Investigation Role of Hormones and Lipid Profile in Diabetes Mellitus Type I Patients

Rieam Dakhel Muhsen[1], Jasim Abdulabbas Abdullah[2]*, Hasan Murtada Al-Kutubi[3]

[1,2] Kerbala University/College of Applied Medical Science – Department of Clinical Laboratories/Iraq

[3] Al-Hasan centers for diabetes and endocrinology in Al-Hussein medical city/Iraq

Email: jassem.omran@uokerbala.edu.iq

Abstract

A study was conducted for 6 months starting from November /2021 to April/2022 in Al-Hassan center for diabetes and endocrinology in Al-Husain medical city of Karbala. The total number of participants are (240) person include (150) patients with type I diabetes mellitus (TIDM), the males (54) (36 %), the females 96 (64%) and (90) healthy control group, males (36) (40%), females (54) (60%). there was a significant increase in concentrations of each hormone (Leptin, Gharlin, Obestatin and CCK) in patient's females than males when compared with control. also observed a significant increase in the levels of total CHO, TG, LDL and VLDL and a significant decrease in the levels of HDL in patients when compared with control, the rise in the lipid profile showed in females larger than males. This study clarified a several relationships between the physiological parameters in patients' group, there were significant positive correlation between age with duration, height, weight and BMI, also found positive correlation between cholesterol and with triglyceride and LDL and positive correlation between TG and VLDL. In addition to, positive correlation between CCK with leptin, Gharlin, Obestatin also there was positive correlation between leptin and both Gharlin, Obestatin.

Keywords: hormones; patients; health

1. Introduction

Diabetes mellitus is one of the most common endocrine disorders resulting from defects in insulin secretion or insulin action[1]. The primary sign of the diabetes is hyperglycemia in the blood, caused by insufficient pancreatic insulin secretion or low insulin-directed fostering of the glucose via target cells. DM could be classified to several the types, yet T1DM and T2DM are the two most common types. For T1DM, insulin renewal therapy is the backbone, while in T2DM, there should be lifestyle modification and a control diet [2] .Loss of functional β-cell mass is the key mechanism leading to diabetes mellitus as long as β-cells are able to compensate, for instance, for insulin resistance, normoglycaemia is preserved , The American Diabetes Association (ADA) defines type I diabetes mellitus (T1DM) as autoimmune β-cell destruction usually leading to absolute insulin deficiency and type II diabetes mellitus (T2DM) as progressive loss of β-cell insulin secretion frequently occurring on the background of insulin resistance. Novel ways of clustering patients with diabetes mellitus into subgroups that predict disease progression and risk of complications are being investigated [3]. T1DM is common worldwide and steadily increasing in frequency of incidence of about 3 % yearly. T1DM is responsible for about 5 % to 10% of total population of individuals who have diabetes, whereas T2DM has almost all cases. The number of individuals affected is predicted to rise to 642 million in 2040. (Mobasseri et al., 2020). In contrast to T2DM, in which both IR and decreased insulin secretion via the cells play a synergistic role, the pathogenesis regarding T1DM is caused by environmental, genetic, and immunologic factors which destroy the beta cells of endocrine pancreas and result in the insulin deficiency. It typically progresses over some period of several months to years throughout which period patients are asymptomatic, glycemic, and positive for the relevant autoantibodies. The autoimmune destruction process occurs in the persons who are genetically susceptible under triggering effects of at least one environmental factor [4]. Leptin and ghrelin are two orexitropic hormones with opposite effects on energy homeostasis, Leptin is one of many adipokines, which are humeral substances that the adipocytes release. Leptin is therefore largely produced by adipocytes and released from the small vesicles within adipocytes on a diurnal pulsatile basis, with higher rates early morning and in the evening. Leptin is circulated in the serum after being secreted in both a bound form and free form [5]. This hormone was at first thought to be used in the treatment of obesity because of its effectiveness in lowering food intake and body weight. Leptin resistance, or the inability of leptin to exert its anorexigenic effects in obese people, is defined as the lack of clinical utility of leptin in obesity. However, obese subjects have since been found to have high levels of circulating leptin and to be insensitive to the exogenous administration of leptin [6]. CCK can be defined as a peptide hormone regarding the gastrointestinal system accountable for stimulating the digestion regarding protein and fat. In the duodenum, the first section of the small intestine, enteroendocrine cells produce and secrete cholecystokinin, also synthesized

doi.org/10.31838/hiv22.02.537 Received: 26.06.22, Revised: 08.08.22, Accepted: 25.08.22

as pancreozymin. The pancreatic digestive tract's enzymes are secreted into the intestine as a result of the gallbladder contracting in reaction to the presence of partially digested food in the duodenum. The hunger is suppressed by this hormone. Cholecystokinin functions as a neurotransmitter in the brain that regulates satiety [7] .

2. Material and Methods

The current work was designed as case control study, which is also known as "prospective study" and "case-referent study [8] involved 240 individuals, 150 subjects of patients with TIDM, and 90 participants apparently healthy control group. Patients of different ages, ranging in age from one to fifty years, of both sexes, were diagnosed with T1DM. In the Al Naqaa laboratory of the Biochemistry Department, samples taken over a six-month period (November 2021 to April 2022) from the Al-Hassan center for diabetes and endocrinology in the Al-Husain medical city in the Kerbala Governorate were thoroughly processed.

Collection samples

With the use of a disposable syringe, five milliliters of venous blood were taken from each participant. Two portions of this blood were separated: (5 ml) was divided between two gel tubes and allowed to clot at the temperature of the room for about 30 min.

The gel tubes were after that centrifuged at 4000 x g to get serum, and the first gel tube containing the serum was utilized to automatically evaluate lipid profile and blood glucose.

The serum of the second gel tube was put into an Eppendorf tube and stored at a (-20oC) temperature until using it to estimate the hormones (leptin, ghrekin, obestatin and CCK).

3. Statistical Analysis

The version twelve of the computer program, SPSS, which has been utilized for data analysis. the data have been represented as mean standard deviation (± Sd). they were estimated differences among groups via using T test with the P value (i.e. the least significant difference) has been found for the comparison amongst the groups, and the results have been considered to have statistical significance at ($p \leq 0.05$).

4. Results and Discussion

leptin

Leptin concentrations for the control group and patients with T1DM are (2.443 and 2.963) nmol/mL, respectively, as can be seen from the statistical analysis regarding the results in table (1): there has been a significant increase (P more than 0.05) in the concentration of leptin in male patients with T1DM when put to comparison with control group. Leptin concentration for female control and patients who have T1DM is (2.029 and 3.059) nmol/ml, respectively. The same table shown a high significant increase (P less than 0.001) in leptin concentration in female patients when put to comparison to the control group. The concentration of leptin for the controls and patients with T1DM is (2.194 and 3.024) nmol/mL, respectively. There is also a highly significant increase (P less than 0.001) in leptin concentration in patients in comparison to controls. Finally, results have shown that there were no significant differences in leptin concentration between females and males in the patient group (p more than 0.05), but that there has been a significant increase (P less than 0.05) in males when compared with the females in control group (leptin concentration, 2.443 and 2.029 nmol/mL, respectively).

Table 1: Concentration of leptin in both patients with TIDM and control groups

Leptin	Patients	Control	P value
	Mean ± SD nmol/Ml	Mean ± SD nmol/mL	
Male	2.963±1.264	2.443±1.37	0.0678 *
Female	3.059±1.492	2.029±0.471	0.0001 **
Total	3.024±1.411	2.194±0.955	0.0001 **
P value	0.6905	0.0432 *	

* Means significance differences (p<0.05) ** means high significance differences (p<0.001)

The serum leptin level in this work's diabetic patients has been significantly higher compared to it in non-diabetic patients, and there have not been any significant gender differences in the T1DM patients. Particularly throughout pubertal development, the leptin data of T1DM patients in comparison with healthy controls are contentious. It has also been discovered that there is a relationship between diabetes HbA1c level and leptin level. The most recent findings contradict Ismail et al (2017). who claimed that there were no appreciable variations in leptin or adiponectin levels between control and diabetic patients. According to a different study Kapustin et al (2020). following comparing the leptin levels regarding pregnant women in groups with the three forms of diabetes and a group of healthy women, they found that, in contrast to the controls, all other groups had high levels of leptin in third trimester. Leptin concentrations measured in the morning tended to be higher in T1DM patients in comparison with controls yet were in the same range with a slight increase in the two groups after lunch. The concentration of leptin significantly reduced in the both controls and patients following breakfast and returned to initial concentrations around lunch time[11]. Disagreement with Abdul Dayem et al. (2017), who discovered that median (IQR) serum leptin level has been considerably lower in diabetic, overweight group II (5.2ng/ml - 24.8ng/ml) in comparison with non-diabetic, overweight group. This was explained by the possibility that the lower leptin concentrations in newly diagnosed T1DM patients may be brought on by an inadequate supply of insulin and increased lipolysis. Although there has not been any statistically significant difference between those two groups in terms of leptin or adiponectin levels, patients with T1DM had

somewhat higher levels than controls [13]. Both fasting and T1DM cause a significant decrease in leptin [14]. Those pathological conditions imply that the insulin results in stimulating the release of the leptin because children with new-onset T1DM and patients with insulinomas have high and low plasma leptin levels, respectively. Insulin therapy raises the levels of the leptin within 24 hours, reaching non-diabetic levels by 3 to 5 days, whereas the removal of the tumor restores plasma leptin to the normal levels [15]. Serum leptin levels in humans have been shown to positively correlate with BMI, body fat percentage, adipocytes' size and fat mass. Obesity-related enlargement of the adipocytes in the humans leads to accelerated leptin secretion and higher serum leptin levels that could result as well from the increased turnover of the cortisol and chronic hyperinsulinemia [15]. Its deficiency or resistance results in hyperphagia, obesity and diabetes mellitus, hormonal and metabolic factors affect leptin inclusive of insulin, steroid, thyroid and estradiol which stimulate, while testosterone inhibits leptin synthesis [16].

Ghrelin

According to the statistical analysis of table (2) for ghrelin, there were no significant differences (P more than 0.05) in concentration of ghrelin in male controls compared with male patients, the mean concentration of ghrelin for control and T1DM patients is (2.391 and 2.415) nmol/mL respectively. Ghrelin levels in female patients have been significantly higher (P less than 0.05) than in controls; their mean concentrations were (2.403 and 1.938) nmol/mL, respectively. Additionally, the concentrations of ghrelin for the control and T1DM patients' group (1.938 and 2.403 nmol/mL, respectively) increased significantly (P more than 0.05). Females and males in the patient group have ghrelin concentrations of (2.403 and 2.415) nmol/mL, respectively, in the same table, showing no significant differences (P more than 0.05). However, a significant rise in ghrelin levels (P less than 0.001) was identified between females and males in the control group (1.938 and 2.391 nmol/mL, respectively).

Table 2: Concentration of ghrelin in both patients with TIDM and control groups

Ghrelin	Patients	Control	P value
	Mean ± SD nmol/mL	Mean ± SD nmol/mL	
Male	2.415±1.18	2.391±0.766	0.9145
Female	2.403±1.344	1.938±0.517	0.0159 *
Total	2.411±1.237	2.119±0.663	0.0398 *
P value	0.9564	0.0012 *	
* means significance differences (p<0.05)		** means high significance differences (p<0.001)	

The results in table (2) support the existence of a relationship between ghrelin and T1DM. others studies demonstrated the ghrelin levels increase before meals and decrease after meals [17]. In comparison to non-diabetic controls and T1DM controls, the levels of ghrelin have been lower in the non-diabetic pregnant and T1DM pregnant women (p less than 0.005 and p less than 0.05, respectively). Both T1DM diabetic and non-diabetic women's lower ghrelin levels throughout pregnancy indicate that the ability to control one's appetite is impacted [18]. Despite studies suggesting that the levels of ghrelin fall with the beginning of T1DM, ghrelin also has protective effects on the β-cells by protecting them from programming death under conditions of T1DM [19]. They have noticed as well that the obesity could affect ghrelin levels because plasma ghrelin concentration levels have been lower in the patients with obesity, and that indicates that the obesity could impact regulations regarding production of ghrelin. Plasma ghrelin concentrations have been lower in the diabetic patients with poor long-term glycemic control compared to patients with the good long-term glycemic control. The fact that the levels of the ghrelin are assayed in research using various methodologies varies significantly across them, nevertheless, according to [20]. Since ghrelin has also been demonstrated to induce lipolysis, variations in its concentration were monitored. In the placebo group, ghrelin concentrations considerably increased. there were a trend toward a fall in the ghrelin in liraglutide group conclude that in the state of fasting, the patients who have inadequately controlled type I diabetes have ongoing ketogenesis and lipolysis, as it has been reflected in the progressive increase in the concentrations of β-hydroxybutyrate and FFA acetoacetate, administrating liraglutide results in inducing dramatic preventions of the increase in the acetoacetate and beta-hydroxybutyrate concentrations besides the reduction of the ghrelin, glucagon, and FFA concentrations [21].

Obestatin

Statistical analysis of obestatin concentration in the table (3) showing there were insignificance increase (P > 0.05) in obestatin concentration of patient males when compared with controls males, the obestatin concentration is (110.072 and 99.694) nmol/mL respectively. But in female's patients observed considerable rise in the obestatin concentration as a comparison to controls group (P < 0.001) the obestatin concentrations of patient's females and control is (113.675and 79.611) nmol/mL respectively. Also, in patients with TIDM observed considerable rise in the obestatin concentration as a comparison to controls group (P < 0.001) the obestatin concentrations of patients and controls is (112.378 and 87.645) nmol/mL respectively. Finally, showed no significance difference (P > 0.05) in obestatin

concentration between males to females for patients' group as concentration (110.072 and 113.675) nmol/mL respectively. Also found high significance increase (P < 0.001) in the obestatin concentrations of patient's females and males of control group (99.694 and 79.611) nmol/mL, respectively.

Table 3: Concentration of Obestatin in both patients with TIDM and control groups			
obestatin	Patients	Control	P value
	Mean ± SD nmol/mL	Mean ± SD nmol/mL	
Male	110.072±61.247	99.694±29.23	0.3467
Female	113.675±59.726	79.611±13.76	0.0001 **
Total	112.378±60.098	87.645±23.381	0.0002 **
P value	0.7258	0.0001 **	
* means significance differences (p<0.05)		** means high significance differences (p<0.001)	

Serum obestatin levels of the T1DM patients in this work were found to be higher than those of the controls in table (3). Kolodziejski et al (2017) reported similar findings, which agree with recent results that found higher serum obestatin levels in both types of diabetes. Obestatin levels were reported to increase in the patients who have the metabolic syndrome, obesity, T1DM, impaired glucose control, and Prader-Willi syndrome (associated with the obesity), while bariatric surgery-induced weight loss in the obese as well as the T2DM patients has shown to have no impact on the levels of the obestatin. A few researches carried out thus far support this idea (Green & Grieve, 2018). Current findings are supported by the role of obestatin, Additionally, it seems to have effects on pancreatic β-cell, most notably increasing the beta-cell mass and activating genes linked to β-cell regeneration and insulin production, inhibiting glucose-induced insulin secretion and preventing lipolysis, acting similarly to insulin by lowering insulin resistance and adipocyte, inflammation that takes place in tissue with a high rate of metabolism, and acting similarly to insulin by reducing adipocyte, inflammation that occurs in tissue with high rate of metabolism, since those are [24].

CCK

As showing in table (4) there have not been any significant differences (P > 0.05) in cck concentration of males patients with TIDM compared to the control group, the cck concentration of patients and control is (20.143 and 19.741) nmol/mL respectively. while there has been a highly significant increase (P < 0.05) in cck concentration in females' patients with TIDM compared with control group, the concentration of cck for T1DM patients and control (21.002 & 13.071) nmol/mL respectively. also there has been a significant increase (P < 0.05) in cck concentration of the patients with TIDM compared to control group (20.693 and15.739) nmol/mL respectively. the same table did not show any significant differences (P > 0.05) in cck concentration between males and females in patients' group (20.143 and 21.002) nmol/mL respectively. but found significant increase (P < 0.05) in cck concentrations between males and females in controls group (19.741 and 13.071) nmol/mL, respectively.

Table 4: Concentration of CCK in both patients with TIDM and control groups			
CCK	Patients	Control	P value
	Mean ± SD nmol/mL	Mean ± SD nmol/mL	
Male	20.143±12.645	19.741±19.422	0.9055
Female	21.002±12.304	13.071±2.686	0.0001 **
Total	20.693±12.392	15.739±12.784	0.0034 *
P value	0.6851	0.0145 *	
* means significance differences (p<0.05)		** means high significance differences (p<0.001)	

Table (4) showed an increase in cck levels of the patients compared to controls, while there aren't any significant differences in the cck concentrations according to gender in the group of patients. Either electrical field stimulation (EFS) or the cholecystokinin octapeptide (CCK8, 10-8M) can lead to eliciting large and significant (P < 0.05) increase in the amylase output from the pancreatic segments in comparison with the basal secretion, insulin (10−6M) alone does not have a significant effect upon the amylase output in comparison with the basal but it improved secretory responses to either CCK8 or EFS [25].

Triglyceride (TG)

From the statistical analyses observations for TG results in table (5) there has been found a significant increase (P < 0.05) in TG concentration for males' patients who have TIDM when compared with controls group, the concentration of TG for patients and controls is (176.259 and 108.166) mg/dl respectively. while observed high significant increase (P < 0.001) in the TG concentrations for females' patients with TIDM when compared with controls group, the concentration of TG for patients and controls is (170.666 and 94.777) mg/dl respectively. also there have been high significant increase (P < 0.001) in concentration of TG for patients when compared to the controls, the concentrations for patients and controls is (172.68 and 100.133) mg/dl respectively. Lastly showed no significant difference in concentration of TG in both patients group and controls group according to the gender.

Table 5: Concentration of TG in both patients with TIDM and control groups			
TG	Patients	Control	P value
	Mean ± SD mg/dl	Mean ± SD mg/dl	
Male	176.259±144.135	108.166±44.487	0.0074 *
Female	170.666±137.094	94.777±50.232	0.0001 **
Total	172.68±139.683	100.133±48.212	0.0001 **
P value	0.8142	0.1985	
* Means significance differences (p<0.05)		** means high significance differences (p<0.001)	

The results in table (5) showed there were an increase in triglyceride concentrations in patients with T1DM compared to healthy subjects, these results similar some studies which indicated increase level of TG. Same findings were reported by Kolodziejski et al (2017) they clarified an increase the levels of TG and found that they were high in the all types of DM compared to the healthy group. In some study, however, overweight T1DM had only significant increased triglyceride and lower HDL levels, showing the typical dyslipidemia of patients with metabolic syndrome [26]. Abd El Dayem etal (2017) have carried out a study on the type I diabetic patients and had shown that there has been a prevalence of the dyslipidemia in the patients where the triglycerides, LDL cholesterol and total cholesterol have been considerably higher whereas the HDL cholesterol has been reduced in comparison to the controls, which is why, should evaluate lipids soon after the diagnosis in the type I diabetic children who are older than 12 years, and it has to be repeated every 5 years in the case where normal results were obtained. Despite the slight increase, there have not been any significant differences in the total cholesterol, total HDL cholesterol and triglycerides between T1DM and healthy participants [27]. In type I diabetes (CACTI) study that reported higher LDL and triglyceride levels in men with type 1 diabetes compared to women[28].

Total Cholesterol (TC)

The results of the table (6) showed there has been high significant increase (P < 0.001) in TC concentrations for all results of T1DM patients groups compared with the controls, the concentrations of TC in male patients compared to controls is (190.592 and 143) mg/dl respectively. And female patients compared to control is (196.166 and 151.111) mg/dl respectively. And the concentrations of TC in patients who have T1DM compared with the controls is (194.16 and 147.866) mg/dl, respectively. while in the same table observed no significant differences in the concentrations of TC (p>0.05) in both groups patients and controls based on gender.

Table 6: Concentration of TC in both patients with TIDM and control groups			
CHO	Patients	Control	P value
	Mean ± SD mg/dl	Mean ± SD mg/dl	
Male	190.592±54.389	143±32.884	0.0001 **
Female	196.166±51.136	151.111±18.838	0.0001 **
Total	194.16±52.393	147.866±25.545	0.0001 **
P value	0.5321	0.1409	
* means significance differences (p<0.05)		** means high significance differences (p<0.001)	

According to current finding in table (6) significantly increase in CHO concentration in patients' group with TIDM while no significant difference according to gender. The diabetes patients had higher diastolic blood pressure, total cholesterol, HbA1c, apoB, LDL cholesterol, body weight, apoA-I, BMI and waist circumference in comparison to the controls, both at the baseline and at five-year follow-ups [29]. Even though diurnal profiles of the cholesterol and triglycerides had shown subtle differences between controls and patients with a slight elevation in the concentration levels in T1DM group, the overall ranges of concentration have been rather similar in the two groups [11]. cholesterol levels in the diabetic patients (158.06mg/dl ± 26.58mg/dl) has been higher in comparison with its levels in the healthy individuals (147.05mg/dl ± 5.51mg/dl) [30].

High- Density Lipoprotein (HDL)

As indicated in table (7) there were insignificant decrease (P> 0.05) in the concentration of HDL in T1DM patients for males compared with the controls, the mean of HDL in T1DM patients for males compared to controls is (40.259 and 42.166) mg/dl respectively. There has been high significant decrease (P < 0.001) in HDL concentration for female's patients who have T1DM compared to controls, the mean of HDL is (38.062 and 46.666) mg/dl respectively. And highly significant decrease (P < 0.001) in HDL concentrations in the patients who have T1DM compared to controls groups, the HDL concentration is (38.853 and 44.866mg/dl) respectively. Finally showed there were insignificant increase (p>0.05) in HDL concentration of males compared to females in patients' group, the mean of HDL (40.259 and 38.062) mg/dl respectively. while showed high significant decrease (P < 0.001) in concentration of HDL of males compared to females in control group, the mean of HDL is (42.166 and 46.666) mg/dl, respectively.

Table 7: Concentration of HDL in both patients with TIDM and control groups			
HDL	Patients	Control	P value
	Mean ± SD mg/dl	Mean ± SD mg/dl	
Male	40.259±8.505	42.166±4.116	0.2148
Female	38.062±7.273	46.666±4.093	0.0001 **
Total	38.853±7.809	44.866±4.642	0.0001 **
P value	0.0972	0.0001 **	
* means significance differences (p<0.05) ** means high significance differences (p<0.001)			

The results of table (7) showed a significant decrease in HDL concentrations in T1DM patients compared to the controls. In comparison with the genetically determined anomalies in the HDL metabolism, low HDL-C much more often happen in the patients who have the metabolic syndrome or DM, chronic renal insufficiency, coronary disease, cardiovascular risk factors and disorders, where the HDL function has been impaired [31]. Another study had shown that T1DM patients usually have normal or even increased plasma HDL cholesterol concentration levels. None-the-less, the composition of HDL protein may be altered without changing the cholesterol content, HDL proteome alteration could lead to dysfunctional HDL particles with decreased capability for protecting from CVD [32]. There have not been any significant differences in the total cholesterol, triglycerides and total HDL cholesterol between the T1DM and healthy participants [27]. It was established that the low HDL-C concentration, an independent CVD risk marker, coincides with the reduction of the protective capacity from the oxidative stress. None-the-less, conflicting results were reported on the low HDL-C levels' prevalence in the T1DM [33]. Which is why, the low concentration of the HDL that was observed in the diabetic patients in comparison with the non-diabetic persons has been considered as a primary cause of the increased CVD risks [34].

Low-Density Lipoprotein (LDL)

Results of table (8) showed high significant increase (P < 0.001) in LDL level in all groups of patients with T1DM as comparison to controls groups, the concentration of LDL for males in patients and controls is (126.333 and 67.833) mg/dl respectively. And the concentration of LDL for females in patients and controls is (134.791 and 76.888) mg/dl respectively. And the concentration of LDL for patients with T1DM as comparison to controls is (131.746 and 73.266) mg/dl respectively. whereas in the same table observed no significant differences (P> 0.05) in the level of LDL in both groups of patients and controls according to gender.

Table 8: Concentration of LDL in both patients with TIDM and control groups			
LDL	Patients	Control	P value
	Mean ± SD mg/dl	Mean ± SD mg/dl	
Male	126.333±40.247	67.833±29.413	0.0001 **
Female	134.791±34.715	76.888±24.246	0.0001 **
Total	131.746±37.018	73.266±26.649	0.0001 **
P value	0.1786	0.1148	
* Means significance differences (p<0.05) ** means high significance differences (p<0.001)			

The results of LDL as shown in the table (8) had high significant increase in level of LDL for diabetic patients compared with the healthy individuals and there were also clarified that there have not been significant differences between males and females in the group of patients, these results are similar and deals with some previous research. LDL cholesterol has been found increased significantly (84.29mg/dl ± 22.71mg/dl) (P < 0.05) in comparison to healthy controls. In addition to that, the level of the cholesterol in diabetic patients (158.06 ± 26.58mg/dl) has been higher in comparison to its levels in the healthy individuals (147.05mg/dl ± 5.51mg/dl) and in the diabetic women, the LDL and cholesterol levels have been noticeably higher compared to their levels in the healthy women[30]. Total LDL-c and cholesterol have been significantly higher while the HDL cholesterol has been decreased in comparison to the controls, indicating increased risk of CVD[12]. Another study indicated high concentrations of LDL in diabetic patients [12]. In another study that has been conducted by (Wedrychowicz etal., 2019) to identify the variation in LDL–c concentrations in the diabetic patients compared to controls, this study had shown a non-significant increase (p>0.05) (2.3±0.6 T1DM, 2.1±0.5 controls). There have not been any significant differences in total cholesterol, total HDL cholesterol and triglycerides between T1DM and healthy participants, LDL being 8 mg/dL (p<0.05) higher in the T1DM compared with the controls [27].

VLDL

The findings of table (9) showed there has been a significant increase (P< 0.05) in concentration of VLDL in T1DM male patients compared to controls, the mean of VLDL for males T1DM patients and controls is (34.962 and 24.166) mg/dl respectively. Also there has been a highly significant increase (P< 0.001) in VLDL concentrations for females with T1DM were compared with the controls, the concentration of VLDL is (36 and 19.888) mg/dl respectively. And observed there has been a highly significant increase (P< 0.001) in VLDL concentrations of patients who have T1DM compared with the controls, the concentration of VLDL is (35.626 and 21.6) mg/dl respectively. While showed no significant difference (P > 0.05) in concentration of VLDL between males and females of patient groups, but there has been a significant increase (P> 0.05) in VLDL concentration in controls groups, the concentration of VLDL (24.166 and 19.888) mg/dl respectively.

Table 9: Concentration of VLDL in both patients with TIDM and control groups			
VLDL	Patients	Control	P value
	Mean ± SD mg/dl	Mean ± SD mg/dl	
Male	34.962±20.164	24.166±10.131	0.0039 *
Female	36±22.981	19.888±8.288	0.0001 **
Total	35.626±22.019	21.6±9.258	0.0001 **
P value	0.7820	0.0309 *	
* means significance differences (p<0.05) ** means high significance differences (p<0.001)			

The present study clarified that the VLDL was significantly rise in the diabetic patients. Some study demonstrated the triglycerides and total cholesterol levels have been high in the diabetics, there were no significant differences in total HDLp, large HDLp and total, medium and large VLDLp, [27]. HDL has an important impact on transferring cholesterol to liver via binding to the scavenger receptor class BI (SR-BI) expressed in hepatocytes or through the transfer to the LDL/VLDL particles by the action of cholesteryl ester transfer protein (CETP), related to the HDL in the plasma [33]. Results of some study had shown significant differences in the HDL, TC and LDL/VLDL levels between the patients and the healthy control group ($p < 0.0001$) [35]. Another study it was also clarified there have not been any significant differences in VLDL concentration between tow group diabetic patients and healthy[36].

References

[1] N. RezRezaeiaei, T. Mardanshahi, M. M. Shafaroudi, S. Abedian, H. Mohammadi, and Z. Zare, "Effects of l-Carnitine on the Follicle-Stimulating Hormone, Luteinizing Hormone, Testosterone, and Testicular Tissue Oxidative Stress Levels in Streptozotocin-Induced Diabetic Rats," J. Evidence-Based Integr. Med., vol. 23, pp. 1–10, 2018, doi: 10.1177/2515690X18796053.

[2] D. B, S. K, L. B, B. RS, and B. PS, "A Modern Review of Diabetes Mellitus: An Annihilatory Metabolic Disorder," J. Silico Vitr. Pharmacol., vol. 03, no. 01, pp. 1–5, 2018, doi: 10.21767/2469-6692.100014.

[3] D. L. Eizirik, L. Pasquali, and M. Cnop, "Pancreatic β-cells in type 1 and type 2 diabetes mellitus: different pathways to failure," Nat. Rev. Endocrinol., vol. 16, no. 7, pp. 349–362, 2020, doi: 10.1038/s41574-020-0355-7.

[4] S. A. Paschou, N. Papadopoulou-Marketou, G. P. Chrousos, and C. Kanaka-Gantenbein, "On type 1 diabetes mellitus pathogenesis," Endocr. Connect., vol. 7, no. 1, pp. R38–R46, 2018, doi: 10.1530/EC-17-0347.

[5] Y. M. Arabi et al., "Leptin, ghrelin, and leptin/ghrelin ratio in critically ill patients," Nutrients, vol. 12, no. 1, pp. 1–11, 2020, doi: 10.3390/nu12010036.

[6] A. G. Izquierdo, A. B. Crujeiras, F. F. Casanueva, and M. C. Carreira, "Leptin, obesity, and leptin resistance: where are we 25 years later?," Nutrients, vol. 11, no. 11, pp. 1–11, 2019, doi: 10.3390/nu11112704.

[7] G. K. Dimitriadis, M. S. Randeva, and A. D. Miras, "Potential Hormone Mechanisms of Bariatric Surgery," Curr. Obes. Rep., vol. 6, no. 3, pp. 253–265, 2017, doi: 10.1007/s13679-017-0276-5.

[8] J. W. Creswell and V. L. P. Clark, "Designing and Conducting Mixed Methods Research Third Edition," Sage Publ., 2017.

[9] M. M. Ismail, T. A. A. Hamid, A. A. Ibrahim, and H. Marzouk, "Serum adipokines & Vitamin D levels in patients with type 1 diabetes mellitus," Arch. Med. Sci., vol. 13, no. 4, pp. 738–744, 2017, doi: 10.5114/aoms.2016.60680.

[10] R. V. Kapustin et al., "Maternal serum leptin, adiponectin, resistin and monocyte chemoattractant protein-1 levels in different types of diabetes mellitus," Eur. J. Obstet. Gynecol. Reprod. Biol., vol. 254, no. September, pp. 284–291, 2020, doi: 10.1016/j.ejogrb.2020.09.050.

[11] P. Trefz, S. C. Schmidt, P. Sukul, J. K. Schubert, W. Miekisch, and D. C. Fischer, "Non-invasive assessment of metabolic adaptation in paediatric patients suffering from type 1 diabetes mellitus," J. Clin. Med., vol. 8, no. 11, pp. 1–22, 2019, doi: 10.3390/jcm8111797.

[12] S. M. Abd El Dayem, M. Abd El Kader, S. Ibrahim, E. Mokhtar, and E. Abd El Megeed, "Leptin and lipid profile in overweight patient with type 1 diabetes," Maced. J. Med. Sci., vol. 5, no. 2, pp. 131–136, 2017, doi: 10.3889/oamjms.2017.033.

[13] A. Wędrychowicz, K. Sztefko, and J. B. Starzyk, "Sclerostin and its significance for children and adolescents with type 1 diabetes mellitus (T1D)," Bone, vol. 120, pp. 387–392, 2019, doi: 10.1016/j.bone.2018.08.007.

[14] Y. Xu and Q. Tong, "Central leptin action on euglycemia restoration in type 1 diabetes: Restraining responses normally induced by fasting?," Int. J. Biochem. Cell Biol., vol. 88, pp. 198–203, 2017, doi: 10.1016/j.biocel.2016.09.027.

[15] G. H. Marques-Oliveira, T. M. Silva, W. G. Lima, H. M. S. Valadares, and V. E. Chaves, "Insulin as a hormone regulator of the synthesis and release of leptin by white adipose tissue," Peptides, vol. 106, pp. 49–58, 2018, doi: 10.1016/j.peptides.2018.06.007.

[16] O. U. Onyemelukwe, D. Ogoina, and G. C. Onyemelukwe, "Leptin concentrations in type 2 diabetes and non-diabetes Nigerian-Africans.," Am. J. Cardiovasc. Dis., vol. 10, no. 4, pp. 444–454, 2020.

[17] M. Warchoł et al., "Association of cord blood ghrelin, leptin and insulin concentrations in term newborns with anthropometric parameters at birth," J. Pediatr. Endocrinol. Metab., vol. 31, no. 2, pp. 151–157, 2018, doi: 10.1515/jpem-2017-0285.

[18] A. Nalla, L. Ringholm, S. N. Sørensen, P. Damm, E. R. Mathiesen, and J. H. Nielsen, "Possible mechanisms involved in improved beta cell function in pregnant women with type 1 diabetes," Heliyon, vol. 6, no. 8, 2020, doi: 10.1016/j.heliyon. 2020.e04569.

[19] A. L. Poher, M. H. Tschöp, and T. D. Müller, "Ghrelin regulation of glucose metabolism," Peptides, vol. 100, no. December 2017, pp. 236–242, 2018, doi: 10.1016/j.peptides.2017.12.015.

[20] B. Özcan, P. J. D. Delhanty, M. Huisman, J. A. Visser, S. J. Neggers, and A. J. van der Lely, "Overweight and obesity in type 1 diabetes is not associated with higher ghrelin concentrations,"

Diabetol. Metab. Syndr., vol. 13, no. 1, pp. 1–7, 2021, doi: 10.1186/s13098-021-00699-4.
[21] K. Green and B. Torre, "Correspondence To:"
[22] P. A. Kolodziejski et al., "Changes in obestatin gene and GPR39 receptor expression in peripheral tissues of rat models of obesity, type 1 and type 2 diabetes," J. Diabetes, vol. 9, no. 4, pp. 353–361, 2017, doi: 10.1111/1753-0407.12417.
[23] B. D. Green and D. J. Grieve, "Biochemical properties and biological actions of obestatin and its relevence in type 2 diabetes," Peptides, vol. 100, no. December 2017, pp. 249–259, 2018, doi: 10.1016/j.peptides.2017.12.006.
[24] H. M. Balaky and I. S. Kakey, "Alterations of obestatin, cardiac markers and lipid profile levels in type 2 diabetes mellitus," Iraqi J. Sci., vol. 62, no. 6, pp. 1804–1815, 2021, doi: 10.24996/ijs.2021.62.6.6.
[25] R. Patel et al., "Mechanism of exocrine pancreatic insufficiency in streptozotocin-induced type 1 diabetes mellitus," Ann. N. Y. Acad. Sci., vol. 1084, pp. 71–88, 2006, doi: 10.1196/annals.1372.038.
[26] P. Fellinger et al., "Overweight and obesity in type 1 diabetes equal those of the general population," Wien. Klin. Wochenschr., vol. 131, no. 3–4, pp. 55–60, 2019, doi: 10.1007/s00508-018-1434-9.
[27] E. Gourgari et al., "Low cholesterol efflux capacity and abnormal lipoprotein particles in youth with type 1 diabetes: A case control study," Cardiovasc. Diabetol., vol. 17, no. 1, pp. 1–10, 2018, doi: 10.1186/s12933-018-0802-0.
[28] V. N. Shah et al., "US CR Methods : Data from the Type 1 Diabetes Exchange registry were utilized to explore gender," J. Diabetes Complications, no. 813, p. #pagerange#, 2018, doi: 10.1016/j.jdiacomp.2018.08.009.
[29] M. Heier et al., "Reduced HDL function in children and young adults with type 1 diabetes," Cardiovasc. Diabetol., vol. 16, no. 1, pp. 1–8, 2017, doi: 10.1186/s12933-017-0570-2.
[30] R. Alghazeer, N. Alghazir, N. Awayn, O. Ahtiwesh, and S. Elgahmasi, "Biomarkers of Oxidative Stress and Antioxidant Defense in Patients with Type 1 Diabetes Mellitus," pp. 198–204, 2018, doi: 10.4103/ijmbs.ijmbs.
[31] W. März et al., "HDL cholesterol: reappraisal of its clinical relevance," Clin. Res. Cardiol., vol. 106, no. 9, pp. 663–675, 2017, doi: 10.1007/s00392-017-1106-1.
[32] E. Gourgari et al., "Proteomic alterations of HDL in youth with type 1 diabetes and their associations with glycemic control: A case-control study," Cardiovasc. Diabetol., vol. 18, no. 1, pp. 1–11, 2019, doi: 10.1186/s12933-019-0846-9.
[33] S. Ganjali, G. M. Dallinga-Thie, L. E. Simental-Mendía, M. Banach, M. Pirro, and A. Sahebkar, "HDL functionality in type 1 diabetes," Atherosclerosis, vol. 267, pp. 99–109, 2017, doi: 10.1016/j.atherosclerosis.2017.10.018.
[34] R. A. K. Srivastava, "Dysfunctional HDL in diabetes mellitus and its role in the pathogenesis of cardiovascular disease," Mol. Cell. Biochem., vol. 440, no. 1–2, pp. 167–187, 2018, doi: 10.1007/s11010-017-3165-z.
[35] M. Bo, G. Arru, M. Niegowska, G. L. Erre, P. A. Manchia, and L. A. Sechi, "Association between lipoprotein levels and humoral reactivity to mycobacterium avium subsp. Paratuberculosis in multiple sclerosis, type 1 diabetes mellitus and rheumatoid arthritis," Microorganisms, vol. 7, no. 10, pp. 1–11, 2019, doi: 10.3390/microorganisms7100423.
[36] Y. Huang et al., "Gut microbiota profiling in Han Chinese with type 1 diabetes," Diabetes Res. Clin. Pract., vol. 141, pp. 256–263, 2018, doi: 10.1016/j.diabres.2018.04.032.