

Association of Serum Ferritin and Lipid Profile in Patients with Thyroid Disorder

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Abstract:

Background: Thyroid hormones are important modulator of intermediary metabolism. They affect synthesis, mobilization and degradation of lipids, although degradation is influenced more than synthesis. Serum ferritin levels also have been reported to be altered in patients with thyroid disease.

Objective: The present study aim to explore the association of lipid profile with serum ferritin in patients with thyroid disorder.

Patients and Methods: In this study One hundred forty subjects were selected from outpatient department of the National Diabetes center/ AL-Mustansiriyah University. Serum Ferritin, free triiodothyronin, free tetraiodothyronin, thyroid stimulating hormone and lipid profile were measured.

Results: Non-significant differences of serum cholesterol, triglyceride, High density lipoprotein, Low density lipoprotein and very Low density lipoprotein level in hypothyroid, hyperthyroid and euthyroid groups were observed. The serum ferritin levels indicate significant increase in hypothyroidism in comparison to their levels in both other groups (hyperthyroidism and euthyroid). Meanwhile a significant increase of serum ferritin was observed in hyperthyroidism in comparison to that level of euthyroid group. Ferritin level was found to be negatively high correlated with lipid profile in hypothyroidism , TSH was also negatively correlated with ferritin level. In hyperthyroidism group ferritin level was high correlated positively with FT4 while a highly significant positive correlation of ferritin with FT3 was observed in euthyroid group.

Conclusion: Conclude that the lipid profile in thyroid disorder patients are various according to ferritin level

Key words: Ferritin, TSH, FT4, FT3, lipid.

Introduction

Diseases of thyroid gland are amongst the most abundant endocrine disorder in the world ⁽¹⁾. Thyroid diseases are primarily conditions that affect the amount of thyroid hormones being produced. Excess production leads to hyperthyroidism while diminished production leads to hypothyroidism⁽²⁾. Thyroid hormones are important modulator of intermediary metabolism. They affect synthesis, mobilization and degradation of lipids, although degradation is influenced more than synthesis. Consequently, thyroid dysfunction particularly hypothyroidism is associated with dyslipidemia which increase the risk of endothelial dysfunction, hypertension and cardiovascular diseases ⁽³⁾. Hypothyroidism, like obesity is one of the pathological conditions most frequently associated with disorders of lipid metabolism⁽⁴⁾ and finally dyslipidemia which is one of the major risk factors of coronary disease⁽⁵⁾.

Hyperthyroidism is a term for overactive tissue within the thyroid gland, resulting in over production and thus an excess of circulating free thyroid hormones: thyroxin (T4), triiodothyronine (T3), or both⁽⁶⁾. Human hyperthyroidism is accompanied by multiple abnormalities with increased energy expenditure and excessive mobilization and utilization of metabolic substrates⁽⁷⁾. With respect to lipid metabolism it is clear that the breakdown of triglycerides (TGs) stored in adipose tissue is enhanced by thyroid hormones excess, resulting in increment

concentration and turnover of non-esterified fatty acids (NEFA)⁽⁸⁾. This increased availability of fatty acids is associated with a rise in the lipid oxidation rate ⁽⁷⁾.

Ferritin is an iron storage protein found in almost all of the body tissues. Serum ferritin levels also have been reported to be altered in patients with thyroid disease ⁽⁹⁾. Thus, changes in the serum concentrations of ferritin. Several groups have documented an association between T3 levels and ferritin expression. Furthermore, administration of T3 to hypothyroid individuals produced a significant increase in the serum ferritin level⁽¹⁰⁾. Although the cause of the T3-induced increase in the serum ferritin level in humans is unknown; increased synthesis of ferritin in the liver may well be an important contributor. These links between T3 and the regulation of ferritin expression suggest that a positive correlation exists between the levels of T4/T3 and ferritin in the serum. Thus, it has been suggested that serum ferritin measurement could be useful for the evaluation of thyroid hormone action on peripheral tissues⁽¹¹⁾.

Serum ferritin levels are assumed to be an atherosclerotic risk factor. Ferritin production is increased in individuals with activated liver production, which has been shown in hyperthyroid conditions⁽¹²⁾.

Objective:

The present study aim to explore the association of lipid profile with ferritin in patients with thyroid disorder.

Patients and Methods:

In this study, a total 140 (60 male and 80 female) subjects were selected from outpatient department of the National Diabetes center/ AL Mustansiriy University. This study divided into three groups (hypothyroidism 26 male and 31 female, hyperthyroidism 20 male and 29 female and euthyroid 14 male and 20 female). The range of the age from 23-55years. The whole procedure was explained to each participant. Permission was taken from the concerned Ethical Committee. Five ml of blood were collected and allowed to clot. Separated serums were collected into plastic microcentrifuge tubes which were labeled appropriately and were stored in ultra-freezer at -20°C until analysis. Demographic characters such as age, height, and weight of all participants were noted. Serum Ferritin, Free T3, Free T4 and TSH were measured by Minividas (Biomerix). While Tc, TG, HDL, LDL, and VLDL were measured by using automated analyser E4 (BIOLABO Kenza240TX). The collected data were analyzed by applying appropriate statistical tests (t-test and Pearson's correlation).

Results: Table 1 indicated that the levels of FT3, FT4, and TSH for hypothyroidism were 3.5 ± 1.23 ng/dl, 11.98 ± 5.2 pg/dl, and 25.79 ± 14.22 mIU/ml respectively while for hyperthyroidism were 7.45 ± 4.68 ng/dl, 27.98 ± 13.88 pg/dl, and 0.05 ± 0.0 mIU/ml respectively. Meanwhile their levels for euthyroid were 4.4 ± 2.08 ng/dl, 13.34 ± 4.81 pg/dl, and 3.82 ± 9.3 mIU/ml respectively. On analysing the lipid profile, non significant differences of serum cholesterol (Tc), triglyceride (TG), High density lipoprotein (HDL), Low density lipoprotein (LDL), and very Low density lipoprotein level (VLDL), in hypothyroid, hyperthyroid and euthyroid groups were observed (Table 1). The serum ferritin levels (ng/dl) in the same groups were 84.06 ± 92.19 , 61.07 ± 89 , and 32.4 ± 39.78 respectively. There was a significant increase ($p \leq 0.05$) of serum ferritin in hypothyroidism in comparison to its level in both other groups (hyperthyroidism and euthyroid), meanwhile a significant increase ($p \leq 0.05$) of serum ferritin was observed in hyperthyroidism in comparison to that level of euthyroid group.

Table 1: Demographic measures and biochemical values.

Parameters	Hypothyroidism(n=57) Mean $\pm$ SD	Hyperthyroidism(n=49) Mean $\pm$ SD	Euthyroid(n=34) Mean $\pm$ SD
Age(year)	42 $\pm$ 11.7	39.6 $\pm$ 14.11	33.9 $\pm$ 11.8
High(cm)	162.14 $\pm$ 9.4	168.3 $\pm$ 10.3	166.5 $\pm$ 8.5
Weight(kg)	86.7 $\pm$ 9.06	84.6 $\pm$ 10.8	82.3 $\pm$ 10.3
BMI (kg/cm ²)	30.86 $\pm$ 3.26	29.16 $\pm$ 3.07	29.7 $\pm$ 2.97
FT3(ng/dl)	3.5 $\pm$ 1.23	7.45 $\pm$ 4.68	4.4 $\pm$ 2.08
FT4(pg/dl)	11.98 $\pm$ 5.2	27.98 $\pm$ 13.88	13.34 $\pm$ 4.81
TSH(mIU/ml)	25.79 $\pm$ 14.22	0.05 $\pm$ 0.0	3.82 $\pm$ 9.3
Ferritin (ng/ml)	84.06 $\pm$ 92.19	61.07 $\pm$ 89	32.4 $\pm$ 39.78
Tc (mg/dl)	201.5 $\pm$ 73.16	216.02 $\pm$ 42.5	209.02 $\pm$ 58.01
TG (mg/dl)	155.85 $\pm$ 98.3	176.34 $\pm$ 91.6	172.44 $\pm$ 64.25
LDL (mg/dl)	127.4 $\pm$ 60.13	136.3 $\pm$ 39.7	129.1 $\pm$ 55.7
HDL (mg/dl)	42.96 $\pm$ 8.78	44.44 $\pm$ 6.2	44.07 $\pm$ 7.4
VLDL (mg/dl)	31.17 $\pm$ 19.66	35.26 $\pm$ 18.3	34.48 $\pm$ 12.85

Ferritin was found to be negatively highly correlated ($p<0.001$) with lipid profile in hypothyroidism, TSH was also negatively correlated ($p<0.05$) with ferritin. On the other hand a highly significant correlation was observed between ferritin and FT4 (Table 2).

In hyperthyroidism group ferritin was highly correlated positively with FT4 ($p<0.001$), while a highly significant positive correlation of ferritin with FT3 was observed in euthyroid group ($p<0.001$).

Table 2: Correlation coefficient of ferritin level with biochemical values

Parameters	Hypothyroidism r value	Hyperthyroidism r value	Euthyroid r value
Age(year)	0.271*	0.262	0.446*
BMI (kg/cm ²)	0.043	0.086	0.184
FT3(ng/dl)	0.237	0.08	0.563**
FT4(pg/dl)	0.435**	0.471**	0.315
TSH(mIU/ml)	-0.320*	-----	-0.123
Tc (mg/dl)	-0.572**	0.052	0.19
TG (mg/dl)	-0.039**	-0.013	0.258
LDL (mg/dl)	-0.515**	0.048	0.143
HDL (mg/dl)	-0.367**	0.09	-0.041
VLDL (mg/dl)	-0.390**	-0.013	0.285

**Correlation is significant at the 0.01 level, *Correlation is significant at the 0.05 level

Discussion

This study found out the relationship between ferritin and lipid profile in patients with thyroid hormone disorder, measured the serum levels of ferritin, FT3, FT4, TSH, and lipid profile in deficient patients having hypothyroidism, hyperthyroidism, and euthyroid. It is observed in this study that the serum ferritin level was significantly increased in hypothyroidism in comparison to both hyperthyroidism and euthyroid. This result was in disagreement with previous study of Mishra A.K. et al who found a significant low level of TIBC, iron and ferritin in subjects with

altered thyroid profile indicated by decreased in blood levels of FT4 and FT3⁽¹³⁾. Etekhari, *et al.*⁽¹⁴⁾ they showed that depletion of iron stores may decrease serum free T4 level. There was statistical significant positive correlation between serum ferritin and free T4 in our study group (hypothyroidism and hyperthyroidism). It was consistent with the study done by Akhter S *et al.* They had showed that there was positive significant correlation between serum ferritin and free T4⁽¹⁵⁾. While a significant positive correlation between serum ferritin and free T3 in euthyroid group. Our study showed that there was significant negative correlation

of serum ferritin with serum TSH in both hypothyroidism and euthyroid ($p \leq 0.05$). On other hand, our results was disagree with study of Völzke H et al who found no association between thyroid function and serum ferritin levels⁽¹²⁾.

Thyroid hormone has a central role in differentiation, development, and maintenance of body homeostasis⁽¹⁶⁾. It has been suggested in various studies that thyroid hormones regulate ferritin expression. The iron regulatory protein (IRP, previously known as the iron-responsive element-binding protein, IRE-BP, and iron-responsive factor, IRF) is a trans-acting RNA-binding protein that binds with high affinity to conserved stem-loop structures, iron-responsive elements (IREs), present in the ferritin, and transferrin receptor (TfR)⁽¹⁷⁾. Previous study suggested that increased serum ferritin of hyperthyroid patients is related to elevated ferritin synthesis in the liver⁽¹⁸⁾.

The results of lipid profile indicate increase of TG level in hyperthyroidism and euthyroid group which is attributable to the decreased activity of lipoprotein lipase that is responsible for the clearance of triglyceride rich lipoprotein.

Increase of total cholesterol and LDL can be attributed to the effect of thyroid hormone on expression of LDL receptors and CYP7A, a rate limiting enzyme in bile acid synthesis⁽¹⁹⁾. Decreased thyroid function not only increases the number of LDL particles but also promote LDL oxidation, thereby increasing the risk of atherosclerosis^(20,21).

Conclusion:

The lipid profile in thyroid disorder patients are various according to ferritin level

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