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Association between Biochemical Parameters (T3, T4, and TSH) and the Lipid Profile in Female Type-2 Diabetes Patients

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Diabetes mellitus (DM) in female is a complex metabolic and endocrine illness induced by environmental and genetic variables that alters the functionality of insulin on peripheral tissues and pancreatic cells, which occurs because cells do not recognize and respond to insulin if it is not treated properly.
The objective: **to analyses lipid peroxidation markers, thyroid hormones, and vitamins E and D in females with type 2 DM (T2DM) to determine whether low vitamin E and D levels affect *HbA1c*.**
***Materials and methods*. The research was conducted in Specialized Center for Endocrinology and Diabetes (Al-Rusafa, Baghdad) for the period from 1.10.2021 to 20.12.2021. The study included 150 blood samples from healthy people (n = 50) and women with T2DM (n = 100). The levels of triiodothyronine (T3), thyroid-stimulating hormone (TSH), cholesterol, *HbA1c*, and glucose were determined by enzyme-linked immunosorbent assay.**
***Results*. The patients with T2DM had significantly higher levels of glucose (229.14 ± 10.62 mg/dL; p < 0.05) than persons in the control group (104.68 ± 21.09 mg/dL), and total cholesterol (235.17 ± 9.14 and 152.42 ± 8.48 mg/dL (p < 0.05), respectively). In patients with T2DM triglyceride levels (314.22 ± 29.73 mg/dL) were higher than controls, although high-density lipoprotein levels were lower. Low density lipoprotein levels were greater than the control group (133.62 ± 9.91 and 73.15 ± 6.72 mg/dL, respectively). The patients with T2DM had lower T3 and T4 concentrations (1.08 ± 0.11 and 58.02 ± 7.42 nmol/L, respectively), while their TSH concentration (4.94 ± 0.51 mIU/L) was greater (p < 0.05) than controls.**
***Conclusions*. Women with T2DM showed increased total cholesterol, triglycerides, low and very low-density lipoproteins. However, T2DM patients had far lower high-density lipoproteins, T3, and T4 levels than controls. A significant difference in the concentration of thyroid-stimulating hormone was found between female with T2DM patients and the control group (p < 0.05).**
Keywords: *low-density lipoproteins, high-density lipoproteins, thyroid-stimulating hormone, thyroxin, diabetes mellitus.*

Зв'язок між біохімічними параметрами (Т3, Т4 і ТТГ) та ліпідним профілем у жінок, хворих на цукровий діабет 2-го типу

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Цукровий діабет (ЦД) у жінок – це складне метаболічне та ендокринне захворювання, спричинене екологічними й генетичними факторами, які змінюють функціональність інсуліну на периферичних тканинах і клітинах підшлункової залози, що відбувається через те, що клітини не розпізнають і не реагують на інсулін, якщо захворювання не лікувати належним чином.
Мета дослідження: проаналізувати маркери перекисного окиснення ліпідів, гормони щитоподібної залози та вітаміни Е і D в жінок із ЦД 2-го типу, щоб визначити, чи впливає низький рівень вітамінів Е та D на концентрацію глікованого гемоглобіну (*HbA1c*).
Матеріали та методи. Дослідження проведено в Спеціалізованому центрі ендокринології та діабету (Аль-Русафа, Багдад) за період із 10.01.2021 по 20.12.2021. Дослідження включало 150 зразків крові здорових людей (n = 50) і хворих на ЦД 2-го типу в жінок (n = 100). Методом імуноферментного аналізу визначали рівні трийодтироніну (Т3), тиреотропного гормону (ТТГ), холестерину, *HbA1c*, глюкози.
Результати. У пацієнтів із ЦД 2-го типу встановлено значно вищі рівні глюкози (229,14 ± 10,62 мг/дл; p < 0,05), ніж у контрольній групі (104,68 ± 21,09 мг/дл), загального холестерину (235,17 ± 9,14 та 152,42 ± 8,48 мг/дл (p < 0,05) відповідно). У пацієнтів із ЦД 2-го типу рівень тригліцеридів (314,22 ± 29,73 мг/дл) був вищим, ніж у контрольній групі, хоча рівень ліпопротеїдів високої щільності був нижчим. Рівень ліпопротеїдів низької щільності був вищим, ніж у контрольній групі (133,62 ± 9,91 та 73,15 ± 6,72 мг/дл відповідно). Пацієнти із ЦД 2-го типу мали нижчі концентрації Т3 і Т4 (1,08 ± 0,11 та 58,02 ± 7,42 нмоль/л відповідно), тоді як концентрація ТТГ (4,94 ± 0,51 мМО/л) перевищувала показник контрольної групи (p < 0,05).
Висновки. У жінок із ЦД 2-го типу спостерігалося підвищення загального холестерину, тригліцеридів, ліпопротеїдів низької та дуже низької щільності. Однак пацієнти із ЦД 2-го типу мали значно нижчі рівні ліпопротеїдів високої щільності, Т3 і Т4, ніж здорові жінки. Достовірна різниця в рівнях тиреотропного гормону була виявлена між пацієнтками ЦД 2-го типу та контрольною групою (p < 0,05).
Ключові слова: *ліпопротеїди низької щільності, ліпопротеїди високої щільності, тиреотропний гормон, тироксин, цукровий діабет.*

Diabetes mellitus (DM) in females is a complex metabolic and endocrine illness induced by environmental and genetic variables that alters the functionality of insulin on peripheral tissues and pancreatic cells. Obesity and excess weight can favor type 2 DM (T2DM) development [1]. Diabetes-related insulinemia may be comparable to euglycemic persons' insulinemia in hyperglycemia. Insulin resistance (IR) is a lowered insulin level [2]. In insulin-resistant cells, insulin hyper secretion compensates for hormonal inactivity. Hyperglycemia occurs when insulin secretion to glucose stimulation is low [3]. T2DM mechanisms of lipotoxicity and glucotoxicity were established in 1990 and supported by studies on animals that were later confirmed in people. Glucotoxicity is the deleterious impact of persistent hyperglycemia on cell function and structure, while hyperglycemia can limit hormone synthesis by reducing insulin messenger ribonucleic acid (RNA). Glucose can destroy genetic information that is important for insulin manufacture. Low activity of phospholipase C, an enzyme needed to create inositol phosphates that secrete insulin by raising intracellular calcium, may also contribute to glucotoxicity. Also, glucose, which functions as a free radical, may cause cell cytotoxicity and death. Randle suggested in 1963 that triglyceride breakdown increases free fatty acid (FFA), which affects the cardiovascular system. Due to enhanced lipolysis, FFA are mobilized and oxidized more in the liver and muscles. In the first phase, glucose use decreases, and hepatic gluconeogenesis increases [4]. This causes hyperglycemia and inhibits insulin production, raising serum glucose levels. FFA deposit as triglycerides in muscles. Increased reactive oxygen species (ROS) in cells reduces insulin gene expression. In T2DM etiology, lipotoxicity favors IR and damages cells. Glucose is a sugar crucial for human health since it participates in many biochemical reactions. It produces adenosine 5'-triphosphate (ATP) and nucleosides through glucose metabolic and pentose phosphate pathways. These processes require many transporter proteins to assist in transferring glucose across cells, and the most notable ones are glucose transporter-2 (GLUT-2) and sodium/glucose cotransporter 1 (SGLT1). Glucose enters small intestinal epithelial cells from the intestinal lumen by crossing the brush boundary membrane via the SGLT1 cotransporter. It exits the cells by traversing the basolateral membrane through the activity of the GLUT-2 transporter, supplying energy throughout the body. Dysregulation of these glucose transporters is involved in the pathogenesis of several metabolic diseases, such as diabetes. Natural loss of GLUT-2 or its down regulation causes abnormal blood glucose concentrations in the body, such as fasting hypoglycemia and glucose tolerance. Therefore, understanding GLUT-2 physiology is necessary for exploring the mechanisms of diabetes and targeted treatment development [5]. Chronic ROS production by mitochondria may contribute to the development of IR, a primary feature of type 2 diabetes. Diabetes and thyroid problems interact in complex ways. T2DM is also linked to subclinical hypothyroidism, nephropathy, cardiovascular disease, and retinopathy [6]. Changes of thyroid function often related to the female reproductive disturbances [7], such as polycystic ovary syndrome [8], infertility, and premenstrual syndrome [9]. The American Diabetic Association screens diabetics for thyroid issues [10]. T2DM in females is a prevalent metabolic illness, which is characterized by high free radical production. Hyperglycemia has been linked to elevated levels of lipid peroxidation and ROS through many mechanisms, including: 1) direct glucose auto-oxidation, 2) activation of glycolysis pathways and the RAGE receptor, and 3) stimulation of nitric oxide-superoxide anion interactions that lead to nitric oxide peroxynitrites and hydroxyl radicals. Polyol and nicotinamide adenine dinucleotide phosphate (NADPH) oxidase activation protein kinase C (PKC). PKC pathway is also increased along with various lipoxygenase enzymes. Low-density lipoprotein (LDL) oxidation affects atherosclerosis in T2DM. LDL makes up the lion's share of the cholesterol in the bloodstream, which is why it's so dangerous. A person's risk of heart disease grows when their blood LDL cholesterol levels rise. Because of the increased pressure in the blood vessels, blood clots may develop or fragments can break off and move through the body, increasing the risk of a heart attack or a stroke and exposing the body to high levels of LDL cholesterol. Polyunsaturated fatty acids (PUFA) lipid peroxidation may be a reliable sign of oxidative stress in diabetes, a lipid peroxidation end product, lowers membrane fluidity and alters membrane-bound enzymes and receptors. Diabetes and vitamin D (also referred to as calciferol) deficiency may cause osteoporosis, metabolic syndromes and polycystic ovary syndrome [11]. Inactivity, obesity [12], and aging are risks. Older males with vitamin D deficiency release more insulin after eating glucose. Multiple studies suggest that 25-hydroxyvitamin D levels predict diabetes-related renal and cardiovascular disease. Diabetes, kidney/liver disease, and vitamin D deficiency may be connected. 25-hydroxyvitamin D improves insulinogenic markers in T2, obesity, and gestational diabetes. The current study aims to analyze lipid peroxidation indicators, such as MDA, thyroid hormones, are connected with elevated T2DM [13]. Can be caused by a variety of environmental and genetic factors. A person's weight is one characteristic that can be changed, but other characteristics, such as age, gender, and genetics, are out of a person's hands. T2DM has been linked to people who don't get enough sleep. However, metabolic processes may be affected. Diet of the mother may influence deoxyribonucleic acid methylation during development of the fetus. *Prevotella copri* and *Bacteroides vulgatus*, two gut bacteria, have been associated to T2DM [14]. World Health Organization (WHO) recommends screening exclusively for high-risk groups. Obese women, those who have had gestational diabetes, or who have polycystic ovary syndrome, and those over the age of 65 years are all considered high-risk groups in the United States, as are those with a close family member who has diabetes [15].

The objective: to evaluate lipid peroxidation markers, represented by MDA, thyroid hormones and finding statistical differences for women in T2DM.

MATERIALS AND METHODS

The study included 150 T2DM patients in the Specialized Center for Endocrinology and Diabetes (Al-Rusafa, Baghdad) for the period from 1.10.2021 to 20.12.2021. The age of participants ranged from 15 till 68 years The sam-

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Table 1

A list of instruments used in this study

Instruments and glasses	Company	Country
Spectrophotometer(UV-Vis)	Biobase	India
ELISA	Labon	China
Centrifuge	Memmert	Germany
Light microscope	Olympus	Japan
Oven	Memmert	Germany
Water bath	Memmert	Germany
Shaking water bath	Memmert	Germany
Sysmex device	Sysmax	Japan
Pipette	BioSan	Germany
Refrigerator	BEKO	Turkey
Different glasses	–	China

Table 2

A list of kits used in this study

Apparatus	Company	Origin
Triiodothyronine (T3)	BioMérieux	France
Thyroxine (T4)		
Thyroid-stimulating hormone (TSH)		
Cholesterol kit	Linear chemicals	Spain
Triglycerides kit		
HDL cholesterol kit		
HbA1c kit	Certified com	Sweden
Glucose kit	BioCon	Germany

Table 3

Glucose levels in the several groups that were examined

Variable	Control (n = 50)	T2DM patients (n = 100)	p-value
Glucose, mg/dL	104.68 ± 21.09	229.14 ± 10.62	0.0001

ples included 150 T2DM patients (100 females) and this study also included 50 healthy women. T2DM patients were diagnosed by an endocrinologist and the statistical mean of blood glucose concentration was considered 100 mg/dL, which is called the optimal level. A reading of more than 200 mg/dL after two hours means diabetes was diagnosed. A reading between 120 and 199 mg/dL means you have prediabetes. Subjects were instructed to fast for 10–12 hours before to the blood and urine tests (patients and healthy people). Ethylenediaminetetraacetic acid tubes (EDTA) and gold-top serum separator tubes were used to preserve the samples. In Eppendorf tubes, the serum blood samples were centrifuged for 10 minutes at 3500 rpm in order to separate them. It was necessary to dissolve all of the samples so that biochemical examination could be carried out. The mean duration of diabetes among subjects who reported diabetes at baseline was 15.6 ± 9.3 years (mean 16.7 years). All instruments and kits used in this study were included, as shown in Table 1 and Table 2.

Glucose-lowering drugs are available in a wide range. In the treatment of T2DM, metformin is the drug of choice. If metformin doesn't work, one might try another oral drug. Thiazolidinediones, glucagon analogs, and dipeptidyl peptidase-4 inhibitors are not included in this list of glucagon-like peptide-1 and glucagon analog analogs. Patients with severe renal or hepatic illness should not use Metformin. As a standalone treatment or in combination with other drugs, insulin injections may be utilized. The vast majority of the time, insulin is unnecessary. Long-acting drugs, such as those taken orally, are almost often given before bedtime. After this, the dose is increased to the therapeutic amount (good control of blood sugar levels). Diabetes patients may improve their blood sugar management by using non-insulin supplements twice day. There seems to be no advantage to long-acting insulin (glargine and detemir), but their high manufacturing costs have rendered them uneconomical since 2010. For pregnant women, insulin is the most effective therapy [16].

Minitab was used to do statistical analysis on the data, which was run on a computer that also had SPSS Statistics for Windows, Version 20.0 and Microsoft Excel XP installed. Various notations were used to represent the data, including the mean, SD, and the lowest and maximum values. According to ANOVA, it was determined whether there were statistically significant differences in results between groups. Duncan's Multiple Range Test was employed to compare the data means on this specific instance. Duncan's Multiple Range test is a post hoc test to measure specific differences between pairs of means.

RESULTS AND DISCUSSION

Glucose concentration:

It appeared in T2DM patients (229.14 ± 10.62 mg/dL) was significantly higher ($p < 0.05$) than in the control group (104.68 ± 21.09 mg/dL; Table 3). Average age of patients was 32.6 years.

Patients with T2DM, according to a recent study, have elevated blood glucose levels. A considerable rise in blood glucose levels has been shown to accompany T2DM in both those without issues and those with them, according to this study's findings [17]. Insulin secretion or resistance, as well as sustained rises in blood sugar levels, can lead to a wide range of diabetes problems such as the breakdown of molecules and membranes. Chronically elevated blood sugar levels are linked to the development of inflammatory damage in the body in diabetics with T2DM [18]. Glucose levels in the blood are maintained by the pancreatic ß-cells, which produce insulin. Peripheral tissue cells with diminished insulin sensitivity are said to be insulin resistant. When insulin levels become chronically elevated, it is known as hyperinsulinemia [19]. The findings of are consistent with data of L. A. Vázquez et al. [20].

Lipid profile

The total cholesterol level in the patients with T2DM (235.17 ± 9.14 mg/dL) was significantly($p < 0.05$) higher than in the control group (152.42 ± 8.48 mg/dL; Table 4). The triglyceride level in T2DM patients (314.22 ± 29.73 mg/dL) was significantly ($p < 0.05$) higher than in the control

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Table 4

Lipid profile of the groups tested

Groups variables	Control (n = 50)	T2DM patients (n = 100)	p-value
Total Cholesterol, mg/dL	152.42 ± 8.48	235.17 ± 9.14	0.0001
Triglyceride, mg/dL	139.52 ± 6.36	314.22 ± 29.73	0.0001
HDL, mg/dL	52.84 ± 3.16	40.51 ± 2.52	0.037
LDL, mg/dL	73.15 ± 6.72	133.62 ± 9.91	0.0001
VLDL, mg/dL	27.51 ± 2.53	62.49 ± 5.61	0.0001

group (139.52 ± 6.36 mg/dL). High-density lipoprotein (HDL) level in T2DM patients (40.51 ± 2.52 mg/dL) was significantly ($p < 0.05$) lower than in the control group (52.84 ± 3.16 mg/dL). LDL levels in T2DM patients (133.62 ± 9.91 mg/dL) were significantly ($p < 0.05$) higher than in the control group (73.15 ± 6.72 mg/dL). Very LDL (VLDL) concentration in T2DM patients (62.49 ± 5.61 mg/dL) was significantly ($p < 0.05$) higher than in the control group (27.51 ± 2.53 mg/dL).

DM with uncontrolled dyslipidemia might worsen the cardiovascular disease already present in diabetics. Obesity, on the other hand, is a well-known risk factor for both T2DM and dyslipidemia [21, 22]. FFA reach the liver and produce dyslipidemia in diabetic patients, resulting in high triglyceride, LDL, and VLDL levels and low HDL levels. Blood Apo lipoprotein B (ApoB) and VLDL production is boosted by increased triglyceride synthesis in the liver. In return for HDL-carrying cholesteryl ester, VLDL exchanges triglyceride for cholesterol ester via cholesteryl ester protein. Increases in triglyceride and VLDL levels are the result of this. Triglyceride-rich HDL is hydrolyzed by lipoprotein lipase, which is found in the liver and excreted in the urine by the kidneys glomeruli [23]. Additionally, IR in the management of Apo lipoprotein A1 (ApoA1) production can produce low HDL-C in diabetes. It has been found IR and eventually ApoA1 dysfunction are the results of an increased inflammatory cytokine like tumor necrosis factor alpha as a third pathogenic mechanism of dyslipidemia in diabetes [24]. It is typical for obesity to result in dyslipidemia, which is characterized by high fasting and post-prandial triglyceride, LDL and low HDL-C levels. Problems with lipid profiles are frequently caused by elevated levels of triglycerides. Patients with diabetes are more likely to have higher levels of triglycerides than those with normal blood sugar levels [25]. This contradicts prior studies, which indicated a significant difference between the increase in blood sugar and the amount of LDL ($p = 0.0102$). Found that if blood sugar levels are greater than usual, the ratio of cholesterol to triglycerides rises above the safe level. This is in contrast to the HDL ratio (at $p = 0.01$ level probability) [26]. This is supported by the results of the investigation. Investigation on the relationship between triglycerides and cholesterol is ongoing. Lipid digestion in diabetic patients' blood is sped up due to insulin's control of lipolipase (LPL), an enzyme protein. According to earlier studies, there was a link between insulin hormone levels

Table 5

Thyroid hormones in studied groups

Hormones	Control group (n = 50)	T2DM patients (n = 100)	p-value
T4 (nmol/L)	74.25 ± 3.81	58.02 ± 7.42*	0.0001
T3 (nmol/L)	1.84 ± 0.25	1.08 ± 0.11*	0.0001
TSH (mIU/L)	3.71 ± 0.42	4.94 ± 0.51*	0.0001

and VLDL levels (325.0) in the type 1 DM (T1DM) [27]. Found a correlation point between fasting blood sugar and IR, with a correlation ratio of 453.0, and blood sugar with triglyceride and HDL, with a correlation ratio of 347.0, which is consistent with the results of the HDL search (322.0). They also established a correlation between IR and the (triglyceride / HDL) concentration of 450.0, which matches the findings of the inquiry into HDL concentration (0.292). For those who have T2DM, the LDL triglyceride content is increased as well as the quantity of dense LDL particles. Diabetes sufferers with *HbA1c* levels over 8% had thicker LDL compared to those with *HbA1c* levels under 8% [28]. Small, thick LDL particles have been associated to an increased risk of cardiovascular disease. According to a number of studies, small dense LDL particles may be atherosclerotic. Macrophages preferentially choose tiny, compact LDL particles that have a lower affinity for the B/E receptor and hence form foam cells, as a result of this process. In order for tiny dense LDL particles to penetrate artery walls, they must have a greater affinity for intimal proteoglycans [29].

T3 concentration in T2DM patients (1.08 ± 0.11 nmol/L) was significantly lower ($p < 0.05$) than in the control group (1.84 ± 0.25 nmol/L), while T4 concentration in T2DM patients (58.02 ± 7.42 nmol/L) was significantly lower ($p < 0.05$) than in the control group (74.25 ± 3.81 nmol/L). TSH levels in T2DM patients (4.94 ± 0.51 nmol/L) were significantly higher ($p < 0.05$) than in the control group (3.71 ± 0.42 nmol/L). Average age of patients (32.6), as shown in Table 5.

TSH and T4 levels in peripheral tissues are changed into T3 as a result of diabetes inhibiting thyroid function [30]. No TSH peak at night and the TSH response to the TSH hormone is reduced in patients with T2DM and euthyroid thyrotropin-releasing hormone (TRH). Although the hypothalamic-pituitary-thyroid axis is under the control of the circadian clock via the suprachiasmatic nucleus pacemaker, daily TSH secretion profiles are disrupted in some patients with hypothyroidism and hyperthyroidism. On the TDI (Time Dependent Inhibition) scale, long-term hyperglycemia has a cumulative effect [31].

Thyroid function tests should be interpreted with care in the presence of diabetes ketoacidosis and other life-threatening acute diseases, such as septic shock, diabetic ketoacidosis is a severe systemic disease which along with reduction in T3 level, T4 level is also decreased, and TSH level is normal (Fig. 1–3). The changes in thyroid hormones are reversed to normal after treatment of ketoacidosis so it is recommended in interpreting results of thyroid function tests in these patients we should consider these facts and thyroid function test should be repeated after treatment.

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Hyperinsulinemia and IR both raise the risk of nodular thyroid disease and the size of the goiter [32]. Compared to non-diabetic controls, T1DM patients exhibited substantially higher blood TSH concentrations (p = 0.008). Researchers who studied thyroid function and thyroid autoimmune disease in Africans with T1DM found similar results to ours [33]. Thyroid hormone levels were significantly lower in T1DM patients compared to both the control and T2DM groups. Subclinical hypothyroidism was found in 21% of the 28 individuals with T1DM. As a result of the Rotterdam Study, patients with higher TSH levels in the normal range had a larger risk of developing T2DM than those with lower TSH levels within this range [34]. Euthyroidism was defined as being within the reference range (0.4–4.2 mIU/L in the Korean analysis, 0.4–4.0 mIU/L in the Rotterdam Investigation, and 0.35–5.0 mIU/L in this study). A higher plasma TSH reference value (0.62–6.68 mIU/L in 6,564 individuals) was found in a different Korean study of the same population which used Western values to establish the range for Korean research. 30% of diabetes patients had greater TSH values than normal controls (p = 0.01), which is a significant difference (p = 0.001) [35]. Hypothyroidism is more common among people with T1DM than in the general population, and women are twice as likely as men to suffer from it (41 vs 19%). 500 Egyptian youngsters with T1DM and 500 Egyptians who were neither diabetic nor hypothyroid were examined. Figures from this investigation show that the prevalence of subclinical hypothyroidism is 11.2% (TSH 5 mIU/L, p = 0.001) [36]. TSH levels in type 1 diabetics were statistically significantly higher than in the control group, at 4.05 and 1.98 mIU/L, respectively (p = 0.008). A common tendency for autoimmune death of pancreatic islet cells and thyrocyte assault on the thyroid is the most plausible explanation. Some research shows that TSH levels in diabetics (1,981.01 vs 2,441.23 mIU/L) are significantly lower than in nondiabetics (p = 0.05). Low thyroid hormone levels in diabetics may be caused by a reduction in TRH synthesis. Hypothyroidism affected 89% of the participants in the research whereas hyperthyroidism affected 11% [37]. Subclinical hypothyroidism and hypothyroidism were the most common thyroid disorders [38]. Hypothyroidism is the most frequent thyroid illness among people with T2DM, according to the research of C. E. Udiong et al. [21]. High and low levels of thyroid hormone in diabetics may be explained by changes in TRH production and release. Diabetics with low T3 levels were shown to have higher fasting glucose, *HbA1c*, and insulin levels, according to our research. In diabetics and non-diabetics, there was no significant difference in TSH concentrations. In a "low T3 state," total and free T3 levels in the blood are low, while T4 and TSH levels are normal, this is because hypothyroidism involves high levels of TSH and low levels of the thyroid hormones T4 and T3. However, in the clinical practice there are often people with low T3 levels with normal T4 and either low or normal TSH [39]. Free T4 levels rise while T3 levels fall as a result of insulin, an anabolic hormone, inhibiting the liver's ability to convert T4 to T3 [40]. Some diabetics have low thyroid hormone levels as a consequence of diabetes-induced decreases in thyroid hormone synthesis (TRH) and the lack of the nocturnal TSH peak. Diabetics with normal thyroid function are influenced by their glycemic state, which affects the levels of TRH and the TSH reaction to it. Diabetics and non-diabetics had no clinically meaningful differences in TSH levels in our study. Diabetics have varied amounts of thyroid hormones, according to results of V. Coiro et al., who discovered that this was the case [41]. Controlling diabetes may enhance TSH responses and the "low T3 state", however C-peptide negative individuals (those who have lost all pancreatic beta-cell activity) may not regain their

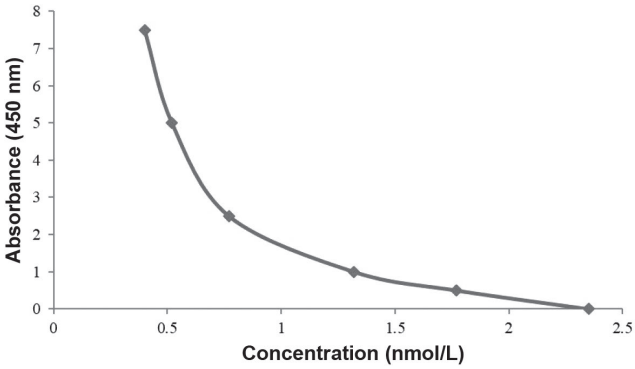

Fig. 1. Standard curve for the determination of T3 concentration

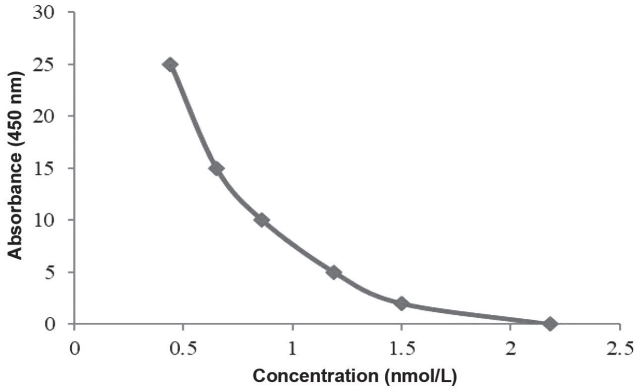

Fig. 2. Standard curve for the determination of T4 concentration

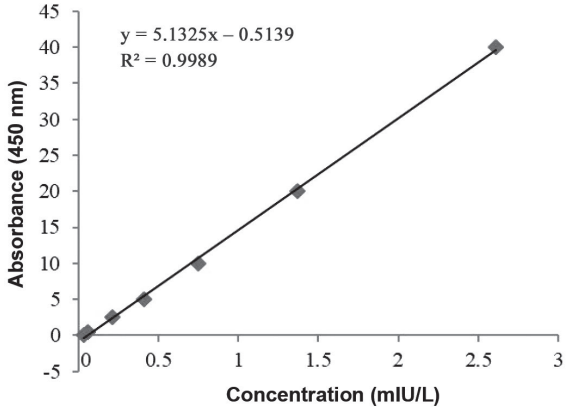

Fig. 3. Standard curve for the determination of TSH concentration

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regular nocturnal TSH peak even with strict diabetes management [42].

Thyroid status variations in T2 diabetics may be due to hypothalamic-pituitary-thyroid axis tolerance, which may explain reduced levels of T4 and T3 production. Since the activity of 5'-Adenine Mono Phosphate Activated Protein Kinase is diminished after acquiring T2DM, thyroid hormone synthesis is reduced. TSH is produced more often when the levels of thyroid hormone are lower [43]. Obesity and increased leptin levels are more common in those with T2DM. Lower levels of thyroid hormone production and greater levels of TSH are the outcome of T2DM being resistant to leptin [44]. T2DM patients' thyroid hormone production decreases as a result of the increased affinity of thyroid hormone to T4 [45]. T2DM causes the thyroidal converting enzyme T4-5'-deiodinase (THBI) to be inactivated. This technique reduces the amount of T4 to T3 conversion [46]. Consequently, T3 declines faster than T4 in diabetics. T3 levels decrease to their lowest point as a consequence of these factors [47]. The hypothalamic-pituitary-thyroid axis is also linked to obesity, stress, and infection, all of which may alter hypothalamus-pituitary-thyroid-axis levels and boost TSH level [48]. Metabolic disorders, diabetes, and thyroid function changes that are often associated with female reproductive disorders, such as polycystic ovary syndrome, infertility, premenstrual syndrome, etc. [49].

CONCLUSIONS

There was a significant difference between the T2DM patients in female and the non-diabetic group in terms of total cholesterol, triglycerides, LDL and VLDL. HDL levels were substantially lower in the T2DM group than in the control group ($p < 0.05$). The age range of these patients ranged from 15 till 68 years. Patients with T2DM in female had lower amounts of T3 and T4 than those in the control group ($p < 0.05$). There was a statistically significant difference in TSH levels between the T2DM patients in female and the control group ($p < 0.05$).

Ethics approval. We hereby declare that all information in this document has been obtained and presented in accordance with academic rules and ethical conduct. I also declare that, as required by these rules and conduct, I have fully cited and referenced all material and results that are not original to this work.

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