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Evaluation the Levels of Thyroid Hormones among Iraqi Pregnant Women

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Abstract

The present study was carried out to evaluate the levels of thyroid hormones among pregnant Iraqi women according to the age.. The study group comprised of (140)of full term pregnant women scheduled follows up the alterations of thyroid hormones, the control group included (50)of healthy women volunteers. Serum concentrations levels of T3, T4 and (TSH) were estimated using (ELFA) technique. In the study groups, blood samples were obtained from various ages pregnant women . Range age of the study groups was (20-40) years. In the control group: serum T3 andT4 levels were decreased slightly with increasing age respectively, while TSH levels were increased slightly with increasing age without significant difference P>0.05 and the values were within the normal range. In the hyperthyroidism which included (45) patients women , there were continuously higher in concentration levels of T3, and T4 than that in the control group, but TSH concentration decreased with highly a significant difference P<0.01.While, in hypothyroidism which included (45) patient women ,the concentrations of T3 and T4 were lower than that in the control group, but TSH increased with a highly significant difference P<0.05.

***Keywords**: Thyroid Hormones; Pregnant Women**;** Enzyme Linked Fluorescent Assay; IRAQ.*

Introduction

Female reproduction system is negatively manipulated by both hyper and hypothyroidism , also female infertility is adversely affected thyrotoxicosis. The thyroid gland makes two thyroid hormones thyroxine (T4) and triiodothyronine (T3)which is the active hormone and is made from T4, [(1)]. Thyroid hormones production is regulated by thyroid stimulating hormone (TSH) which is made by pituitary gland in the brain, [(1,2)].When the thyroid hormones concentrations levels are low in the blood the pituitary releases more TSH and when the levels in the blood are high the pituitary respond by decreases TSH production. The thyroid functions normally, if (TSH) (T3) (T4) areall normal through pregnancy [(1,3)]. The most common causes of maternal hyperthyroidism during pregnancy (80-85 %) is graves' disease [(4)].The diagnosis of hyperthyroidism is based on history , physical exam and laboratory testing .

The most common cause of hypothyroidism during pregnancy is the autoimmune disorder known as Hashimato's thyroiditis. Untreated or in adequately treated hypothyroidism has been associated with maternal anemia (low red blood cell, count) myopathy (muscle pain , weakness), placental abnormalities , low birth weight infants and bleeding. Because of the important effects of thyroid hormones on the pregnant women and her baby, this project was done,[(3,5)].

This study aimed to determine serum concentrations of thyroxine (T4), triiodo thyronine (T3)and thyroid stimulating hormone (TSH) , because of their critical role during pregnancyfor the health of mother and baby (hypo or hyperthyroidism), so the condition can be recognized and treated immediately before or after birth .

Materials and Method

This study was carried out during the period from June 2013 to October_2013 . A group of(ninety) pregnant women with disturbances of thyroid gland hormones (forty five) for each of hypo and hyperthyroidism . (Fifty)pregnant women as a healthy control were included in this study , with age range 20-40 years . They were attending the Specialized center for Endocrinology Hospital women and children in the province of Muthana. The patients and control were grouped depending on their age to four groups (20-24)

(25-29)(30-34)(35-40).

Venous blood samples (5 ml) were collected from patients and centrifuged after clotting at 3000 rpm for 10 min for hormone determination . patients sera were taken by micropipettes and stored at 2-8℃ in disposable tubes for up to 48 hours until assay to obtain more accurate results .

Quantitative Determination of T3 (VIDAS) Test:

The assay principle combines an enzyme immunoassay competition method with a final fluorescent detection (ELFA) was used to determine total triiodothyronine(T3) in human plasma (lithiumheparin). The Solid Phase Receptacle (SPR) serves as the solid phase as well as the pipe ting device for the assay .Reagents for the assay are ready –to-use and predisposed in the sealed reagent strips .All of the assay steps are performed automatically by the instrument.The reaction medium is cycled in and out of the SPR several times.The sample is taken and transferred into the well containing the T3 antigen labeled with alkaline phosphate (conjugate) Competition occurs between the antigen present in the sample and the labeled antigen for the specific anti-T3 antibodies (sheep) coated on the interior of the SPR. Unbound components are eliminated during washing steps. During the final detection steps, the substrate (4-Methyl-umbelliferyl phosphate) is cycled in and out of the SPR. The conjugate enzyme catalyzes the hydrolysis of this substrate into a fluorescent product (4-Methyl-umbelliferone) the fluorescence of which is measured at 450 nm. The intensity of the fluorescence is inversely proportional to the concentration of antigen present in the sample. At the end of the assay ,results are automatically calculated.

Results are calculated automatically by the instrument in relation to the calibration curve stored in memory (4-parameter logistic model) and are expressed in nmol/l. Samples with a concentration greater than 9 nmol/l, may be diluted by 1/2 in C1 control or normal serum .The result will be calculated taking into account the dilution factor and the concentration of C1 or normal serum used . The results of a VIDAS T3 assay must be interpreted as part of a complete clinical profile and association with thyroid function tests,including at least a TSH assay.

Quantitative Determination of T4 (VIDAS) Test:

The assay principle combines an enzyme immunoassay competition method with a final fluorescent detection (ELFA)was used to determine total thyroxine (T4) in human plasma (lithium heparin). The Solid Phase Receptacle (SPR) serves as the solid phase as well as the pipetting device for the assay .Reagents for the assay are ready –to-use and predisposed in the sealed reagent strips.all of the assay steps are performed automatically by the instrument.The reaction medium is cycled in and out of the SPR several times.The sample is taken and transferred into the well containing the T4 antigen labeled with alkaline phosphate (conjugate). Competition occurs between the antigen present in the sample and the labeled antigen for the specific anti-T4 antibodies (sheep) coated on the interior of the SPR.

Unbound components are eliminated during washing steps.During the final detection steps, the substrate (4-Methyl-umbelliferyl phosphate) is cycled in and out of the SPR. The conjugate enzyme catalyzes the hydrolysis of this substrate into a fluorescent product (4-Methyl-umbelliferone) the fluorescence of which is measured at 450 nm. The intensity of the fluorescence is inversely proportional to the concentration of antigen present in the sample .At the end of the assay ,results are automatically calculated .

Results are calculated automatically by the instrument in relation to the calibration curve stored in memory (4-parameter logistic model) and are expressed in nmol/l. Samples with a concentration greater than 320 nmol/l, retested after diluted by 1/2 in T4 free human serum(1volume of sample and 1 volume of T4 free human serum)and retested in the VIDAS T4 assay .if the dilution factor has not been entered when the work list was created, multiply the result by the dilution factor to obtain the sample concentration . interpretation of test result should be made taking into consideration the patient's history , and in association with thyroid function assessment ,including at least a TSH assay.

Quantitative Determination of TSH (VIDAS) Test:

The assay principle combines an enzyme immunoassay competition method with a final fluorescent detection (ELFA)was used to determine total thyroid-stimulating hormone (TSH) in human plasma (lithium heparin).The Solid Phase Receptacle (SPR) serves as the solid phase as well as the pipetting device for the assay .Reagents for the assay are ready –to-use and predisposed in the sealed reagent strips. all of the assay steps are performed automatically by

the instrument. The reaction medium is cycled in and out of the SPR several times. The sample is taken and transferred into the well containing the AntiTSH antibody labeled with alkaline phosphate (conjugate). The sample/conjugate mixture is cycled in and out of the SPR . the antigen binds to antibodies coated on the SPR and to the conjugate forming a "sandwich" .Unbound components are eliminated during washing steps. During the final detection steps, the substrate (4-Methyl-umbelliferyl phosphate) is cycled in and out of the SPR. The conjugate enzyme catalyzes the hydrolysis of this substrate into a fluorescent product (4-Methyl-umbelliferone) the fluorescence of which is measured at 450 nm. The intensity of the fluorescence is inversely proportional to the concentration of antigen present in the sample. At the end of the assay ,results are automatically .

The TSH Results are calculated automatically by the instrument Using calibration curve which are stored by the instrument (4-parameter logistic model),the concentrations are expressed in μLu/ml(2nd IRP 80/558). Samples with TSH a concentration greater than 60μLu/ml, must be realized after dilution in TSH diluted (R1) .if the dilution factor has not been entered when the work list was created, multiply the result by the dilution factor to obtain the sample concentration . interpretation of test result should be made taking into consideration the patient's history ,and the result of any other tests performed.

Statistical analysis: Data were summarized, analysed and presented using two software programs; these were the statistical package of social sciences (SPSS version 23) and Microsoft Office Excel 2010. The level of significance was considered significant at $P< 0.05$ and highly significant at $P< 0.01$.

Results and Discussion

Table (1) Shows that the values of T3,T4 decreased slightly with age and TSH decreased slightly with age without significant difference P>0.05 and the values were within the normal range .The above results agreed with the observation of other studies [6,7]. A healthy pregnant woman can adopt herself with this scenario and thyroid in pregnancy produce an extra amount of thyroid hormoneson condition of a healthy thyroid gland in combination of enough iodine an essential element in the thyroid hormone structure[8,9].

Table (1) Distribution of healthy females(as a control group)according to the age and its relation with T3,T4 and TSH:

Age group years		No.	T3 level(nmol/l)	T4 level(nmol/l)	TSH level(μIU/ml)
(20-24)	Mean	14	2.1871	89.9553	3.4724
	Std. Deviation		±.08432	±5.67140	±.53197
(25-29)	Mean	13	1.8542	77.5892	2.4117
	Std. Deviation		±.06815	±2.90794	±.24653
(30-34)	Mean	12	1.5592	69.2883	1.5675
	Std. Deviation		±.11493	±2.23568	±.20627
(35-40)	Mean	11	1.2356	63.1444	.9689
	Std. Deviation		±.14063	±1.02542	±.20925
Total	Mean	50	1.7852	77.2014	2.3100
	Std. Deviation		±.36709	±11.03601	±1.02926

* Normal value:T3=0,4-9nmol/l

T4=6-320nmol/l

TSH=0,3-5 μIU/ml

In addition, the pregnancy is a physiological period which can be associated with various thyroid malfunctions . The serum concentration of TSH,T3,T4 are the least thyroid parameter which should be evaluated during pregnancy to have a clear picture of a healthy fetus and maternal life . The normal range for thyroid hormone during pregnancy are altered and when thyroid hormone are assessed those specific values should be taken into consideration. Pregnancy itself might have an adverse effect on thyroid function ,leaving the pregnant woman with subclinical ,overt hypo and hyperthyroidism .It seems that autoimmunity to the thyroid during pregnancy is the major cause for hypothyroidism in particular[10,11].

Table (2) shows the values of T3,T4 increased with age and TSH decreased with age without significant difference P>0.05 between the first and second group, while there was significant difference P<0.05 between the first and second group with the third group and highly significant difference P<0.01 between the first and second group and the fourth group and significant difference P<0.05 between the third and the fourth group . The protein responsible for the transportation of female sex hormones ,defined as Sex Hormone Binding Globulin (SHBG). The protein responsible for the transportation for female sex hormones ,defined as and also the serum estrogen level concentration are elevated during hyperthyroidism .Therefore , correlation between SHBG and female sex hormones during periodical cycles and pregnancy should be taken into close consideration . The correlation between SHBG and female sex hormones is a matter under scrutiny[12,13].

Table (2) Distribution of patients with Hyperthyroidism according to the age range and its relation with T3,T4 and TSH:

Age group years		No.	T3 level(nmol/l)	T4 level(nmol/l)	TSH level(μIU/ml)
(20_24)	Mean	13	6.8550	268.7967	.2533
	Std. Deviation		±.56013	±26.93433	±.00816
(25-29)	Mean	12	6.1317	187.9117	.2183
	Std. Deviation		±.07111	±8.66305	±.01169
(30_34)	Mean	11	4.9471	165.0443	.1657
	Std. Deviation		±.56988	±6.84556	±.01697
(35_40)	Mean	9	3.2863	132.3079	.1089
	Std. Deviation		±.45297	±7.11519	±.01883
Total	Mean	45	4.6582	168.1049	.1604
	Std. Deviation		±1.41758	±46.02076	±.05514

Tables (1) and (2) Showed that there was a highly significant difference P<0.01 between the values of T3 , T4 and TSH in patients compared with the control group . The above results agreed with the observation of other studies, ([14,15]). The most common cause (80%-85%) of maternal hyperthyroidism during pregnancy is Grave's disease and occurs in one of 1500 pregnant . in addition to other usual causes of hyperthyroidism ,very high levels of HCG , seen in severe forms of morning sickness my cause transient hyperthyroidism .[16, 17]. Many changes occur in thyroid function during the transition phase from the non-pregnant to the pregnant state , changes which stabilize by the end of second trimester or the onset of the third trimester . There is biochemical evidence of functional stimulation of the thyroid, such as in serum thyroglobulin levels, preferential T3 secretion increased T3/T4 ratio and slight increases in basal TSH at delivery[18,19].

Table (3) Showed that the values of T3,T4 decreased with age and TSH decreased with age. There was a highly significant difference P< 0.01 between the

first group and other groups and significant difference P< 0.05 between the second and third group with highly significant difference P< 0.01 between the second and fourth group, while there was a significant difference between the third and fourth group P<0.05.

Table (3) Distribution of patients with Hypothyroidism according to the age range and its relation with T3,T4 and TSH:

Age group years		No.	T3 level(nmol/l)	T4 level(nmol/l)	TSH level(мIU/ml)
(20_24)	Mean	13	.9150	51.6200	58.7650
	Std. Deviation		±.02121	±.38184	±.33234
(25_29)	Mean	12	.6950	43.3550	52.1550
	Std. Deviation		±.04359	±4.13330	±3.04706
(30_34)	Mean	11	.4925	31.6150	46.1175
	Std. Deviation		±.09032	±3.65275	±3.35450
(35-40)	Mean	9	.3320	19.4700	37.3500
	Std. Deviation		±.03347	±5.50463	±3.15824
Total	Mean	45	.5493	33.3647	46.4913
	Std. Deviation		±.21322	±12.69400	±8.23578

Table (1) ,(3) Showed there was a highly significant difference P< 0.01 between the values of T3 , T4 and TSH in patients compared with the control . The above results agreed with the observation ofother studies, [20-22] . The most common cause of hypothyroidism is the autoimmune disorder known as hashimoto's thyroiditis. Hypothyroidism can occur during pregnancy due to the initial presentation of hashimoto's thyroiditis , in adequate treatment of a woman already known to have hypothyroidism a variety of causes , or over –treatment of a hyperthyroid woman with antithyroid medications . Approximately , 2.5% of women will have a slightly elevated TSH of greater than 6 and 0.4% will have a TSH greater than 10 during pregnancy ,[23-25] .The incidence of hypothyroidism as normal cause among female is indirectly correlated with age and the prevalence of hypothyroidism in elderly female is about ten times higher compared to younger age in their twenties,[26,27].

Ethical Clearance: The Research Ethical Committee at scientific research by ethical approval of both environmental and health and higher education and scientific research ministries in Iraq

Conflict of Interest: The authors declare that they have no conflict of interest.

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