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Article

Effect of Parasite Infection on the Lipid Profile and Thyroid Hormones in thyroiditis patients

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ABSTRACT

This study investigated parasitic infection's effect on the thyroid gland's functions by hypo- or hyperthyroidism and inflammation by measuring some physiological and immunological indicators. 130 blood and stool samples were collected from both genders, including 80 samples from people with thyroid disorders and 50 samples from healthy people. Hormone levels and Lipid profile were estimated by using the Cobas e411 device. The general stool examination was conducted to confirm the presence of a parasitic infection and determine the type of parasites. As for the type of parasites found, the most affected were *Entamoeba histolytica*, *Giardia lamblia*, *Blastocystis hominis*, and the last parasite, *Cryptosporidium.* Hormonal tests, and depending on the level of hormones, it was found that 44 out of 80 patients showed a decrease in hormone levels, which were counted as hypothyroidism. In contrast, 36 showed an increase and were counted as hyperthyroidism. The results of cholesterol level, triglycerides and low-density lipoprotein for hypothyroidism showed an increase in patients without parasites, higher than those parasitic infected compared to the control. Conclusion: This study showed that infection with a parasite affected the performance of the thyroid gland.

Keywords: Parasites; Thyroid Disorders; Thyroid Hormones; Lipid Profile.

INTRODUCTION

Parasites are microscopic creatures that live in or on another organism, receiving their food from the host and inflicting harm [1]. The parasite can attack different organs, for example, the thyroid gland, which is one of the most important endocrine glands in the body, as its hormones (T4 and T3) have an important role in regulating the body's basic metabolic rate, the generation of heat, contribute to fat metabolism by stimulating lipolysis, and production fatty acids as an energy source [2].

The thyroid is a bi-lobed gland, often described as resembling a butterfly or bow tie. It is positioned in the neck, between the Cervical 5 (C5) and thoracic 1 (T1) vertebrae, just below the thyroid cartilage (Adam’s apple) of the larynx [3], which are connected by a small piece of tissue called the isthmus; around half of the individuals also possess an additional third lobe, usually triangular shaped and known as the pyramidal lobe [4,5].

Thyroxine (T4) and triiodothyronine (T3) are classical thyroid hormones with relatively well-understood actions. In contrast, the physiological role of thyroid hormone metabolites, also circulating in the blood, is less well characterized [6], T3 and T4 are synthesized from iodine and tyrosine, they elevate optimal growth, development, function and conservation of all body tissues. The synthesis and secretion of these hormones affect a hormone released via the pituitary gland called thyroid-thyroid-stimulating hormone (TSH). This gland also produces calcitonin, which plays a role in calcium homeostasis [7]. Parasitic infection like *G. lamblia* and *E. histolytica* produces alterations in thyroid function. They cause a decrease in the level of Triiodothyronine (T3) and Thyroxin (T4) hormones [8].

On the other hand, there is evidence that *Toxoplasma* can interfere with the thyroid's normal function. This parasite is responsible for the alterations that are carried about in the lipid profile. These changes are characterized by a considerable reduction in cholesterol, triglycerides, LDL, and vLDL levels, as well as a significant increase in the level of HDL [9]. This study aimed to study the relationship between parasitic infection and thyroiditis by determining the type of thyroiditis (hyperthyroidism or hypothyroidism) by measurement of T3, T4 and TSH hormones. Investigating the types of parasites present in patients with thyroiditis. Studying the effect of parasites in patients suffering from thyroiditis (hypothyroidism or hyperthyroidism) on Lipid Profile and comparing them with healthy people and patients suffering from thyroiditis without parasite infection.

MATERIALS AND METHODS

Study group: The patients were selected according to their signs of thyroid problems that were evaluated by the medical consultation staff and, in most cases, included diarrhea, mood changes, anger, anxiety, depression, weight loss, weight gain, oily skin, dry skin, sensitivity to temperature changes, and others. The blood samples were collected from 80 Iraqi patients with a problem with the thyroid gland and 50 healthy considered controls from both genders, aged (20-50 years).

General stool examination (GSE)

Macroscopic examination

This included examining stool samples with the naked eye to detect the physiological characteristics (color, consistency, odor, blood, mucus, and to see the adult worms if present).

Microscopic examination. Wet mount method

This examination uses the wet mounts method of stool sample exam. The examination was done by taking a small part of the stool with a wooden stick and putting it on a slide with a normal saline drop. After mixing the stool sample well with normal saline, put the cover slide carefully to prevent the formation of air bubbles, then examine under a microscope by low power (10x) and high power (40x), as well as using lugol's iodine solution in the wet mount, with the same procedure of using normal saline[10,11].

Staining with permanent stains

According to Garcia, [12] staining of slides was performed. The staining was done with Giemsa stain to detect *Entamoeba histolytica* and other parasites. The staining with safranin stain was used to detect *Blastocystis hominis*. The staining with methylene blue to detect *Giardia lamblia* (trophozoite of parasite appears in dark blue color). Staining with ziehl-neelsen stain to detect *Cryptosporidium parvum* (Oocyct of parasite appears in red).

Measurement of T3, T4 and TSH hormones

According to the manufacturer information company of the Cobas-Roche/ Germany kit (06437206, 2017), levels of T3 and T4 in serum were estimated. The same company manufactures the kit used in the device Cobas e411, and the method to work is the automatic system. The level of T4(Triiodothyronine) in serum was estimated according to the manufacturer information company of the Cobas-Roche/ Germany kit (11731459, 2018). The kit was used in the device Cobas e411, and the method to work is the automatic system.

Measurement of Lipid Profile

According to the manufacturer information company of BioSystem/ USA (M115250.22, 2019), cholesterol levels and triglyceride levels were estimated in each serum sample. According to the manufacturer information company of BioSystem/ USA (M115223i-27, 2019), high-density lipoprotein (HDL) levels were estimated in each serum sample.

RESULTS

Distribution groups of the study

The total subjects in this study included 130 blood and stool samples: 80 samples from people suffering from thyroid disorders and 50 samples from healthy people of both sexes. Then, they were distributed according to hormonal tests (T3, T4 and TSH) for hypothyroidism, hyperthyroidism and normal. After stool examining the stool, the total samples were divided into hypothyroidism with and without the parasite and hyperthyroidism with parasites and without parasites.

Distribution of thyroiditis according to thyroid hormones

The hormonal tests for thyroid function (T3, T4, TSH) showed that 80 people suffer from a thyroid disorder. Depending on the level of hormones, whether it is high or low, it was found that 44 people showed a clear decrease in the level of hormones, and they were counted as hypothyroidism. Their results are shown in Table 1.

Tested groups	**Thyroid hormones function**		
Normal	T3 ng/dL	T4 ng/dL	TSH µIU/mL
Mean±Std. Er	B 1.13±0.07	B 106.22±1.41	B 1.92±0.10
Hypothyroidism	T3	T4	TSH
Mean±Std. Er	C 0.78±0.11	C 65.31±8.17	C 1.29±0.45
Hyperthyroidism	T3	T4	TSH
Mean±Std. Er	A 1.61±0.51	A 179.61±11.18	A 5.56±0.7
P value	0.01	0.001	0.01

Table 1. Serum level of thyroid hormones in patients and control. Data expressed as mean±Std. Error. LSD test was used to calculate the significant differences between the tested mean. The letters (A, B and C) LSD for columns represented the levels of significance, the highly significant start of the letter (A) and decreasing with the last one. P value ≤ 0.05. Similar letters. Mean there are no significant differences between tests mean. *T: triiodothyronine, *TSH: thyroid stimulating hormone,*Std: standard deviation, Er: error.

Numbers and types of parasites in study groups

After examining the stool by using some special stains to diagnose parasites, the present four types of parasites were detected in this study: *Entamoeba histolytica, Giardia lamblia, Blastocystis hominis and Cryptosporidium parvum.*The rate of parasite infection with these parasites in hypothyroidism is shown in Table 2.

	E.histolytica	***G.lamblia***	***B.hominis***	***C.parvum***	**Total**
Hypothyroidism	19	16	9	1	45
Hyperthyroidism	7	5	4	1	17
Control	1	3	2	0	6

Table 2. Numbers and types of parasites in study groups.

Lipid Profile Results

The result showed in Table 3 that the level lipid profile (Ch, Tg, LDL, VLDL) increased in the hypothyroidism group more than in the hyperthyroidism group compared with control, while the hyperthyroidism without parasites results compared with the control group as shown in Table 4. At the same time, the level of HDL increased in hyperthyroidism more than in hypothyroidism with and without parasites compared with the control group. There was no significant difference in the effect of different parasites diagnosed in this study (*E. histolytica*, *G. lamblia*, *B. hominis*) on each (Tg, HDL, VLDL), as shown in Table 5.

Tested groups	**Lipid profile/hypothyroidism**				
Normal	**Ch mg/ml**	**Tg mg/ml**	**HDL mg/dl**	**LDL mg/ml**	**VLDL mg/ml**
Mean	C 155.82	C 128.13	B 25.62	C 34.96	A 95.09
±Std. Error of Mean	1.94	3.36	0.67	0.49	1.99
Hypothyroidism With parasites	CH	TG	HDL	LDL	VLDL
Mean	B 197.00	B 148.00	A 33.61	B 132.79	B 29.61
±Std. Error of Mean	3.74	5.83	0.56	3.70	1.17
Hypothyroidism Without parasites	CH	TG	HDL	LDL	VLDL
Mean	A 213.56	A 159.31	A 34.06	A 145.75	B 32.10
±Std. Error of Mean	6.43	7.57	0.70	6.59	1.47
P value	0.001	0.001	0.05	0.001	0.03

Table 3. Lipid profiles among hypothyroidism patients and control group. Data expressed as mean±Std. Error. LSD test was used to calculate the significant differences between tested mean, the letters (A, B and C) LSD for columns represented the levels of significance, The highly significant start of the letter (A) and decreasing with the last one. P value ≤ 0.05. Similar letters Mean there are no significant differences between tests mean. *Std: standard deviation.

Tested groups	**Lipid profile/hyperthyroidism**				
Normal	Ch mg/mL	Tg mg/mL	HDL mg/dL	LDL mg/mL	VLDL mg/mL
Mean	B 155.82	C 128.13	B 25.62	B 34.96	A 95.09
±Std. Error of Mean	1.94	3.36	0.67	0.49	1.99
Hyperthyroidism With parasites	CH	TG	HDL	LDL	VLDL
Mean	A 166.13	B 143.88	A 34.08	A 103.19	B 28.78
±Std. Error of Mean	3.15	8.96	0.98	2.74	1.79
Hyperthyroidism Without parasites	CH	TG	HDL	LDL	VLDL
Mean	A 162.60	A 153.85	A 34.30	A 97.45	B30.79
±Std. Error of Mean	3.05	7.61	0.74	2.81	1.51
P value	0.01	0.01	0.05	0.01	0.05

Table 4: Lipid profiles among hyperthyroidism patients and control group. Data expressed as mean±Std. Error. LSD test was used to calculate the significant differences between the tested mean. The letters (A, B and C) LSD for columns represented the significant levels. The highly significant start of the letter (A) and decreasing with the last one. P value ≤ 0.05. Similar letters Mean there are no significant differences between tests mean.

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	Lipid profile/thyroiditis				
Parasites types	Ch mg/mL	Tg mg/mL	HDL mg/dL	LDL mg/mL	VLDL mg/mL
***E. histolytica*/Mean**	190.88	143.65	33.92	A 127.19	28.75
±Std. Error of Mean	4.70	6.06	0.68	4.55	1.21
***G. lamblia*/Mean**	188.33	148.57	33.48	A 125.05	29.71
±Std. Error of Mean	4.23	6.01	0.63	3.87	1.20
***B. hominis*/Mean**	176.31	141.77	33.82	B 114.08	28.35
±Std. Error of Mean	4.50	10.96	1.01	4.01	2.19
P value	NS	NS	NS	0.05	NS

Table 5. Compare the effect of parasite species on lipid profile. Data expressed as mean±Std. Error. LSD test was used to calculate the significant differences between the tested mean, the letters (A and B) LSD for columns represented the significant levels, The highly significant start of the letter (A) and decreasing with the last one. P value ≤ 0.05. Similar letters Mean there are no significant differences between tests mean. *Std: standard deviation.

DISCUSSION

Hyperthyroidism disorders of the thyroid gland can result in excess T3 and T4 production and the compensatory decrease of TSH [13]. The antibodies bind TSH to initiate and increase T3 and T4 synthesis and production regardless of a decrease in the level of TSH by a negative feedback mechanism exerted by T3 and T4 on the pituitary and hypothalamus [14]. Taylor *et al.* (2018) showed the incidence of hyperthyroidism is lower compared with hypothyroidism in the general population. Yasri and Wiwanitkit [15] found that infection with parasitic diseases leads to deficiency and disorder of parathyroid gland hormones. The study by Zhang et al., [2] showed that the thyroid-stimulating hormone (TSH) was raised in response to low total T4 and T3 and explained that the parasites could attack the thyroid gland. Also, its hormones (T3 and T4) are important in regulating the body's basic metabolic rate generation of heat. They contribute to fat metabolism by stimulating lipolysis, producing fatty acids as an energy source. In a study conducted by Wsoo *et al.* [16] from the period of July 2015 to July 2016 in Ranya Town, Iraqi Kurdistan, 2013 individuals were screened, they concluded that the highest prevalence was hyperthyroidism 7.6%, followed by subclinical hypothyroidism 6.01%, they revealed that the women had a greater susceptibility than men in each age group. A cross-sectional study performed in Baghdad-Iraq, in a period of 6 months from July to December 2018, with the participation of 1800 cases, revealed that the prevalence of hypothyroidism (primary and subclinical) was higher than hyperthyroidism (primary and subclinical). The highest prevalence was recorded with subclinical hypothyroidism at 14.1%, and the disease frequency was higher in adults ages and females approximately three times than in males [17]. Khan *et al*. [18] concluded that levels of TC, Tg, LDL, and VLDLand TC/HDL ratio elevated in hypothyroid patients but disagreed with the same study that concluded a significant decrease in HDL observed in hypothyroid patients and disagreed with their results in hyperthyroid patients which revealed low HDL levels with no significant changes in TC, Tg, LDL-C, VLDL-C, and TC/HDL ratio. The study conducted by Rizos *et al*. [19] found that hyperthyroidism exhibits an enhanced excretion of cholesterol and an increased turnover of LDL, resulting in a decrease in total and LDL cholesterol. At the same time, HDL levels are unaffected and remain normal or decreased in hyperthyroidism. Another effect of T3 is the up-regulation of apolipoprotein AV (ApoAV), which plays a major role in Tg regulation. Indeed, increased levels of the above have been associated with decreased levels of Tg [20]. Moreover, a decrease in LPL activity is found in hypothyroidism, decreasing the clearance of TG-rich lipoproteins [21]. Goldberg *et al.* [22] showed that hypothyroid patients with elevated TG levels associated with increased levels of VLDL and occasionally fasting chylomicronemia also exhibit elevated levels of HDL-C mainly due to increased concentration of HDL2 particles. Indeed, a reduction of HL activity results in a decrease in HDL2 catabolism. Moreover, Ferri *et al*. [23] showed that decreased cholesteryl ester transfer protein (CETP) activity results in reduced transfer of cholesteryl esters from HDL to VLDL, thus increasing HDL-C levels. According to Peppa *et al*. [24], one of the main reasons hypothyroidism is a risk factor for atherosclerotic cardiovascular disease is that dyslipidemia is a prevalent finding in the condition. In one study, more than 90% of hypothyroid patients were found to have dyslipidemia[25]. The study conducted by Mansfield *et al*. [26] showed that 71% of patients with hypothyroidism had some form of dyslipidemia, and 32% had an isolated hypercholesterolemia. Similarly, Taylor *et al.* [27] showed decreased prevalence of hyperthyroidism is evident in hyperlipidemic patients, since only 3 out of the 248 patients with thyrotoxicosis. Lalla *et al*. [28] reported that the levels of TC and LDL-C tend to decrease in patients with hyperthyroidism. This is due to increased LDL receptor gene expression, which enhances LDL receptor-mediated catabolism of LDL particles. Furthermore, hyperthyroidism results in enhanced LDL oxidability related to FT4 levels [29]. Gautam *et al.* [30] a decrease in HDL-C levels is also observed in hyperthyroidism due to increased CETP-mediated transfer of cholesteryl esters from HDL to VLDL and increased HL-mediated catabolism of HDL2, while triglyceride levels remain unchanged. Thyroid function significantly affects lipoprotein metabolism as well as some cardiovascular disease (CVD) risk factors [29].Thyroid hormones can influence HDL metabolism by increasing cholesteryl ester transfer protein (CETP) activity, which exchanges cholesteryl esters from HDL to VLDL and Tg in the opposite direction [31]. In addition, thyroid hormones stimulate the lipoprotein lipase (LPL), which catabolizes the Tg-rich lipoproteins, and the hepatic lipase (HL), which hydrolyzes HDL2 to HDL3 and contributes to the conversion of intermediate-density lipoproteins (IDL) to LDL[32]. The lack of central leptin function in *Entamoeba histolytica*, infected mice increases activation of the hypothalamic–pituitary–adrenal axis, leading to increased glucocorticoid and decreased thyroid and growth hormone levels that could indirectly affect immune and intestinal functions important in amebic infection [33]. The role of *Entamoeba histolytica* in the increased levels of lipids is noticed in the current results because of its effect on leptin. Since leptin is a key body weight regulating adipokine released in proportion to the adipose tissue mass, without leptin, the body thinks it has no body fat, which signals intense, uncontrolled hunger and food consumption [34]. Infection with intestinal parasites (without thyroid disorders) decreases lipid profile, as shown in Al-Shamari and Jabir [35], who concluded that cholesterol levels were decreased in giardiasis patients. In contrast, the other lipids were normal in the same patients because *Giardia lamblia* consumed the host's cholesterol in the cell's biosynthesis. It goes back to the parasite's inability to synthesize cholesterol since one of the main complications of giardiasis is lipid malabsorption, so steatorrhoea (foul-smelling, greasy stool) is a clinical sign of giardiasis. According to research done by Al-Khamesi [9] reported that *T. gondii* plays an important role in changes in the lipid profile. These changes are characterized by a significant decrease in the levels of cholesterol, triglycerides, LDL and VLDL, as well as a significant increase in the level of HDL. In addition, thyroid function may be affected by this parasite. Ma'ani *et al.* [36] found that the *Giardia* parasite may consume only cholesterol and neglect the other lipids, which showed that cholesterol starvation triggers trophozoite differentiation into cysts. Also, Barash [37] found that *Giardia lamblia* trophozoites may inhibit lipolysis. The degree of inhibition increased with a longer duration of lipase exposure to trophozoites. The study by Montoro-Huguet *et al*. [38] showed a decrease in triglyceride levels and high-density lipoproteins. A study by Al-Hadrawy[39] showed that changes in cholesterol and lipid levels show a greater association with an active infection that results in intestinal amoebiasis and that *E. Histolytica* infection leads to reduced cholesterol absorption from the intestine.

CONCLUSIONS

In the current study, the younger age groups with thyroiditis are more likely to be infected with parasites—the effect of parasites on the immune factors more than the physiological factors in thyroiditis patients.

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