

## Research article

## An evaluation of blood glucose and lipid profile in female hypothyroidism patients in Kerbala province, Iraq

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### ABSTRACT

**Introduction and Aim:** Hypothyroidism is a common metabolic disorder caused by inadequate secretion of the thyroid hormone by the thyroid glands. The condition impacts various metabolic processes including glucose synthesis, lipid synthesis, mobilization and metabolic rate. This study aimed to evaluate the physiological factors associated with female hypothyroidism patients of Kerbala province of Iraq.

**Materials and Methods:** Fifty females (35 with hypothyroidism and 15 normal) aged between 20-49 years were included in the study. Blood sample was collected from each individual and subjected to thyroid function test (TFT), lipid profile test (LPT) and fasting blood glucose (FBG).

**Results:** The study showed a significant ( $P \leq 0.001$ ) increase in thyroid stimulating hormone (TSH) levels as compared to control. While a significant decrease was seen in thyroxin (T4) levels in comparison to controls, no significant difference was seen for triiodothyronine (T3) levels in both groups. Low-density lipoprotein (LDL), Triglycerides (TG), total cholesterol (TC) was significantly increased ( $P \leq 0.001$ ) while high density lipoprotein (HDL) was observed to significantly decrease as compared to control group. High significant elevation ( $P \leq 0.001$ ) in fasting blood glucose (FBG) was seen in patients with hypothyroidism as compared to control.

**Conclusion:** The results obtained in this study show that hypothyroidism in females to be significantly associated with increase in dyslipidemia and blood glucose levels.

**Keywords:** Hypothyroidism; blood glucose; lipid profile; glycemic status; Kerbala.

### INTRODUCTION

The thyroid, a butterfly shaped gland consisting of two lobes is situated on either side of the trachea. The thyroid gland releases the hormones, thyroxin (T4) and triiodothyronine (T3) that regulate metabolism and other vital bodily functions (1). Hypothyroidism is a condition in which the thyroid gland produces reduced quantity of the thyroid hormones T4 and T3 resulting in the pituitary gland to secrete more TSH because of secondary activation (2). Hypothyroidism has been further classified as primary (deficiency in thyroid hormone), secondary (deficiency in TSH), tertiary (deficiency in thyrotropin-releasing hormone TRH), central (includes both secondary and tertiary) and peripheral (permanent congenital hypothyroidism) based on thyroid hormone production (1). Based on the severity the prevalence of this disorder ranges from 2-15% within a population. Women are affected more than men, and both sexes become more affected as they get older. Symptoms commonly seen in hypothyroidism include generalized weakness and/or weariness dry coarse skin, weight gain, tiredness, and constipation (2).

Thyroid hormones also influence lipid production and distribution. The most important effect on lipid

metabolism includes increase concentration of free fatty acids (FFF) in plasma as a result of mobilization of triglycerides (TG) from the adipose tissue, There is an increase in serum total cholesterol (TC), apolipoprotein (B), lipoprotein (A) and low density lipoprotein cholesterol (LDL-C) in patients with overt hypothyroidism (3), which results in an increase in cholesterol levels. According to research, metabolic syndrome is responsible for 25% new-onset of cardiovascular disease (CVD), hyperlipidemia and insulin resistance (4). Thyroid hormones also play a significant role in glucose homeostasis management, including modifications of circulating insulin levels and counter-regulatory hormones, intestinal absorption, hepatic synthesis, and glucose uptake by peripheral tissues (fat and muscle) (5). Increased gluconeogenesis and glycogenolysis to create free glucose are among the changes in carbohydrate metabolism seen in hypothyroidism (6).

This study aimed to evaluate dyslipidemia and glucose levels of female hypothyroidism patients and determine the correlation of these parameters between patients and normal healthy controls.

**MATERIALS AND METHODS**

**Study design**

This study included fifty adult females in the age range of 20-49 years, who were tested for physiological parameters related to thyroid function. The subjects were divided into 2 groups. Group I: consisting of normal females (n=15) and Group II: consisting of females (n=35) with thyroid disease.

**Inclusion criteria**

Females who have being clinically diagnosed with thyroid disease.

**Exclusion criteria**

Females with chronic disorders such as hyperlipidemia, diabetes, hypertension, liver disease, and malignancy.

**Samples collection and experiments**

Venous blood (5 ml) was drawn from each subject aseptically, followed by separation of serum by centrifugation. The serum obtained was subjected to biochemical assays. Thyroid stimulating hormones TSH, T3 and T4 concentrations were measured using the Vidas® Thyroid kit (BioMerieux SA 376 Chemin 69280 Marcy-l'Etoile - France). Fasting blood glucose (FBG) was estimated by colorimetric enzymatic method (Spain kit). Lipid profile test (LPT) included total cholesterol (TC), high-density lipoprotein (HDL), Low density lipoprotein (LDL) and triglycerides (TG), which was estimated by enzymatic colorimetric methods using kits CHOD-PAP and GPO-PAP (Spectrum, Egypt) and Spin-react (SPINREACT, Spain).

**Statistical analysis**

Data obtained was subjected to statistical analysis using the student's t-test (SPSS software, ver.24). A P-value ≤0.001 was considered statistically significant.

**RESULTS**

We analyzed the difference in TSH, T3 and T4 hormonal levels in hypothyroid and normal females. Our results showed that, while there is a significant increase in the TSH, T4 was significantly lower in cases as compared to controls (Table 1).

Hypothyroid subjects also exhibited an increase in lipid profile parameters TC (257.66±11.25), TG (222.60±19.13), HDL (39.31±0. 80), and LDL (103.80± 7.66) levels in comparison to control group, the difference of which was statistically significant increase (P≤0.001) (Table 2).

**Table 1:** Thyroid hormone levels in normal and hypothyroid female patients

Parameters	Group	n	Mean	SEM	P value
TSH (µIU/ml)	normal	15	2.13	0.18	0.001
	patient	35	9.90	0.55	
T3 (ng/dl)	normal	15	1.82	0.10	0.720
	patient	35	1.76	0.09	
T4 (µg/dl)	normal	15	102.40	4.74	0.001
	patient	35	64.96	3.56	

n= number of subjects; SEM= Standard Error Mean

Similarly, in hypothyroid cases a significant increase in FBG levels was seen as compared to normal (Table 3). A correlational analysis to determine the association between age and the serum parameters tested revealed that there was no positive correlation between age and lipid profiles or thyroid hormone levels (Table 4) or FBG levels (Table 5). However, significant positive correlation was seen between FBG and T4 hormone levels (Table 5). There was no correlation found between age and lipid profile or between FBG and lipid profiles (Table 6). No significant difference was found between age groups of patients with serum lipid profiles (TC, TG, HDL and LDL), thyroid function tests (TSH, T3 and T4) and fasting blood glucose (FBG) levels (Table 7).

**Table 2:** Lipid profile of female hypothyroidism patients as compared to normal healthy females

Parameters	Groups	n	Mean	SEM	P value
TC (mg/dL)	normal	15	156.67	7.00	0.001
	patient	35	257.66	11.25	
TG (mg/dL)	normal	15	106.27	15.96	0.001
	patient	35	222.60	19.13	
HDL(mg/dL)	normal	15	57.13	6.81	0.001
	patient	35	39.31	0.80	
LD (mg/dL)	normal	15	103.80	7.66	0.001
	patient	35	155.40	10.17	

n= number of subjects; SEM= Standard Error Mean

**Table 3:** Fasting blood glucose (FBG) levels in normal and hypothyroidism female patients

Parameter	Groups	n	Mean	SEM	P value
FBG (mm/l)	normal	15	99.47	10.63	0.001
	patient	35	170.11	14.71	

n= number of subjects; SEM= Standard Error Mean

**Table 4:** Correlation between age, lipid profile and thyroid hormonal levels in females with hypothyroidism

Parameters	Age	TC	TG	HDL	LDL	TSH	T3
TC (mg/dL)	-.177						
TG (mg/dL)	-.135	-.057					
HDL (mg/dL)	.179	-.149	-.209				
LDL (mg/dL)	-.047	.295	.254	-.129			
TSH (μIU/ml)	-.125	-.086	.011	.004	.195		
T3 (ng/dl)	-.168	.209	-.249	-.006	-.287	-.044	
T4 (μg/dl)	.040	.184	.012	.270	.025	-.153	.063

**Table 5:** Correlation between age, thyroid hormone and fasting blood glucose (FBG) in hypothyroid female patients

Parameters	Age	TSH	T3	T4
TSH (μIU/ml)	-.125			
T3 (ng/dl)	-.168	-.044		
T4 (μg/dl)	.040	-.153	.063	
FBG (mm/l)	.136	-.007	-.180	.504**

\*\*significant correlation at the 0.01 level (2-tailed)

**Table 6:** Correlation between age, fasting blood glucose (FBG) and lipid profile test in hypothyroid patients

Parameters	Age	FBG	TC	TG	HDL
FBG	.136				
TC (mg/dL)	-.177	.038			
TG (mg/dL)	-.135	.082	-.057		
HDL(mg/dL)	.179	.272	-.149	-.209	
LDL (mg/dL)	-.047	.140	.295	.254	-.129

**Table 7:** Relationship of age with lipid profile, thyroid function and FBG

Parameters	Age groups	n	Mean	SEM	P value
TC (mg/dL)	20-29	11	253.55	19.35	0.36
	30-39	11	280.64	22.30	
	40-49	13	241.69	17.06	
TG (mg/dL)	20-29	11	233.82	37.38	0.74
	30-39	11	234.55	44.83	
	40-49	13	203.00	18.40	
HDL (mg/dL)	20-29	11	39.36	1.25	0.30
	30-39	11	37.64	1.60	
	40-49	13	40.69	1.27	
LDL (mg/dL)	20-29	11	144.36	14.87	0.53
	30-39	11	172.27	22.14	
	40-49	13	150.46	16.03	
TSH (μIU/ml)	20-29	11	9.94	0.91	0.96
	30-39	11	10.08	1.05	
	40-49	13	9.71	0.95	
T3 (ng/dl)	20-29	11	1.82	0.17	0.32
	30-39	11	1.92	0.20	
	40-49	13	1.59	0.11	
T4 (μg/dl)	20-29	11	68.36	4.97	0.58
	30-39	11	59.39	7.10	
	40-49	13	66.79	6.36	
FBG (mm/l)	20-29	11	157.09	21.93	0.62
	30-39	11	160.64	23.56	
	40-49	13	189.15	29.54	

n= number of subjects; SEM= Standard Error Mean

## DISCUSSION

Hypothyroidism, a common hormonal disorder has been strongly linked to thyroid hormone secretion and metabolic rate (9). These hormones affect protein, carbohydrates and fat metabolism and decreased hormonal levels could result in clinical conditions such as decreased fertility, coma, congestive heart failure, and electrolyte abnormalities (7). The significantly increase in TSH levels seen in cases as compared to normal subjects in this study, could be attributed to the deregulation of the hypothalamus pituitary axis causing neuroendocrine dysfunction (8). Furthermore, decrease in T4 hormone levels in the case of hypothyroidism most often manifests by decrease physical and mental activity due to reduction in metabolic function (9). The increase in TSH and T4 levels and a decline in T3 hormonal levels seen in this study are in agreement with previous studies (13-15). Studies have shown that the pituitary gland secretes thyroid stimulating hormone as a result of the negative feedback process. High levels of T3/T4 exert a negative feedback on the anterior pituitary decreasing TSH secretion, while low levels of T3/T4 increase TSH serum concentrations (10).

As regards age factor our observation was compatible with an earlier study that focused on hypothyroid women (11). Women are shown to be six times more prone than males to have hypothyroidism which could be related to the secretion of high level of estrogen that leads to antagonistic effect on the hormones T3 and T4 that competes with them for binding sites on the receptor proteins. Research also showed that increased disturbance of thyroid gland in females is related to sexual hormone progesterone and estrogen that can cause nervous tension during menstrual cycle or pregnancy (17). Estrogen also regulates the transport proteins that bind to thyroxin (TBG) by decrease removal process from the blood and enhanced production that estrogen hormone causes activated immune system for increased production of anti-thyroid antibodies (ATA; 12)

Our results showed that lipid profiles, FBG and thyroid hormone levels are not related to age in normal and hypothyroid patients which is in agreement with a previous study (13). Our study also found an increase in lipid profiles (TC, TG, LDL) and decrease in (HDL) in hypothyroidism patients which agrees with an earlier study, wherein they report a high increase in LDL, TC levels in 88 women aged 20–35 years with hypothyroidism at Misan City as compared to control (14). Also result in agreement with (14) found increase in (LDL) low density lipoprotein and decrease in (HDL) HDLs are increased risks factors for cardiovascular diseases (CVD) due to endothelial dysfunction, coagulation disturbances metabolic, hormonal, and hemodynamic changes related with altered lipid profile (10). A statistical significant link

observed between high blood TC, TG, LDL, and low HDL levels among patients in this study, is consistent with an earlier study (15), wherein it was reported that the increase in LDL, TC and TG of hypothyroidism may be related to secretion of thyroid hormones which in turn can have an effect on the metabolism of HDL by transfer of cholesterol ester transfer protein (CETP) from (HDL2) to very low density lipoproteins (VLDL) and TG (13) found highly increase statically ( $p \leq 0.0001$ ) in TC, LDL while decrease in (HDL) but there is no any significant change in TG associated to control (3). The study also found hyperlipidemia and increase atherosclerotic development in the patients of hypothyroidism due to elevated LDL-C, TC, and TG related with thyroid hormones deficiency, this fact expression when thyroid hormone modulated LDL receptors in which decrease binding ligand of lipoprotein receptors produce by liver finally Increase level of TC and TG. Studies also found the same result of hyperlipidemia in the patients suffering from hypothyroidism (20,21).

The thyroid gland plays an important role in the glucose homeostasis (16). Increased concentration of FBG in females with hypothyroidism seen in this study agrees to a previous study (17) and has been attributed to thyroid dysfunction associated with poor glycemic control. In a recent study, FBG was considered a risk factor for hypothyroidism in patients with "type2 diabetes mellitus"(18). In yet another study, high prevalence of thyroid dysfunction (24.2%) was found in women associated with type 2 diabetes mellitus between age of 51-70 years and obesity (BMI >30 kg/m<sup>2</sup>) (19). Although the mechanism of thyroid dysfunction with diabetes mellitus is still unclear, it has been suggested that thyroid antibodies and autoimmune etiology to be the causative factors, involved in the complex interaction for insulin signals pathway and modulation feedback mechanism of thyroid hormones (24-26).

The increase in blood glucose is associated with insulin resistance, as an inverse correlation exists between insulin resistance and cells function and stimulating thyroid hormone concentrations, which is mediated by  $\beta$ -cells dysfunction (20). Studies have shown that 66.7 percent of 60 type 2 diabetic Kurdish females had primary hypothyroidism (21). Other experiment by (22) occur on 415 patients at Al-Diwaniya Teaching Hospital found increase of abnormal thyroid morphology (ATM) and increase disorders in thyroid function in the patients of female diabetic mellitus, and this agree with a similar study in Baghdad (23). Our result also agree with (24) increase FBG in females of hypothyroidism in Baghdad that can be related to because the majority of hypothyroidism patients have glucose and insulin metabolic problems, such as insufficient insulin production hyper-insulinemia, altered peripheral glucose elimination. Hypothyroidism can cause

insulin-resistant status, due to insulin receptor defects and pathogenesis mechanisms which include abnormal phosphorylation of insulin signaling proteins, altered composition of muscle fiber, decrease in trans-capillary insulin delivery, reduce glycogen synthesis, and impaired mitochondrial oxidative phosphorylation (25).

## CONCLUSION

Hypothyroidism disorder causes increase in LDL, TC, TG levels, leading to dyslipidemia which could be a risk factor for cardiovascular disease in these patients. Hypothyroidism has a major effect on glucose metabolism which could lead to diabetes in these patients.

## CONFLICT OF INTEREST

Authors declare that there is no conflict of interest.

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