, IgM, IgA & C3, C4) بطريقة الأنتشار المناعي الشعاعي المفرد (SRID).

وجد في هذه الدراسة قيمة معنوية عالية لقلّة T3, T4 للمرضى مقارنة بالأصحاء (المجموعة القياسية) وأن T4 لدى الجنسين له قيمة معنوية عالية بين المرضى و الأصحاء. ووجد أن هناك اختلافاً واضحاً في مستوى IgM, IgG لدى مرضى نقص إفراز الغدة الدرقية مقارنة بدراسات أخرى عدا IgA بين المرضى و الأصحاء ولا وجود لأختلاف معنوي بين مستوى C3, C4 بين المرضى و الأصحاء.

الاستنتاجات : يستنتج من هذه الدراسة ان مستوى (T4) في المصل يهبط بشكل عالي المعنوية لدى مرضى نقص إفراز الغده الدرقية مقارنة بمجموعة السيطره مما يؤدي الى زيادة (TSH) لدى المرض المعنيين كذلك ظهر عوز معنوي بمستوى الغلوبين المناعي (M,G) بينما اتخفض قليلا مستوى IgA ومكوني المتمم الثالث والرابع مقارنة بمجموعة السيطرة

## Abstract:

Hypothyroidism is a term that means a decrease of circulatory T3, T4 and an increase of TSH hormone.

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**The aim of the study was to evaluate the relationship between secretion of thyroid hormones and sensitivity of immunoglobulins & complement in patients with hypothyroidism.**

**The study was conducted in Education Laboratories of Medical City during the period between 1/10/2009 -1/7/2011; on 35 patients with hypothyroidism. Their ages' range between 30-40 years (17males & 18 females); compared with 25 apparently healthy control group (13 males & 12 females), their ages range between 25-35 years. Clinically the patients were examined and thyroid hormones (T3, T4 & TSH) were estimated by RIA besides the level of C3, C4 & total serum levels of Igs which estimated by SRID technique. The study showed that there was a significant decrement in T3 & T4 level in comparison with healthy control group. Furthermore, there was a significant difference between the level of T4 among both patients' sexes (males & females).**

**Moreover, there were significant differences in the level of IgG & IgM in comparison with control group. There were no significant differences in C3 & C4 concentrations in comparison with healthy control.**

**It can be concluded that hypothyroidism results in highly significant reduction in T4 levels which results in highly significant elevation in TSH levels in addition to decrement in IgG & IgM levels (with slightly decrement in IgA , C3 and C4 levels) among hypothyroidism patients in comparison with their levels among healthy control.**

### **Introduction:**

Thyroid gland is the largest organ specialized in endocrine function in human body. It secretes hormones into blood stream. Thyroid hormones contain (59-65%) of trace element iodine [I]. Thyroid hormones are:

1) Tetraiodothyronin (Thyroxin) (T<sub>4</sub>) :It consists of four iodine atoms and it is abbreviated as (T<sub>4</sub>), it acts as pro-hormone which is stored in thyroid gland and released to the blood circulation, it exerts physiological action in various tissues [2] .the reference range of T<sub>4</sub> is 64-148 mlu/L [3].

2) Triiodithyronine (T<sub>3</sub>):Triiodithyronine is a thyroid hormone with three iodine atoms is abbreviated as (T<sub>3</sub>), about 20%, body (T<sub>3</sub>) comes from thyroid gland 80% is derived from T<sub>4</sub>-deiodation which takes place in many organs in the body specially in the liver [4]. The reference range of (T<sub>3</sub>) is 1.5-3.3 n mol/L

Hyperthyroidism and hypothyroidism are common endocrine problems [3]

Hyperthyroidism develops when body is exposed to excessive amounts of thyroid hormone.

Hypothyroidism means deficiency of thyroid hormone. There are some signs and symptoms observed in patients with hypothyroidism such as, slowing of mentality, dry skin, weight gain, deafness, hoarseness of voice, hair loss and slow speech.

There are four types of hypothyroidism

1. Congenital hypothyroidism
2. Primary hypothyroidism
3. Secondary hypothyroidism
4. Tertiary hypothyroidism [5]

Thyroid Stimulating Hormone (TSH) (Thyrotropin) is secreted from the pituitary gland which is located at the base of brain. It is controlled by hypothalamic hormone Thyrotropin Releasing Hormone (TRH) [6]. The immune system is a large and complex series of elements widely distributed throughout the body, it has many

effects against pathogens, and reaction against foreign substances while there is no reaction against self components.

The biological components of immune response which is fundamental in immunology and allergy are specific for pathogen. [7] Humoral immunity involves humoral solution in biological fluid, including effectors of non specific immunity (Complement) and specific immunity (antibodies) [1]. Immunoglobulin (Ab) is defined as a glycoprotein, synthesized by the cells of lymphoreticular system and released to the plasma and other body fluids [5]. The basic unit structure for an immunoglobulin molecule is composed of four polypeptide chains each two are identical referred to as heavy and light chains. Immunoglobulins react specially with the antigen that produces (Ab-Ag) complexes. According to the heavy chain (Igs) are classified into 5 classes (isotopes) [8]:

**IgG:** This type is the most important group, it constitutes (70-75%) of total immunoglobulin pool, and 80% in serum; the molecular weight of IgG is (150,000) Dalton [9].

**IgM:** This is an isotype that accounts for approximately (5-10) % of immunoglobulin in pool; the molecular weight is (900,000) Daltons. This class of Ig is essential in primary overly Ig especially bacterial infection [10].

**IgA:** This immunoglobulin constitutes about (5-15) of total Igs in the serum, which is found in two forms monomer and dimer [11].

Complement system is an important part of the body defense mechanism against infection .the complement system consists of about 30 proteins most of these proteins and glycoproteins are synthesized in the liver, it response to bacterial infection [12]. There are three pathways of complement activation.

- 1) Classical pathway
- 2) Alternative and imitated by a number of other factors
- 3) Lectin Pathway

Complements Component C3 constitutes 70% of total protein in the complement system, may be used in some (Ag –Ab) reactions, it is synthesized in the liver, macrophages, fibroblasts, lymphoid tissue and skin [13].

Complements component C4 is synthesized in bone, lung, tissues, may be passed in the alternative complement pathway when immune complexes are not involved, or may be used in very complicated series of reactions that follow many (Ag-Ab) reaction [13].

## **Materials & Methods**

### **Materials**

### **Patients & Consuls**

Thirty five sera samples have been collected from untreated newly diagnosed hypothyroid volunteer patients (included (17♂, 18♀) their ages ranging from (30-40) years. All patients have been diagnosed by consultant committee of the Medical City Hospital during the period from (Oct / 2009 – July/ 2010). Twenty five control volunteer subjects (12♀ +13♂) aged (25-35) years.

All subjects were tested for thyroid functions (T3, T4 & TSH), immunoglobulin isotypes (IgA, IgG & IgM) & complement (C3 & C4) concentrations.

### **Methods:**

The work was done at Teaching–Laboratories and Medical City laboratories during Sep. (2009-2010). All subjects were sent for thyroid function tests assay by immunoradiometric assay system for hormones determination [5].

TSH: The  $p^{25}$  labeled signal-antibody binds to an epitope of (TSH) molecule especially different from that recognized by biotin-capture –Ab, the formation of a capture-Ab-Ag Signal (Ab- Complex) also referred to as a sandwich " that measured the concentration of (TSH) in gamma counter [14].

Thyroxin "T4" is measured by  $I^{125}$  RIA system, this assay is based on competition between unlabelled "T4" and fixed quantity of  $I^{125}$  labeled "T4" for limited number of binding sites or "T4" specific Abs. Triiodothyroxine "T3" Level was determined by using  $I^{125}$ RIA system with the same principle [15].

The estimation of Igs & complements' components (C3& C4) was carried out by single radial immunodiffusion (SRID) test [11].

### **Results and Discussion:**

Hypothyroidism results from failure to maintain adequate tissue levels of thyroid hormone, if "T4" is decreased, it would cause an increase in the secretion of TSH by pituitary & this causes stress in Igs & complements C3, C4, [1].

The study included (18 ♀, 17♂) hypothyroidism patients with age ranged between (30-40) years compared to (25) control subjects (12♀, 13♂), their age between (25-35) years as shown in table (1) at Teaching Lab. Medical City between Sep./ 2009-Mar/ 2010 .

The serum T3 level for healthy control & hypothyroid patients show no significant difference as shown in table (2). This finding agrees with [2, 3].

So the serum T4 level shows highly significant decrease in hypothyroid patients' sera compared to healthy control group as shown in the same table. This study agreed with Oppenheimer [4]. In our study showed that the TSH level increased in hypothyroid group compared to healthy control group as shown in table1. This agrees with Sing *et al.*, [5].

The serum "T3" level for healthy subjects & hypothyroid patients show no significant difference also. Table (3) showed "T4" level in females & males, which showed highly significant difference between two sexes compared with control subject.

Then the total level of Igs in the sera of hypothyroid patients & the control were listed in the table (4) in addition to the level of complements' components C3 & C4 for the same groups. Igs concentrations were measured in mg/dL. It was clear, that there were highly significant differences between hypothyroid patients' sera level of IgG & IgM in comparison with healthy group, that mean are reported deficiency, except for IgA level in patients' sera in comparison with controls [15].

The cut off values for these results depended on the data of the normal healthy individuals.

Also this table showed that there were no significant differences in C3& C4 level between patients & control. That mean of C3, C4 were slightly deficiency in hypothyroid patients in comparison with healthy control evidences are accumulating that the complement system is an important mediator in the immunologic defense of the body.

### **Results**

**Table (1): Age & gender distribution of the studied groups.**

Studied group statistic	Hypothyroidism	Healthy control
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Rang of Age	30-40	25-35
Mean ± SD	34.71± 3.30	29.64±3.23
Male No (%)	17-(48.6%)	12-(48%)
Female No (%)	18-(51.4 %)	13-(52%)
Total No (%)	35-(100%)	25-(100%)

No Significant difference between both sexes (P=0.343), though the frequency of females is higher (51.4%)

**Table 2: The thyroid status of patients and controls.**

	Hypothyroidism	Healthy subjects	P value
T3	0.28±0.07 (0.2-0.4)	2.26±0.27 (1.7-2.7)	0.0001*
T4	27.29±7.19 (18-48)	109.44±14.00 (86-128)	0.0001*
TSH	26.83±8.77 (15.0-48.0)	2.06±0.26 (1.5-2.5)	0.0001*

\*Significant differences between the two means using t-test for two independent means at 0.05 level of significance

**Table3: Level of T3 & T4 among patients and controls according to their gender.**

	Hypothyroidism			Healthy subjects		
	Male	Female	P value	Male	Female	P value
T3	0.30±0.07 (0.2-0.4)	0.26±0.06 (0.2-0.4)	0.049*	2.28±0.26 (1.8-2.7)	2.25±0.29 (1.7-2.6)	0.810
T4	31.88±6.48 (25-48)	22.94±4.78 (18-30)	0.0001*	111.85±12.77 (89-128)	106.83±15.34 (86-128)	0.382
TSH	29.35±7.74 (18-48)	24.44±9.23 (15-42)	0.099	2.02±0.31 (1.5-2.5)	2.09±0.20 (1.8-2.4)	0.521

\*Significant difference between the two means using t-test for two independent means at 0.05 level of significance.

**Table 4: Levels of total serum Igs, C3 & C4 complements Components among sera of the studied groups.**

	Hypothyroidism	Healthy subjects	P value
IGA	331.76±147.72 (112-628)	351.40±73.56 (190-460)	0.543
IGG	1296.43±307.47 (614-1830)	1566.16±289.65 (1130-2011)	0.001*
IGM	174.26±78.70 (36-340)	251.56±73.08 (110-340)	0.0001*
C3	162.97±44.34 (15-240)	167.88±32.57 (120-215)	0.640
C4	44.57±10.67 (25-64)	35.32±9.29 (23-55)	0.001*

\*Significant difference between the two means using t-test for two independent means at 0.05 level of significance.

**Table 5: level of some immunological parameters among the studied groups distributed according to gender.**

Concentration	Hypothyroidism			Healthy subjects		
	Male	Female	P value	Male	Female	P value
Mg/dL						
IGA	314.56±167.12 (112-628)	348.00±129.54 (115-590)	0.511	321.15±74.05 (190-420)	384.17±59.77 (280-460)	0.029*
IGG	1234.71±328.30 (614-1640)	1354.72±283.24 (795-1830)	0.254	1481.92±229.69 (1180-1820)	1657.42±328.67 (1130-2011)	0.133
IGM	154.00±85.84 (36-338)	193.39±68.22 (93-340)	0.141	248.15±56.92 (157-320)	255.25±89.94 (110-340)	0.814

C3	160.18±54.22 (15-238)	165.61±33.90 (120-240)	0.723	161.38±32.72 (125-215)	174.92±32.28 (120-210)	0.309
C4	42.05±10.74 (25-64)	46.94±10.33 (26-64)	0.178	37.15±9.52 (24-55)	33.33±9.01 (23-50)	0.314

\*Significant difference between the two means using t-test for two independent means at 0.05 level of significance.

### **Conclusion:**

This study has shown that, serum (T4) level show highly significant decrease in hypothyroid patients sera in contrast to healthy control group & that lead the (TSH) level in our patients group, so the Igs (G & M) show a significant deficiency while IgA & complement components (C3& C4 ) for our patients group have slightly significant when compare with healthy control .

### **References:**

- 1-Margare S. "Gene Engineering in Endocrinology" Humana Press Inc; 2000.
- 2-Bunevicius R, Kazanavicius G., Zalinkevicius R., & Prange A. J. "Effect of thyroxine as compared with place triiodothyronin in patient with hypothyroidism." N. Engl. J. Med. 340: 424-422, 1999.
- 3-Eastham R. D., *Biochemical values chemistry*, 7<sup>th</sup> Ed. Bristol John Wright, 1983.
- 4-Oppenheimer JH. "Thyroid hormone action at the nuclear level." Ann. Intern. Med. 102: 374, 1985.
- 5-Singh N., Jerome M., & Hershman M.D., "Hypothyroidism: Best practice of Medicine." Endocrinology and Metabolic disease, 116-183, 2002.
- 6-Alexanderl VM, & Scarpello " " J. Clin. Endocrinol. 48, 419, 2008.
- 7-Roitt I, Brostoff J., & Male D. "*Immunology*" 5<sup>th</sup> Ed. Published by Mosby, London, UK, 1998.
- 8-Riott I, Luan Roitt, & Male J. "*Immunology*" 6<sup>th</sup> Ed., Party, PP: 65-75, 2002.
- 9-Kindt T.G., & Osborne B.A. "*Immunology*" 4<sup>th</sup> Ed., W. H. Freeman Company .New York, U.S.A., 2000.
- 10-Benjamin E., Coico R., & Sunshine G. "*Immunology*" 4<sup>th</sup> Ed. Inc., USA 870-80, 2000.
- 11- Hyde R.M. "*Immunoglobulin*" 4<sup>th</sup> Ed. Published by Lippincott Williams and Wilkins. Philadelphia, 2004.
- 12-Peakman M., & Vergin D.R. "*Basic and clinical of immunology*" 1<sup>st</sup> Ed., Churchill Livingston, New York PP: 17, 1997.
- 13-Matsuhita M. *et al.*, "Complement-activating complex off Colin & Mannose binding lection-associated serine protein protease." J. Immunol. N. 164: 2281-2284, 2006.
- 14-Fischbach B. "*A Manual Labortory and Diagnostic Tests*" 7<sup>th</sup>E. Chapter 3, PP: 164-170, 2001.
- 15-Demer LM. & Sencer CA. "laboratory Medicine Practice Guidelines: Laboratory Support for the Diagnosis and Monitoring of Thyroid Disease." J. Thyroid, 13(1): 57-67, 2008.