Biochemical Study of Gonad Hormones in Sera of Iraqi Patients with Thyroid Disorder

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Abstract:

The objective of this study was to evaluate the alteration in levels of gonado trophins hormones i.e.,Leutizing (LH),Follicular(FSH) in sera of patients with thyroid disorders and molecular binding study of (LH ,FSH) with their antibodies

The study was conducted at the specialized center for endocrinology and diabetes from January / 2009 to March / 2010.Two hundreds and twenty three Iraqi subjects, 109 patients with thyroid disorders at age range between (40-50) years and 114 healthy individuals as control group were included in this study.

The majority of patients were female with hyperthyroidism and (49.54 %) were at age range between(40 - 50) years.

The levels of hormones(LH,FSH.tri iodothyronine(T3).thyroxine(T4), thyroid stimulating hormoneTSH) were measured by using Enzyme Linked Flourscent Assay(ELFA, while residual studies used Immuno Raido Metric Assay(IRMA) method only.

It was found that production of TSH was increased with about (15-20) fold in hyperthyroidism over that in control.Sixty percent of patients with hyperthyroidism were underweight BMI≤20.0 (kg/m^2) while (44.5%) of patients with hypothyroidism were overweight BMI(25.0-29.9)kg/m^2 .

The mean level of LH and FSH had increased significantly ($p<0.01$) in patients with hyperthyroidism and in females more than in males compared to control group. In contrast , for hypothyroidism the level of LH& FSH were decreased significantly ($p<0.01$)

It can be concluded that patients with hypo and hyper thyroidism would altered their serum LH&FSH levels in female more than in male due to the effects of T3 and T4 on pituitary secretions

Key words: Gonadal Hormones, LH, FSH, Thyroid Disorder.

Introduction:

Thyroid gland is the largest organ specialized for endocrine function in human body(1). It produces two hormones, L–Thyroxin (T4), Tetraio-dothyronine and (Triiodo-thyronine, T3) [1,2].Thyroid disorders can be classified to Hyperthyroidism (thyrotoxicocsis), which is an excessive secretion of thyroid hormone while Hypothyroidism (Myxedema) is a decrease in the production of thyroid hormones. There are several other types of hypothyroidism such as goiter, Hashimotos disease [3,4]. Glycoprotein hormones. including luteinizing hormone (LH) , Follicle – stimulating hormone (FSH), Thyroid – stimulating hormone (TSH) .They secreted from pituitary gland. LH and FSH both are subjected to feed back loops regulation (short feed back inhibition on the anterior loop of the pituitary)by ovarian and testes hormones testosterone & progesterone [5-8] The FSH ,LH, and TSH

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receptors are members of the super family of G- protein coupled receptors in the cell membrane .They interact with target proteins, such as adenylate cyclase c-AMP [2] .Increased levels of LH and FSH are seen in primary ovarianfailure,while the decrease in their levels are seen in secondary ovarian failure which is an indication of a pituitary or hypothalamus disorder [9]. The current study was conducted to:

1.Evaluate the levels of (LH and FSH) in sera of patients with thyroid disorder and find out whether this disease would altere or has an effect on (LH and FSH) levels then studying the correlation between the age,BMI ;sex and the disease according to the Gonadotrophins hormone levels.

2.Study the molecular binding between each 125I-anti LH or125I-anti FSH antibody with its hormones (LH or FSH) in sera of thyroid disorder females patients with in low & control hormonal levels.

Subjects & Methods

Patients and Control Study Design

The present study was conducted at the specialized center for endocrinology and diabetes with period of collection from January / 2009 to March / 2010. Patients with thyroid disorders were 109, age range (12-50)years (69females & 40 males).,while the healthy subjects were 114 (77females & 37 males)as control group, age range(13-50)years.

Materials and Methods:

1- Total serum protein was determined by using Lowry *et al*., method. [10]

2- ELFA & IRMA methods were used to estimate the hormones levels of(TSH, T3, T4,FSH, and LH) in sera of patients & control groups

3-Quantitative determination was made using ELFA (enzyme linked fluorescent assay) technique on the Vidas Instrument by using kit for LH, FSH, TSH, T3, T4 hormone. Biomerieux-(France)

4- The molecular binding of gonadotrophins (LH & FSH) with its labeled antibodies(Abs) were made and studied.

Results & Discussion

Depending on the results in Table (1) patients with thyroid disorders can be classified into two groups : group A : patients with hyperthyroidism in which their mean T3 levels were significantly higher than control group ($p<0.01$) (8.727±16.61),(1.988±0.96) nmol\ml respectively , also the mean value of T4 showed a significant increase($p <0.01$) compared to control (105.5 ± 36.75) , (87.58 ± 18.33) nmole\ml respectively, while TSH level shows a significant decrease ($p <0.01$) (0.062 ± 0.0422) compared to control group (1.8517 ± 1.0097) nmole\ml.

The results were in agreement with previous studies.They found that hypo thyroidism can be characterized by the increase in TSH production with about (15-20) fold over that in control and T4 levels were low, while elevated T3 &T4 concentrations are indicated of hyperthyroidism . It is well known that secretion of TSH is regulated by negative feed back from serum thyroid hormones concentrations [11-14].

Table (1) :Levels of TSH, T3 andT4 in sera of patients and control groups.

Group	No.	TSH Mean±Std. (μIU/ ml)	Std. Error	T3 Mean±Std. (nmol/ ml)	Std. Error	T4 Mean±Std. (nmol/ ml)	Std. Error	P. Value
Control	114	1. 8517±1. 0097	0. 094	1. 988 ± 0. 96	0. 09	87. 58±18. 33	1.71	
Hyper thyroidism	35	0. 062 ± 0. 0422	0. 007	8.727 ± 16. 61	2. 8	105. 5 ± 36.75	6. 21	P<0.01
Hypo thyroidism	74	21. 616 ± 19. 93	2. 3	1.416 ± 0.78	0. 09	58. 93 ± 29. 19	3. 39	P<0.01

The distribution of subjects according to age is illustrated in Table (2) which shows that the majority of patients (49.54 %) were at age range between (40-50) years.[15]

Table (2) Distribution of patients, controls according to age range.

Age range (Year)	Patient No.	Patient %	Control No.	Control %
10-19	10	9.18	13	11.4
20-29	11	10.09	21	18.4
30-39	34	31.19	22	19.3
40-50	54	49.54	58	50.9
Total	109	100	114	100

The effect of gender on patients of thyroid disorder is shown in Table (3). This Table reveals that most of the patients were females (57.1%) for group A hyperthyroidism and (66.2%) for group B hypothyroidism. Baskin, Freal and Surks found that hypothyroidism is more than hyperthyroidism and women show a much higher risk of hypothyroid than more with greater than 5:1 ratio and eight folds in hyperthyroidism [16-18].

According to the data found at the statically department of bio and health at the Ministry of Health in Iraq (statically guide 2009), the number of patients with hypothyroidism are more than hyperthyroidism and female patients are more than male, and in the north,and middle of Iraq more than in the south , this may be explained due to the environment or kinds of diet in Iraq [19].

Table (3) Distribution the patients according sex

Groups	Female No.	Female %	Male No.	Male %	Total No.	Total %
Group A: Hyperthyroidism	20	57.1%	15	42.9%	35	33.11
Group B: Hypothyroidism	49	66.2 %	25	33.8%	74	67.89
Total	69		40		109	100

Body mass index (BMI) is another factor that had been studied in this research. As shown in Table (4), most patients with hyperthyroidism (60%) were underweight BMI≤20.0 (kg/m^2) while (44.5%) of patients with hypothyroidism were overweight BMI 25-29.9(kg/m^2). These percentages agree with Larsen &others ; symptoms of hyperthyroidisum include weight loss while for hypothyroidism include weight gain[20 -22] .

Table (4) Distribution of patients according to body mass index (kg/m^2).

($kg\backslash m^2$)	Classes	Hyperthyroidism		Hypothyroidism	
		No.	%	No.	%
<20.0	under weight	21	60%	10	13.5 %
20→24.9	health weight	6	17.1%	3	4%
25→29.9	over weight	3	8.6%	33	44.5%
≥30.0	obesity	5	14.3%	28	38 %
Total		35	100%	74	100%

In measurement the level of LH,FSH hormones in the sera of the patients under study it cleared from Table (5), the mean level of LH &FSH had increased significantly ($p<0.01$) in patients with hyperthyroidism and in females more than males compared to control group .

In contrast , in hypothyroidism patients, levels of LH and FSH were decreased significantly ($p<0.01$) and in females more than males. The data agree with Ashok khar et al who found that T3,T4 were significantly inhibit the release of gonadotrophin in the presence of gonadotrophin releasing hormone GnRH (using rat pituitary cell calture)[23].JF Bruni , et. al studied the effect of hypo &hyper thyroidism on serum LH&FSH in both intact and castrated male & female rats; they found that hypothyroidism results in decreased release of LH and FSH in rats [24].

Table (5): LH& FSH levels according to sex of patients &control groups

Groups		No.	LH mean±Std	Std. Error	FSH mean±Std	Std. Error	P. Value
Hypo thyroidism	Female	49	2.907±3.365	0.48	5.392±8.056	1.15	P<0.01
	Male	25	0.227±1.911	0.38	2.046±2.512	0.50	
Hyper thyroidism	Female	20	8.11±9.615	2.15	18.016±29.158	6.5	P<0.01
	Male	15	15.234±16.02	4.13	33.597±28.03	8.67	
Control	Female	77	5.125±7.046	0.80	10.149±18.74	2.1	
	Male	58	0.6619±0.574	0.09	12.546±2.643	0.41	

In conclusion for the current study ,the following points can be drawn :

1- The majority of Iraqi patients with thyroid disorder were at ages (40-50) years and in hypothyroidism more than those with hyperthyroidism , and in females more than in males .

2- The levels of LH and FSH were elevated for patients with hyper thyroidism while the low LH&FSH levels were found in patients with hypothyroidisum .

3-Most of the patients in hypothyroidism were with over weight BMI 25- 29.9 Kg\m^2, while patients in hyperthyroidism most of them was considered to be under weight BMI<20.*0*

From all above, we can say that Iraqi females with hypothyroidisum would decrease releasing LH &FSH. In other word they will be infertility in the future .

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دراسة كيمياحياتية لهرمونات المناسل فى امصال المرضى العراقيين بخلل الدرقية

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الخلاصة:

تهدف الدراسة الحالية الى تقييم التغيرات فى مستويات هرمونات المناسل المغديةللدرقية(اللوتوزينى وهرمون الجريب)فى امصال المرضى بخلل الدرقية ودراسة الارتباط الجزيئى مابين( ) ومضاداتها .

الجزء العملى:اجريت الدراسة فى المركز التخصصى للغددلصم والسكرى بجمع مئتان وثلاثة وعشرين عينة من امصال العراقيين ابتداءا كانون الثانى/2009 الى ادار/2010. شملت العينات 109 لمرضى بخلل الدرقية بمدى العمر ما بين (40-50)سنة و114 لاشخاص اصحاء كمجموعة سيطرة بنفس المدى من العمر . اغلب المرضى كانوا نساءمصابات بارتفاع الدرقية وان (49.54%)منهن كانوا بمدى من العمر مابين (40-50) سنة.

تم قياس مستويات هرمونات الثايروكسين (T4) وثايرونين ثلاثى اليود(T3) والمحفز للدرقية(TSH) و(LH,FSH) باستخدام تقنية الفحص التفلورى للانزيم المرتبط(ELFA) واستخدم تتقنبة الفحص الراديوى المناعى المترى لبقية الدراسات(IRMA)

النتائج: اظهرت نتائج الدراسة ارتفاع انتاج TSHبمقدار20-30 مرة عند المصابين بارتفاع الدرقية اكثر من الاصحاء.ان 60%من المرضى بارتفاع الدرقية لديهم انخفاض فى الوزن ($BMI\leq 20.0$ (kg/m^2) بينما(44.5%) من المرضى بانخفض الدرقية كانواعندهم زيادة فى الوزن . kg/m^2(25.0-29.9)BMI.

كانت معدل مستوى ال LH and FSH ارتفاع ملحوظ $p>0.05$ عند مرضى ارتفاع الدرقية و للاناث اكثر من الذكورمقارنة بالاصحاء.في حين مرضى انخفاض الدرقية كانت مستويات ال FSH and خفضة بصورة ملحوظة($p<0.01$).

الاستنتاج:يمكن القول ان مرضى ارتفاع وانخفاض الدرقية سبعانون من تغير فى هرمونات المناسل LH&FSH لاسيما النساء اكثر من الرجال بسبب تاثيرات هرمونات الدرقية T3وT4 على افرازات الغدة النخامية.