A Comparative Estimation of Metabolic and Hormonal Parameters Among Iraqi Hypothyroid Patients

Hind Shakir Ahmed

ABSTRACT:

BACKGROUND:

Thyroid hormones have a crucial physiological role to maintain balance of metabolism of body. Deficiency of iron can produce hypothyroidism. Hypothyroidism causes several lipid metabolism disorders. Visfatin and leptin are adipocytokines and have been suggested as important regulators in patients with thyroid dysfunction.

OBJECTIVE:

The aim of the present study was to estimate the circulating levels of lipids, iron, visfatin, and leptin in newly diagnosed hypothyroid patients.

PATIENTS AND METHODS:

The current study was conducted in medical city teaching hospital on 45 newly diagnosed cases of hypothyroidism aged 35-50 years and compared with 45 healthy individuals as control group during the period from June 2016 to January 2017. This study investigated the serum concentrations of lipid profile, some iron status parameters and hematological parameters, total- and free-, triiodothyronine, tetraiodothyronine, thyroid stimulating hormone, visfatin, and leptin in hypothyroid patients and compared them with the controls.

RESULTS:

There was a significant increased in serum total cholesterol and triacylglycerol in hypothyroid patients compared to the control, ($P=0.001$). There was a significant decreased in hemoglobin, serum iron, and ferritin while a significant increased in total iron binding capacity in hypothyroid patients compared to the control, ($P\leq0.05$). Means value of thyroid stimulating hormone levels were significantly increased in hypothyroid patients compared to the control group. On the other hand, the levels of total- and free-, tetraiodothyronine, free triiodothyronine were significantly decreased in hypothyroid patients as compared to the control group. There was a significant increased in visfatin and leptin concentrations in hypothyroid patients compared to the control group, ($P\leq0.05$).

CONCLUSION:

These data suggest that thyroid hormone insufficiency may lead to deficiency of iron and lipids abnormalities. Thus, estimation of iron and related parameters with lipids may be quite useful during the diagnosis and treatment of hypothyroid patients. Also, alterations in thyroid status change serum visfatin and leptin in hypothyroid patients. It is advisable to routinely investigate them for early detection allowing its early management.

KEY WORDS: hypothyroidism, hematological parameters, visfatin, and leptin

INTRODUCTION:

Hypothyroidism is a common endocrine disorder results from decreased secretion of total thyroxine (TT4) and total triiodothyronine (TT3) leading to inadequate thyroid action. It is more common in females than males [(1)]. Biochemically, hyposecretion of T4 and T3 leads to distinct raise in serum thyroid stimulating hormone (TSH) levels because of hypersecretion of pituitary TSH [(2)].

Department of Chemistry, College of Education for Pure Science (Ibn Al-Haytham)/
University of Baghdad.

Thyroid hormones serve as regulators of diverse processes in the body. They stimulate resting metabolic rate and heat production, influence cell proliferation and development, modulate response to further hormones, and alter metabolism of carbohydrate, protein and lipids [(3)]. Hypothyroidism may cause diverse types of anemia through decreasing the oxygen metabolism. Anemia that normalizes due to T4 replacement, even in the presence of normal serum iron is found in around 25% of hypothyroid patients [(4)].

Iron metabolism is very intricately connected to thyroid hormone metabolism. Assessment of serum ferritin, iron, and total iron binding capacity (TIBC), which measures percent saturation of transport form transferrin with iron, might be of great implication in hypothyroidism. Regular thyroid status is dependent on the incidence of numerous trace elements e.g., iron, iodine, selenium, and zinc for both the synthesis and metabolism of thyroid hormones [5].

Thyroid dysfunction, particularly hypothyroidism, is associated with dyslipidemia as thyroid hormones are significant modulators of intermediary metabolism [6]. Thyroid dysfunction results in alterations of appetite, body weight, muscle mass and adipose tissue [7]. In addition to typical clinical symptoms directly correlated to thyroid hormones and TSH, patients suffer from thyroid dysfunction are expected to present with high incidences of insulin resistance, type 2 diabetes mellitus and cardiovascular diseases [8-10]. Thyroid-stimulating hormone receptors have been found in the adipose tissues; this indicates that it can complete a central role in the regulation of adipose tissue metabolism [11].

Visfatin is one of the main abundant adipocytokines newly revealed with the capacity to modulate several functions. Visfatin, also identified as nicotinamide phosphoribosyltransferase (NAMPT) as well as pre-B-cell colony-enhancing factor, it is a highly conserved, 52-kDa protein found in alive species from bacteria to humans with suggested enzymatic, immunological, and metabolic properties [12]. Visfatin has been analyzed in hypothyroidism in vitro and in vivo studies, but results are inconclusive [13].

Leptin is a 146-amino acid protein hormone encoded by the ob gene, a peptide hormone, has been shown as one of the major significant hormones secreted by adipose tissue. Also, it acts a regulatory function in inflammation and immunity status, and has an impotent function in the instruction of immune responses [14]. Leptin affects the neuroendocrine system at numerous levels, including the hypothalamic-pituitary-adrenal, thyroid, gonadal, and growth hormone axes [15].

Therefore, The aim of the present study was to estimate the circulating levels of lipids, iron, visfatin, and leptin in newly diagnosed hypothyroid patients.

PATIENTS AND METHODS:

The current study was conducted at Medical City Hospital on 45 newly diagnosed cases of hypothyroidism (21 males and 24 females) aged 35-50 years from June 2016 to January 2017. For comparison, 45 healthy individuals constituted the control group. Patients with history of any drug intake or any infection/illness, pregnant females, diabetic patients, patients with thyroid cancer were excluded from the study.

Height was deliberated in centimeters (cm) and weight in kilograms (kg), using a calibrated spring balance. Body mass index (BMI) was calculated by dividing weight (kg) with height (m^2).

Fasting blood samples were collected and hemoglobin was analyzed by spectrophotometer. The serum hence obtained was separated into 3 divisions; for thyroid, iron, and lipid profiles.

First part of the serum was analyzed using the Randox kit for total cholesterol (TC), triacylglycerol (TAG), and high density lipoprotein cholesterol (HDL-C). For iron profile, serum was analyzed for circulating levels of iron and ferritin.

The third part of the serum was analyzed for circulating levels of TT3, TT4, free T3 (FT3), free T4 (FT4), and TSH by enzyme linked immunosorbent assay (ELISA) technique. Serum visfatin and leptin levels were estimated in patients and controls by ELISA technique using human visfatin and leptin ELISA Kit.

STATISTICAL ANALYSIS:

Statistical analysis was performed by Statistical Package for Social Sciences (SPSS). Means and standard deviations (SD) were deliberated for all parameters. T-test was used to contrast the means of diverse variables in both groups. P value $\leq$ 0.05 was measured significant.

RESULTS:

Clinical and anthropometric distinctiveness of the studied groups were summarized in table 1. The means of age in the present study was (42.2±8.0) years in hypothyroidism. There were 21 males and 24 females. There was a significant raised in age, weight, BMI, systolic blood pressure (SBP), and diastolic blood pressure (DBP) in hypothyroidism as compared in healthy group, ($P \leq 0.05$).

The lipid parameters were compared between hypothyroidism and healthy group, table 2. There was a significant raised in serum TC, TAG, TC/HDL-C ratio, and TAG/HDL-C ratio in hypothyroidism as compared in healthy group, ($P=0.001$).

Table 1: Clinical and anthropometric distinctiveness of the studied groups.

Parameter	Hypothyroidism (n=45)	Healthy (n=45)	P-Value
Age (years)	42.20±8.0	38.70±3.24	0.05
Male/Female	21/24	21/24	-
Height (cm)	1.44±0.20	1.76±0.30	0.06
Weight (kg)	73.20 ± 12.60	67.80 ± 10.90	0.001
BMI (kg/m^2)	35.50±4.45	21.90±1.93	0.001
SBP (mmHg)	136.52±6.70	125.0±7.50	0.001
DBP (mmHg)	85.66±4.50	83.33±1.50	0.05

Table 2: Comparison of lipid profiles between the studied groups.

Parameter	Hypothyroidism (n=45)	Healthy (n=45)	P-Value
TC (mg/dl)	202.55±10.44	145.0±0.23	0.001
TAG (mg/dl)	265.0±12.25	120.0±2.95	0.001
HDL-C (mg/dl)	38.0±5.80	42.75±6.8	0.001
TC/HDL-C	5.33±4.84	3.37±1.26	0.001
TAG/HDL-C	6.97±6.44	2.81±2.51	0.001

Table 3 demonstrates the comparison of iron and hematological profiles between hypothyroidism and healthy group. There was a significant reduced in Hb, serum iron, and ferritin while a significant increased in TIBC in hypothyroidism compared to healthy group, (P≤0.05).

Table 4 illustrates the comparison of iron and hematological profiles between hypothyroidism and healthy group. There was a significant decreased in TT4, FT3, and FT4 in hypothyroidism as compared in healthy group, (P=0.001). Also, there was a reduced in TT3 in hypothyroidism, but it was not significant. A significant raised was noticed in serum TSH, visfatin, and leptin in hypothyroidism as compared in healthy group, (P≤0.05).

Table 3: Comparison of iron and hematological profiles between the studied groups.

Parameter	Hypothyroidism (n=45)	Healthy (n=45)	P - Value
Hb (g/dl)	9.85±0.50	13.85 ± 1.12	0.05
Iron (µg/dl)	42.10 ± 8.12	72.30 ± 12.70	0.001
ferritin (ng/ml)	17.45 ± 10.50	35.0 ± 15.80	0.001
TIBC (µg/dl)	278.40 ± 16.07	238.0 ± 12.50	0.001

Table 4: Comparison of hormonal profiles between the studied groups.

Parameter	Hypothyroidism (n=45)	Healthy (n=45)	P-Value
TT3 (nmol/l)	0.71±0.43	1.32 ± 0.30	0.06
TT4 (nmol/l)	46.0±0.89	72.60 ± 1.82	0.001
FT3 (ρmol/l)	2.12±0.35	6.15±0.57	0.001
FT4 (ρmol/l)	2.32±0.81	15.96±3.20	0.001
TSH (µmol/l)	9.56±2.82	1.80±1.50	0.05
Visfatin (ng/ml)	10.12±1.98	6.0±0.54	0.05
Leptin (ng/ml)	9.75±2.40	2.21±0.43	0.001

DISCUSSION:

In the current study, the means ± SD of age in hypothyroid patients was (42.2±8.0) and (38.70±3.24) in healthy group and female predominance is more than the male of total cases. Similar findings were reported by Desai et al [16]. Also, BMI of hypothyroid patients were evaluated and compared with healthy group. Increased levels of BMI (>25) were seen in hypothyroid patients.

Thyroid hormones are complicated in controlling metabolism of macromolecules involving lipids and carbohydrates [17].

Dyslipidemia was seen among hypothyroid patients, and higher significantly levels of TC and TAG were noticed in hypothyroid patients as compared in healthy group which concurs with the information's of the earlier study [18]. Current study showed a significant increased in serum TC, TAG, and LDL-C in hypothyroid patients as compared in healthy group, which is in accordance with other studies [19, 20].

Decreased thyroid secretion significantly increases the plasma cholesterol levels because the decreased rate for conversion of cholesterol to bile acids and consequent diminished loss in the feces due to decreased number of LDL receptors on liver cells. According to Khan et al study, significant increased in levels of TC in hypothyroid patients compared to healthy [21]. Study done by Lakshmi et al showed that there was a significant reduce in HDL levels in hypothyroid patients compared to healthy which is in agreement with the present results [22]. The lipids ratios predict cardiovascular disease risk better than isolated lipoprotein subfractions. This study showed there was a significant increased (P=0.001) in TC/HDL ratio in cases compared to healthy. If the ratio of TC/HDL-C is more than 3.5, risk is more [23]. Moreover, TAG/HDL-C ratio also significantly increased in cases compared to healthy, which is in agreement with the study of Alamdari et al [24].

The elevated rate of hypothyroidism in the study subjects may be refer to elevated rate of thyroid autoimmunity and insufficiency of micronutrients such asiron [25]. On the other hand, several studies showed an association between body iron status including; iron metabolism, ferritin, and serum iron with thyroid hormones functions [26, 27]. The hypothyroidism influence body iron status, blood cells and cause anemia with a variety of severities. Blood indices such as Hb also may change through thyroid dysfunction [28].

The current results demonstrate a significant decreased in Hb levels for hypothyroid patient compared to healthy group. Dorgalaleh et al., revealed that red blood cell, Hb, and hematocrit in patients with hypothyroidism were significantly lowered than healthy groups; whereas these parameters were elevated in hyperthyroidism [29]. In this study, the levels of iron and ferritin were found to decrease in hypothyroid patients while that of TIBC to increase in patients suffering from hypothyroidism as compared to healthy group. These results are in accordance with other studies which reported that iron deficiency may be associated with low levels of thyroid hormones [30, 31]. These findings suggest that anemia led to higher levels of TSH. Similarly, it was noticed that iron deficient patients had significantly lesser FT3 level. In a further study in Bangladesh among general population, serum TSH level was significantly elevated and serum FT4 was significantly lesser in iron deficient subjects than healthy, nevertheless, serum FT3 was almost similar between iron deficient subjects and healthy [32]. These results may be due to the fact that anemic and iron deficient patients have elevated risk for hypothyroidism, and hypothyroidism is connected with anemic and iron deficient patients. As a result, these findings suggest for the probability that iron insufficiency may impair thyroid metabolism as reported in preceding experiments. Both primary steps of thyroid hormone synthesis are catalyzed by heme containing enzyme, thyroid peroxidase. Severe iron insufficiency may lesser thyroid peroxidase activity and obstruct with the synthesis of thyroid hormones thereby leading to hypothyroidism [33]. Studies have discovered that iron insufficiency anemia impairs thyroid metabolism and as well decreases plasma TT3 along with TT4 concentrations and reduces peripheral exchanging of T4 to T3 [34].

Furthermore, leptin, produced by adipocytes, regulates appetite and energy expenditure and influences thyrotropic axis with TSH secretion [35]. Serum levels of leptin are proportional to BMI. In the present study, BMI and serum levels of leptin were significantly different between healthy and hypothyroid patients which are in agreement with the study of Versini et al [36]. This association between serum leptin and thyroid functions may be partly mediated by TSH, TSH has a direct effect on leptin secretion by simulating TSH-receptor on adipocytes [37].

Visfatin has been documented as a cytokine with a wide variety of immune and inflammatory activities, involving instruction of inflammatory cytokines, and regulation of macrophage as well as lymphocyte proliferation [38].

In this study, visfatin concentration depends on FT3 and FT4. These findings about the association of visfatin with FT3 and FT4 levels are in accordance with the results of *in vitro* and *in vivo* studies. Therefore, this study suggests that pattern of visfatin changes varies in different FT3 concentration, which is in agreement with the study of Sawicka-Gutaj et al [39]. This might

prove that visfatin level in hypothyroidism depends on thyroid hormones level and might assume that factor should be taken into consideration to assess visfatin level in patients with thyroid dysfunction. In addition, it might be there is a probable involvement of visfatin in pathogenesis of chronic autoimmune thyroiditis.

CONCLUSION:

This data suggest that thyroid hormone insufficiency may guide to deficiency of iron and lipids abnormalities. Thus, assessment of iron and related parameters with lipids may be quite useful during the diagnosis and treatment of hypothyroid patients. So, alterations in thyroid status alter serum visfatin, and leptin in hypothyroid patients. It is desirable to routinely investigate them for early detection allowing its early management.

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