Original Article

Evaluation Serum levels of Leptin,CRP and Lipid profile in Hypothyroid Women in Kirkuk city/Iraq

Nursan A.B. Hassan[1], Sahlah Kh. Abbas[2]
[1]M.s.c student College of Science, university of Kirkuk
[2]Profesor of immunology, College of Science, university of Kirkuk
Email: Nuresmer93@gmail.com
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Abstract

Leptin is a hormone primarily produced by the adipose tissue in proportion to the size of fat stores with a primary function in the control of lipid reserves,this study aimed to evaluate the influence of hypothyroidisim on serum levels of Leptin,CRP and lipid profile,blood sample was collected from 75 women age ranged between (15-49) years 65 of the them had hypothyroidisim while 10 of the samples were healthy control, The results showed no significant diffirence in serum Leptin (p =0.1),while there was significant high concentration of serum leptin in obeses hypothyroid women in compared to non obeses hypothyroid women Serum Cholesterol ,Triglyceride , VLDL in addition to serum LDL were significantly higher in patient compared to control group,the Serum CRP levels were significantly Higher in hypothyroid patient compared to the control, circulating thyroid hormones do not appear to play a significant effect on Leptin Levels in patients with hypothyroidisim While it Causes Dyslipidemia,with a significant increase in the serum levels of CRP as an inflamantory marker linked between hypothyroidism and risk factors of cardiovascular events.

Keywords: Hypothyroidisim, Leptin, CRP.

INTRODUCTION

The thyroid gland is a vital butterfly shaped endocrine gland its one of the largest of the endocrine glands, located immediately below the larynx on each side of and anterior to the trachea, normally weighing15 to 20 grams in adults. The thyroid secretes two major metabolic hormones, thyroxine and triiodothyronine commonly called T4 and T3, respectively. Both of these hormones profoundly increase the metabolic rate of the body[1,2]

Hypothyroidism is a common endocrine disorder with reduced production of thyroid hormones. It is a common disease with different frequency in different countries. It is characterized biochemically by a reduction in serum T3 and T4 levels that result in an increase in serum thyroid stimulating hormone (TSH) concentration[3,4]Women are affected more than men[5]

Leptin is a 167-amino acid protein hormone encoded by the OB gene and secreted by adipocytes in response to an increase in fat mass,its seems to be a key molecule in the feedback loop that regulates energy balance ,leptin has a dual action in decreases the appetite and icreases energy consumption causing more fat to be burned [6]Its participates with thyroid hormones in thermogensis process[7]

Leptin is considered to play a role in maintenance of energy balance and body weight by neuroendocrine mechanisim,the serum leptin levels were correlated with Body mass index (BMI) and Thyrotropin (TSH) hormone in hypothyroid women,the receptor of this hormone is located in different parts of the body , its not only regulates lipid and energy homeostaisis but is also affects neuroendocrine and immune function[8,9]

The hormone is regulated by several mediates including Insulin,Glococorticoids and thyroid hormones ,Leptin is mainly produced in hypothalamus and probably affects the thyroid axis in hypothalamus and achievates Jak state,and its also impact on the para-ventricular cores which is effective for Thyrotropin releasing hormonr (TRH) gene regulation[10,11]

Adipokines serve as a protective factors in the development of disorders in the state of thyroid dysfunction ,abnormal levels of leptin in hypothyroidisim have been reported a controversial results [12] In hypothyroidism, increased thyroid stimulating hormone (TSH) and decrease in T3 and T4, results in increased of body weight and alteration of lipid profile. These changes are associated with glucose and insulin metabolism along with adipose tissue metabolism [13,14]. Alteration of thyroid profile may affect leptin and adiponectin secretions and can lead to further complications.

Lipids are biological compounds that are usually hydrophobic in nature and soluble in organic solvents in many situations. They are essential parts for the cell membrane structure and has vital role in signaling between cells and body metabolism [15] Lipids are expressed by phospholipids, cholesterol, triglycerides (TGs), fatty acids, sterols, and others. They are indissoluble in plasma, so they carried via lipoproteins, which vary in sizes, structures and densities [16] T3 plays an important role in lipid metabolism by regulating the genes that responsible of lipid biosynthesis and lipid hydrolysis[17] Satyajit and Arindam shows a that there is a strong relationship between hypothyroidisim and Dyslipidemia [18]

C-reactive protein is a homopentameric acute-phase inflammatory protein, named native CRP (nCRP), is characterized by a dislike arranging of five conforming non-covalently bound [19] CRP is produced firstly in the liver hepatocytes, but also by smooth muscle cells, macrophages, lymphocytes, endothelial cells, and adipocytes [20] The acute phase response develops in a wide range of chronic and acute inflammatory conditions such as fungal ,viral and bacterial infections, rheumatism and autoimmune disorders. These conditions lead to the release of interleukin-6 and other cytokines , which in turn stimulate the synthesis of CRP and fibrinogen in the liver [21,22]Ahmad and his assistant showed that abnormal thyroid hormones levels impacts the CRP levels[23]

MATERIALS AND METHODS:

The present study was conducted on 75 women age ranged between (15-49) years 65 of them were had hypothyroidisim and they were under hormonal treatment while 10 as control group,the samples were collected from private laboratories in Kirkuk city in the period between September 2021 until February 2022.

The Patients were diagnosed by senior physician through the symptoms and according to the T3 and T4 and TSH values in the serum

The blood was drown and the serum was separated and stored in the Refrigerator at 8-2 C° until completing the collection of the samples .

We used a full auto analyzer called Beakman coulter access 2 to determine the hormones this device works on the principle of Immunefluorescence assay system to evaluate the levels of T3,T4 ,TSH and uses ELISA SunLong Biotech kit to determine the serum leptin ,and for the lipid profile and CRP we used a full auto devise called Erba XL-180 that work on the principle of Turbidimetric immunoassay.

Statical Analysis

Data were analyzed using spp statistics 21.0(Chicago,Inc.,USA).The results are givin as mean ± standard deviation ,T test was used to compare two group between cases and controls.The Pearson correlation coefficient was used to calculate among the study parameters.A p value less than 0.05 was considered significant.

RESULT AND DISCUSSION:

The results showed no significant difference in age ($p \leq 0.15$) while recorded a significant increase in BMI ($P<0.001$) between hypothyroid patient and control group as shown in Table 1

Table 1: Characteristics of the study including (Age,BMI) in hypothyroid patient and control group.

Characteristics	Control	Hypothyroid	P value
	Mean ± SD		
Age(Years)	**28.9** ± 1.01	**31.9** ± 1.09	0.15
BMI(kg/m^2)	**22.0** ± 0.21	**27.0** ± 0.64	<0.001

The result of BMI agreed with [24] and [25] also [26] showed that there is a positive relationship between TSH levels and both body weight and BMI while they have a negative relationship with T3 and T4.

The thyroid hormones are responsible of the basal metabolic rate (BMR) in hypothyroid status the decrease in the T3 and T4 concentration lead to a lack in the rate of the metabolism and that's why hypothyroidisim causes obesity[27]

Our Findings Showed a significant difference (decrease) in serum T3 levels (P≤ 0.011) and T4 levels (P≤0.001) and a significant increase in TSH levels (P<0.001) in hypothyroid patients compared to the control group as shown in Table 2

Table 2: Serum Levels of T3,T4,TSH in Hypothyroid patient in comparison to Controls

Prameters	Control	Hypothyroid	P-Value
	Mean ± SD		
TSH(nmol/L)	1.82±0.09	17.11±2.07	<0.001
T4(nmol/L)	118.61±2.33	91.00±3.43	0.001
T3(nmol/L)	1.67±0.02	1.45±0.03	0.011

These results agreed with other results [28] and [29] and also with [24], Chin and his assistants estimated that the raising of TSH levels in hypothyroid patients would be a compensative response to counteract the decrease levels of THs trying of hypothalamus to acquire into a homeostasis [30].

The Anterior pituitary gland produces TSH after it is induced by TRH from the hypothalamus. This production depends on Thyroid hormone levels in circulation. Because of the inverse correlation between TSH and THs levels or the negative regulatory relationship between Thyroid Hormones and the pituitary gland, this hormone is considered a sensitive indicator for Thyroid function in clinical diagnosis because it influence by small alteration in T4 concentration. [31]

The result recorded a significant increase in serum cholesterol (P≤ 0.001) level and serum triglycerides(P≤ 0.001) and LDL value (P≤ 0.033) and VLDL (P≤ 0.001) hypothyroid patients compared to control group as shown in Table 3

Table 3: Serum Levels of lipid profile in Hypothyroid patient in comparison to Controls

Parameter	Control	Hypothyroid	P-value
	Mean ± SD		
Cholesterol(mg/dl)	149.85±17.4	180.93±36.39	0.001
Triglycerides(mg/dl)	97.71±22.88	186.79±99.26	0.001
HDL(mg/dl)	50.57±7.74	46.65±9.0	0.24
LDL(mg/dl)	77.28±14	93.04±33.0	0.033
VLDL(mg/dl)	20.0±5.4	37.48±20.25	0.001

These results agreed with previous studies[32] and [29] and also with [33].Hypothyroidism is a common cause of hyperlipidemia in humans and animals,it have an impact on every major metabolic signaling including lipid metabolism. These hormones effect on the composition, metabolism and disintegration of lipid but, the disintegration is affected more than composition. Through a variety of mechanisms, Thyroid hormone regulates the synthesis of cholesterol in the liver which is consider the main organ for cholesterol production, Thyroid dysfunction may result in Dyslipidemia (lipid abnormalities) which is correlated with endothelium disorders, hypertension, and cardiovascular disease. Hyperlipidemia, reduces cholesterol removal, lacks antioxidant system and impacts on thyroid hormones regulation of antioxidant enzymes.. In hypothyroidism patients the greatest chronic lipid abnormality is hypercholesterolemia[14,34].

Triglycerides are raised because of an increased esterification of fatty acids at hepatic level. Also, low levels of THs reduce activity of lipoprotein lipase (LPL), the enzyme important for removal of TG, therefore result in rise levels of TG in serum [35].

THs control the LPL, which is responsible for removing TG present in VLDL-c and chylomicrons molecules. It activates the breakdown of TG into non-esterified fatty acid and transports it to the Adipose Tissu and storage as TG after re-esterification[36]

Our findings showed no significant differences in the serum leptin level in the hypothyroid patients compared to control group as shown in Table 4

Table 4: Serum Levels of Leptin in Hypothyroid patient in comparison to Controls

Parameter	Control	Hypothyroid	P-value
	Mean ± SD		
Leptin(pg/ml)	959±37	1108.86±245.42	0.46

Yaturu et al indicate that serum leptin levels did not differ with change in the status[37].also [38] and [39] have not found any significant change in leptin levels.

While there was a slight increase in leptin concentrations in hypothyroid patients when compared to controls. Variations in plasma TSH contributes to the regulation of leptin pulses by regulating its mRNA expression [38,40] along with stimulating adipocytes directly to secrete leptin in peripheral tissue [39].

One of the explanations for the association between leptin and TSH is the hypothesis that TSH stimulates the release of leptin by adipocytes and then leptin stimulates the release of TSH to compensate for the increase in the fat mass[41,42]

Our findings showed a significant increase in serum level of C-reactive protein in hypothyroid patient compared to the control group as shown in the Table 5

Table 5: Serum level of CRP in hypothyroid patient in comparison to Controls

Parameter	Control	Hypothyroid	P-value
	Mean ± SD		
CRP(mg/l)	1.0 ± 0	1.9 ±0.29	0.003

These results agreed with previous studies [32] and [43],the cause of CRP levels increase in hypothyroid is due to decrease in serum levels of CRP clearance in hypothyroidism [44].

The results showed a significant increase in the BMI ($P<0.01$) in obeses hypothyroid patients compared to non obeses hypothyroid patients that's means there is a positive correlation between the obesity and BMI also serum levels of leptin showed a significant increase ($P\leq0.03$) in obese hypothyroid compared to no obeses which shows a positive correlation between obesity and serum leptin levels as shown in Table 6.

Table 6: Correlation of the parameters with obeses and non obeses hypothyroid patients

Parameters	)18(Obeses n=	Non obeses n=(47)	P-value
	Mean ± SD		
BMI	32.85±0.35	24.56±0.38	<0.01
T3	1.48±0.03	1.43±0.03	0.75
T4	86.71±2.60	92.62±3.74	0.37
TSH	13.99±2.09	22.42±5.05	0.34
Leptin	1183±24	1051±35	0.03
Cholesterol	189.58±5.00	177.97±4.29	0.34
Triglyceride	173.52±7.76	191.80±13.62	0.29
HDL	45.82±1.07	46.93±1.15	0.66
LDL	96.82±4.05	91.82±4.14	0.55
VLDL	35.76±1.64	38.13±2.77	0.46
CRP	2.68±0.45	1.54±0.17	0.29

These results agreed with [26] who showed that obeses subjects had significantly higher leptin levels ,when the fat cells increase, leptin levels increase proportionally [45,46], the increased expression of the ob gene in the adipocytes of obese people suggests that this is due to increased synthesis of leptin[47,48].

Our findings showed a significant negative correlation between the leptin levels and T3 while recorded a non significant negative correlation with T4 hormone ,but there was a positive non significant correlation between Leptin and TSH,a strong Positive correlation was seen between Leptin and Triglyceride and VLDL,whereas there was a positive non significant correlation between leptin and Cholesterol ,We recorded a strong negative correlation between Leptin and HDL,a non significant negative correlation was seen between leptin and LDL,non significant positive correlation was recorded between Leptin and CRP as shown in Table 7

The results showed non significant negative correlation between Triglyceride and T3 and T4 hormones While it showed a strong positive correlation with TSH hormone ,Triglyceride correlated positively significant with Cholesterol levels ,also its recorded a strong negative significant correlation with HDL and a strong positive significant correlation with VLDL,While there was a negative non significant correlation with LDL,Triglyceride correlated negatively non significant with CRP as shown in Table 7.

The cholesterol recorded a negative non significant correlation with T3 and T4 hormones while it does correlated strongly positive significant with TSH hormone,there was a positive significant correlation between cholesterol and Triglyceride ,VLDL ,the results showed a strong negative correlation between cholesterol and HDL While there was strong positive correlation between cholesterol and LDL,cholesterol correlated negatively non significant with CRP as shown in Table 7.

HDL levels recorded a positive non significant correlation with T3 and T4 hormones while its correlated negatively non significat with TSH hormone,there was a strong significant correlation between HDL and (Cholesterol ,Triglyceride,VLDL and Leptin) ,HDL recoded a significant negative correlation with LDL,while its correlated positively non significant with CRP as shown in Table 7.

The present study recorded a non significant positive correlation between LDL and (TSH,T4) hormones while recorded a negative non significant correlation between LDL and (T3,Triglyceride,VLDL,CRP,Leptin) ,LDL correlated strongly positive significant with cholesterol while it does correlated negatively significant with HDL as shown in Table 7.

Our finding showed a negative non significant correlation between VLDL and (T3,T4,LDL,CRP), while recoded a strongly negative correlation with HDL,the results showed a strong positive correlation between VDLD and (TSH,Triglyceride,Leptin) also it showed a positive significant correlation with cholesterol levels as shown in Table 7.

T3 hormone correlated strongly positive significant with T4 hormone while it correlated strongly negative significant with TSH hormone,the study recorded a positive non significant correlation between T3 and CRP,whereas T4 hormone correlated strongly positive significant with T3 hormone while its correlated negatively non significant with TSH and CRP,TSH showed a negative strong significant correlation with T3 hormone while it does correlated negatively non significantwithT4andCRP .

CRP correlated negatively non significant with (T4,TSH,Triglyceride, cholesterol,LDL,VLDL) While its showed a non

Table 7: Correlations between the study parameters

		T3	T4	TSH	T.G	CHO	HDL	LDL	VLDL	CRP	LIPTIN
T3	Pearson Correlation		.535**	-.343**	-.206-	-.178-	.174	-.030-	-.237-	.053	-.249-*
	Sig. (2-tailed)		.000	.006	.103	.159	.170	.811	.059	.679	.047
	N		64	64	64	64	64	64	64	64	64
T4	Pearson Correlation	.535**		-.085-	-.048-	-.175-	.179	.021	-.087-	-.009-	-.240-
	Sig. (2-tailed)	.000		.505	.706	.167	.156	.870	.496	.942	.056
	N	64		64	64	64	64	64	64	64	64
TSH	Pearson Correlation	-.343**	-.085-		.528**	.423**	-.220-	.164	.545**	-.075-	.170
	Sig. (2-tailed)	.006	.505		.000	.000	.080	.195	.000	.553	.179
	N	64	64		64	64	64	64	64	64	64
T.G	Pearson Correlation	-.206-	-.048-	.528**		.261*	-.666-**	-.044-	.990**	-.171-	.420**
	Sig. (2-tailed)	.103	.706	.000		.037	.000	.727	.000	.176	.001
	N	64	64	64		64	64	64	64	64	64
CHO	Pearson Correlation	-.178-	-.175-	.423**	.261*		-.337-**	.738**	.304*	-.139-	.128
	Sig. (2-tailed)	.159	.167	.000	.037		.007	.000	.015	.273	.312
	N	64	64	64	64		64	64	64	64	64
HDL	Pearson Correlation	.174	.179	-.220-	-.666-**	-.337-**		-.290-*	-.640-**	.076	-.393-**
	Sig. (2-tailed)	.170	.156	.080	.000	.007		.020	.000	.550	.001
	N	64	64	64	64	64		64	64	64	64
LDL	Pearson Correlation	-.030-	.021	.164	-.044-	.738**	-.290-*		-.057-	-.042-	-.039-
	Sig. (2-tailed)	.811	.870	.195	.727	.000	.020		.657	.743	.761
	N	64	64	64	64	64	64		64	64	64
VLDL	Pearson Correlation	-.237-	-.087-	.545**	.990**	.304*	-.640-**	-.057-		-.165-	.419**
	Sig. (2-tailed)	.059	.496	.000	.000	.015	.000	.657		.194	.001
	N	64	64	64	64	64	64	64		64	64
CRP	Pearson Correlation	.053	-.009-	-.075-	-.171-	-.139-	.076	-.042-	-.165-		.142
	Sig. (2-tailed)	.679	.942	.553	.176	.273	.550	.743	.194		.262
	N	64	64	64	64	64	64	64	64		64
LIPTIN	Pearson Correlation	-.249-*	-.240-	.170	.420**	.128	-.393-**	-.039-	.419**	.142	
	Sig. (2-tailed)	.047	.056	.179	.001	.312	.001	.761	.001	.262	
	N	64	64	64	64	64	64	64	64	64	

** Correlation is significant at the 0.01 level (2-tailed).//// * Correlation is significant at the 0.05 level (2-tailed)

significant positive correlation with (T3,HDL,Leptin) as shown in Table 7

Conclusions

Serum TSH was significant higher while serum levels of T3 and T4 was significantly lower in hypothyroid patients . circulation thyroid hormones do not appear to play any significant effect on leptin level in hypothyroid womens compared to control group ,While its shows a significant effect(Increase) on serum Cholesterol and Triglyceride and VLDL levels in hypothyroid women compared to control group,CRP showed a significant increase in hypothyroid women compared to control group,Leptin levels correlated positively significant with BMI in obeses hypothyroid compared to non obeses

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