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RESEARCH ARTICLE - MEDICAL TECHNIQUES

To Investigate the Associations of Dyslipidemia and BMI, as Risk Factors Leading to Insulin Resistance and Development of Type2 Diabetes Mellitus in Baqubah City

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Abstract

Insulin resistance is a condition in which persons with type 2 diabetes make insulin but is unable to use it properly to transfer glucose into cells, resulting in high blood glucose levels. Obesity, particularly visceral fat (fat surrounding the organs) is a major cause of insulin resistance. The homeostasis model evaluation is the gold standard method for determining whether or not a person is insulin resistant. This article tries to investigate the development of the values of some parameters among type 2- diabetic patients versus normal levels of healthy control groups these parameters included FBS, HbAIc (%), FIL, HOMAIR age BMI and lipid profile. The results found that the means values of FBS(mg/dl), HbAIc (%), FIL (miu /L), HOMAIR were (175.96± 39.68, 9.74±1.82 , 18.99±5.98 , 8.136±2.53) respectively versus normal levels of control group (85.44±7.58, 4.92±.500 , 5.79 ± 0.5, 1.22±0.17). While means of age and BMI (kg/m²) of cases were (54.27±13.35, 32.20±2.23) versus the mean for the control group (47.12±10.77, 26.04±1.65) respectively. The levels of total cholesterol (mg/dl), triglycerides (mg/dl), LDL (mg/dl) and VLDL (mg/dl) among type-2 diabetic patients were(238.19±8.27, 183.48±7.66, 117.20±8.59, 36.69±4.28) respectively versus normal concentrations among control groups with mean values (146.03±7.48, 137.54±7.43, 87.55±6.92, 23.6±5.58) respectively, While the mean value of HDL-C was (40.34±9.82) in patients and (52.31± 4.94) in control. In all these parameters there were highly significant differences between case and control (with (p-value= >0.001) and the mean values of patients with type 2 DM were more than control except the values of HDL-C were in patients less than in control. This study found that the results of the tests FBS, HbAIc (%), age BMI and lipid profile in patients with diabetes type 2 in comparison to the control group have a significant correlation with FIL, HOMAIR.

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Keywords: Insulin resistance; HOMAIR; Lipid profile, BMI; Type 2 diabetes.

1. Introduction

Diabetes mellitus is a condition in which the body does not create enough insulin or does not respond correctly to it (insulin resistance), resulting in abnormally high blood sugar (glucose) levels and defective insulin action or excessive glucagon release [1]. Obesity or recent weight increase (Body mass index 25 kg/m2), positive family history of diabetes, aging, composition of bad food, and lifestyle risk factors (ex; alcohol intake, physical activity, smoking, dyslipidemia) are all connected with the development of type 2 diabetes [2]. Obesity causes inflammation, higher leptin levels, and lower adiponectin levels, all of which lead to insulin resistance and lower insulin production [3].

Obese people have excessive levels of serum-free fatty acids and triglyceride accumulation inside their cells. Intracellular insulin signaling is inhibited, resulting in insulin resistance and apoptotic beta-cell death. It causes inflammatory cytokines to be released, which leads to insulin resistance [4]. Obesity causes insulin receptor signaling to be disrupted, resulting in hyperinsulinemia. After years of compensatory hyperinsulinemia, beta cell failure ensues. By attempting to maintain a normal blood glucose level, the beta cells are overworked. By the time diabetes is diagnosed, the beta cells are unable to secrete adequate insulin, [3, 4]. Insulin resistance is a medical disease that frequently occurs in people with type 2DM, as opposed to individuals with type 1DM, who have a shortage of insulin in their blood. Insulin resistance occurs when beta cells in the pancreas continue to produce insulin to regulate blood glucose levels, but the cells that are sensitive to it do not respond, resulting in hyperinsulinemia and hyperglycemia [5]. The gold standard method for determining insulin resistance is the homeostasis model evaluation. This approach is used to assess the health of the beta cells in the pancreas and their ability to release insulin, as well as to monitor diabetes.

Nomenclature

DM	Diabetes Mellitus	FBS	fasting blood sugar
Homa-IR	Homeostasis model assessment- Insulin Resistant	SD	standard deviation
kg/m²	Kilogram per square meter	%	percent
SPSS	statistical package of social sciences	mmol/L	millimole per liter
RBC	red blood cells	mg /dl	milligram per deciliter
T2DM	type 2 diabetes Miletus	FIL	fasting insulin level
BMI	body mass index	ANOVA	One-way analysis of
TG	triglyceride	P	probability value
HDL	high density lipoprotein	H.S	high significant
LDL	low density lipoprotein	miU/mL	milli-international units per liter
VLDL	very low density lipoprotein	TNF	tumor necrosis factor
β cells	Beta cells	IL	interleukin
α	alpha		

This is a test; that is done when the patient suffers from diabetes, but this does not appear during the tests period, is used to develop the appropriate treatment to maintain this sugar level in patients with type 2 diabetes, and also for how likely it is that you will develop diabetes in the future[6].

For the examination, the patient must be fasting for at least 8 hours, the blood sugar level is performed in addition to the insulin ratio test, and the equation is applied to the value of insulin resistance [7]. The application of the Homa-IR equation is as follows;

Insulin resistance = [(fasting glucose mg/dl) x (blood insulin µU/mL)] / 405

Or Insulin resistance = [(fasting glucose mmol/L) x (blood insulin µU/mL)] / 22.5[8].

Dyslipidemia is a complication of diabetes. The presence of excessive quantities of cholesterol, triglycerides, and other lipoprotein types in the blood due to diet and lifestyle is particularly common in type 2 diabetes (non-insulin-dependent diabetes), affecting approximately 72 percent to 85 percent of patients. In affluent countries, hyperlipidemia (abnormally high blood lipid levels) is the most frequent kind of dyslipidemia. Dylipidemia can be caused by a long-term increase in insulin levels in the blood, or by a long-term increase in insulin resistance. Body Mass Index (BMI) is a simple calculation based on a person's height and weight that is a valid predictor of body fatness for most people. It was previously known as the Quetelet index. BMI = kg/m2 is the formula, where kg is the weight of a person in kilograms, and m2 is their height in meters squared (kg/m²). Commonly used to classify underweight (BMI<18), normal weight BMI(18.5-24.9), overweight BMI (25-29.9), and obesity BMI(≥30) in adults [10].

2. Subjects and Methods

This study was conducted in consultation clinics in Baquba Teaching Hospital / Iraq, during the period from January- March 2022. It consists of 150 participants divided into 2 groups (100 patients with type 2 DM and 50 healthy controls from medical staff and relatives) ages (30 to 78 years) for both groups.

Five ml of blood was obtained from vein puncture using a 5 ml disposable syringe, for a period from 9 to 10 am and for a fasting period of 8 to 12 hours, the blood sample was divided into two parts: The first part of the blood was put in vacutainer gel tube. After blood clotting at room temperature of about (25 Cº), it was separated by centrifugation at (3000 rpm for 5 min) to collect serum and used to assay fasting blood glucose level, fasting insulin level, and lipid profile (total cholesterol, triglyceride, HDL, LDL, VLDL). The second part (2.5 ml) of the blood sample was used to measure HbA1c after being placed in a tube containing an anticoagulant (ethylene diamine tetra acetic acid /EDTA); it is measured on the same day.

3. Procedure

FBS, HbA1c, Lipid profile examine by cobas E.411, insulin level examined by The COBAS INTEGRA 400 plus analyzer.

4. Statistical analysis

"Statistical Package for Social Sciences version (SPSS)"version 26.00 was used for data analysis, and the data are expressed as means ± standard deviation. Differences between studies groups were evaluated by One-way analysis of variance (ANOVA)"(Fisher's exact probability test) and the chi-square test" were used to analyze the association. "P-values less than 0.05 were considered statistically significant.

5. Results and Discussion

5.1. Diabetic parameters assessment

Table 1, Fig. 1; represent fasting serum glucose (FSG) high levels among type 2- diabetic patients(175.96± 39.68 mg/dl) versus levels of the healthy control group (85.44±7.58). Statistically, these differences were highly-significant (P-value <0.001). This finding agrees with *Tayek et al.*and *Kumar et al.* where it was found that fasting sugar is high in diabetic patients compared to control where its level was normal [11,12]. The results in Table 1, Fig. 2 show that the level of fasting insulin in diabetic patients was high(18.99±5.98) compared to healthy people(5.79 ±.5), even if both values within the normal value of the FIL (2-25miu/L), but there were highly significant differences between cases and control with (P-value <0.001). These results are consistent with *Enteshary et al.* where it was also found that the level of insulin is high in patients with type 2 diabetes and is lower in the control [13,7].Insulin resistance or insufficiency of insulin is one of the causes of high blood sugar, in this case, where insulin is produced by the pancreas, but the cells of the body resist it, causing high fasting sugar, and this is common in the development of type 2diabetes [14]. The results presented in the Table 1, Fig. 3 observe a higher percentage of cumulative glucose in patients with type 2 diabetes compared to healthy people the levels of HbAIc (%) with means (9.74±1.82) versus (4.92±.500) for

healthy control groups, These differences were highly significant with (P-value <0.001). These results are in agreement with *Liu et al.* where it was found that the percentage of cumulative sugar in diabetic patients was more than the normal limit compared to the healthy people, where HbA1c is within the normal limit [15]. The cumulative sugar is known as glycated hemoglobin, and it is the product of glucose sticking in the body with red blood cells (RBC), and the human body is unable to use glucose effectively and properly, and this is what drives it to stick to red blood cells and then accumulate in the body. RBCs are usually effective for a period of two to three months, which is precisely why cumulative glucose readings are taken for this same period [16]. HbA1c levels can be utilized as a diagnostic tool for detecting insulin resistance in its early stages. We suggested adopting HbA1c levels as a simple and less expensive test because research identified a beneficial connection between HbA1c and HOMA-IR levels in the obese group (no need to fasting) [17]. The result of this study table (1,fig4) found that levels of HOMAIR were high in levels among type-2 diabetic patients(8.136±2.53), While the level of control was (1.22±0.17). The differences between patients and control were highly significant (P-value <0.001). This finding is similar to the study of Horáková *et al.* Where the study found that the proportion of insulin resistance increased after applying the resistance equation: The HOMA-IR was calculated with the following formula (glucose levels in mmol/L, insulin levels in mIU/L); HOMA − IR = glucose × insulin /22.5 [18].IR is typically defined as decreased sensitivity and responsiveness to insulin-mediated glucose disposal and inhibition of hepatic glucose production.IR plays a significant pathophysiologic role in T2DM. It is commonly associated with visceral adiposity, glucose intolerance, hypertension, dyslipidemia, endothelial dysfunction, and elevated levels of markers of inflammation [19].

Table 2, Fig. 5 shows that Eighty-three (83%) out of 100 types 2 diabetic patients were within obese groups (BMI ≥30 Kg/m2) while the rest cases of the diabetic patients 17 (17%) were overweight group (BMI 25-29.9 Kg/m2) and 35 (69.4%) out of 25 was over weight in control. No normal weight was found in patients while there were 15 (30.6%) normal weight in control and no obese subjects in control Statistically these differences were highly significant with (p-value= > 0.001). Also, these findings matched those of Palmer & Toth. who found that BMI was one of the Factors that increase the chance of developing type 2 diabetes [20]. Obesity has long been considered a risk factor for insulin resistance. Obesity is related to higher lipid levels in adipose tissue, which leads to greater fat accumulation and insulin resistance. Obesity can cause inflammation in the body, which leads to an increase in the production of inflammatory cytokines, which can impair insulin sensitivity. Studies indicating elevated levels of the proinflammatory cytokines IL-6 and TNF- in people with insulin resistance and T2DM support this idea. Alternatively, adipose tissue hormone production may be disrupted, increasing the generation of adipokines that promote insulin resistance. [21].

Table 1 Comparisons between the levels of diabetic parameters among cases and controls

Parameters	Study Groups	No.	Mean	Std. Deviation	T-test	P-value
FBS	Case	100	175.96	39.68	15.9	<0.001
(mg/dl)	Control	50	85.44	7.58		H.S
FIL	Case	100	18.99	5.98	21.9	<0.001
(miu /L)	Control	50	5.79	0.50		H.S
HbA1c	Case	100	9.74	1.82	18.3	<0.001
(%)	Control	50	4.92	.500		H.S
HOMAİR	Case	100	8.136	2.53	27.10	<0.001
	Control	50	1.22	0.17		H.S

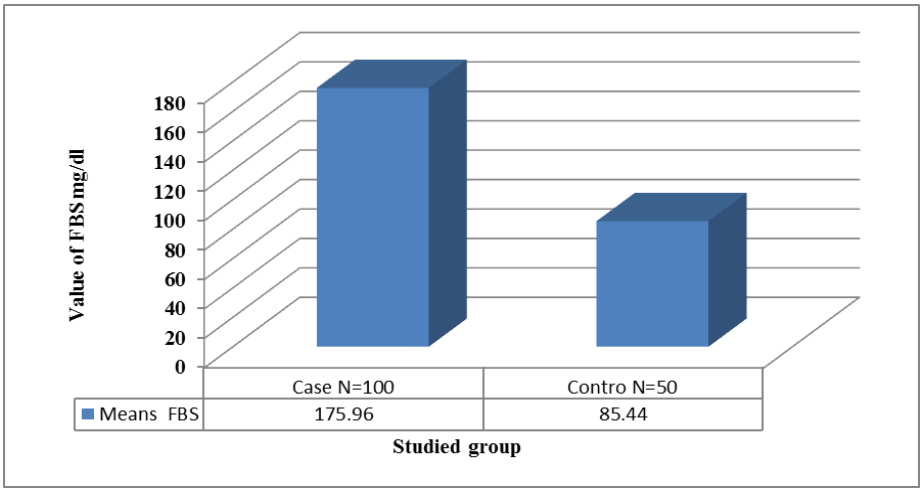

Fig 1. Mean concentrations of FBS (mg/dl) for studied group (case number=100, control number=50), where SD of patient= 39.68, while SD of control= 7.58 and P-value <0.001(H.S).

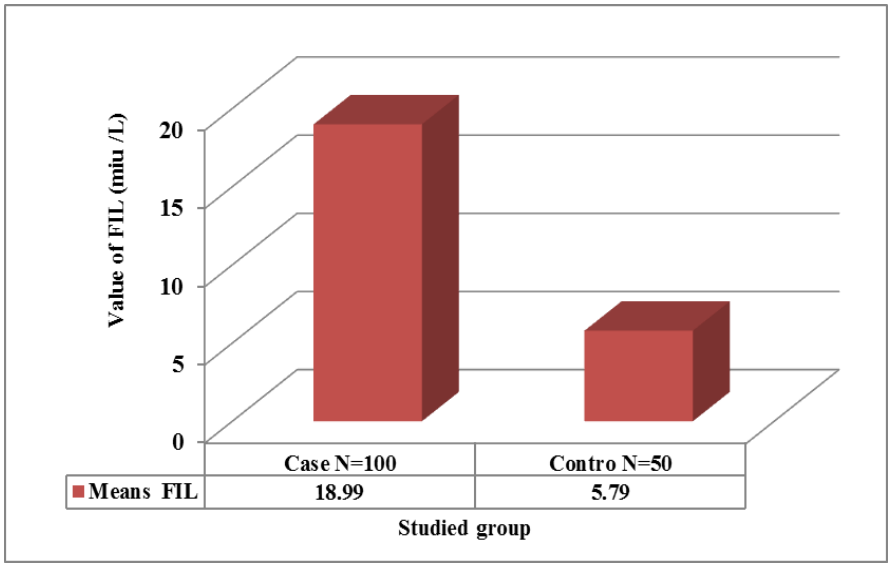

Fig 2. Mean concentrations of FIL (miu/L) for studied group (case number=100, control number=50), where SD of patient= 5.98, while SD of control= 0.50 and P-value <0.001(H.S)

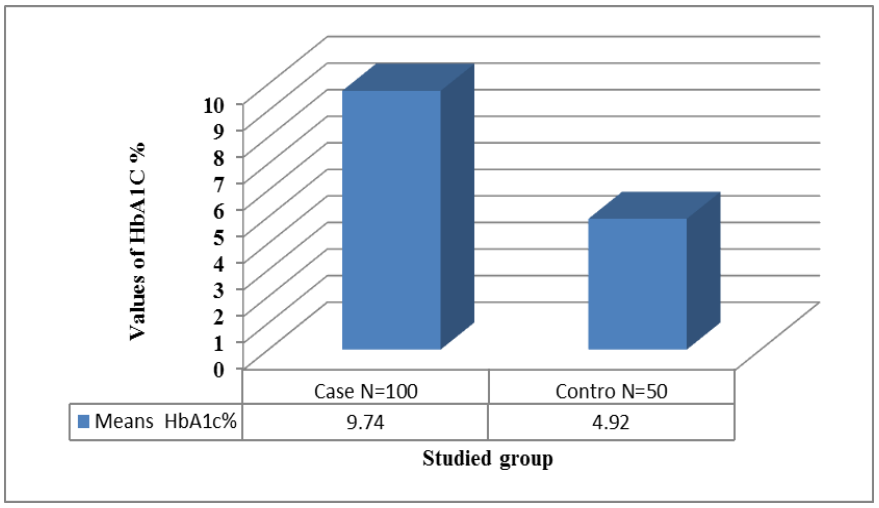

Fig 3. Mean concentrations of HbA1c (%) for studied group (case number=100, control number=50), where SD of patient= 1.82, while SD of control= 0.500and P-value <0.001(H.S)

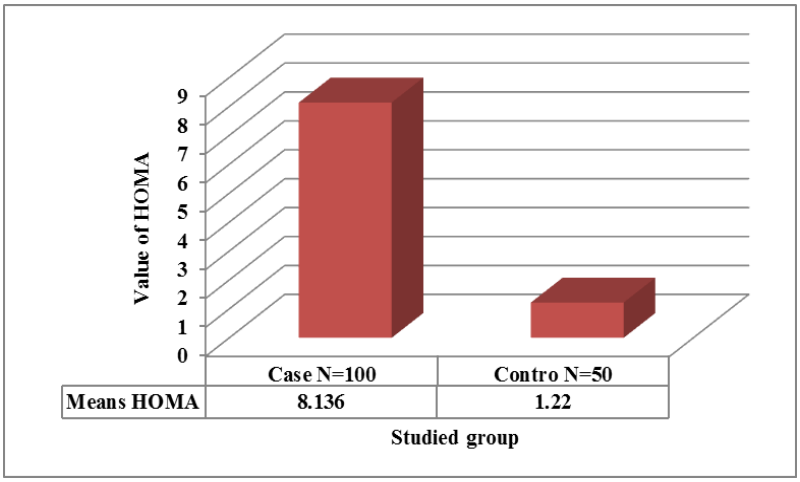

Fig 4. Mean concentrations of HOMA for studied group (case number=100, control number=50), where SD of patient=2.53, while SD of control= 0.17and P-value <0.001(H.S).

Table 2 Demographical characteristics of the studied groups.

Parameters		Patients (N=100)	Control(N=50)	Sign.
BMI (Kg/m^2) No. (%)	Normal Weight (18.5-24.9)	0 (0.0%)	15 (30.6%)	Chi-square=97.1 P-value= 0<.001 (H.S)
	Over Weight (25-29.9)	17 (17%)	35 (69.4%)	
	Obese ≥30	83 (83%)	0 (0.0%)	
	Mean ± SD	32.20±2.23	26.04±1.65	t-test = 17.2 P-value=<0.001

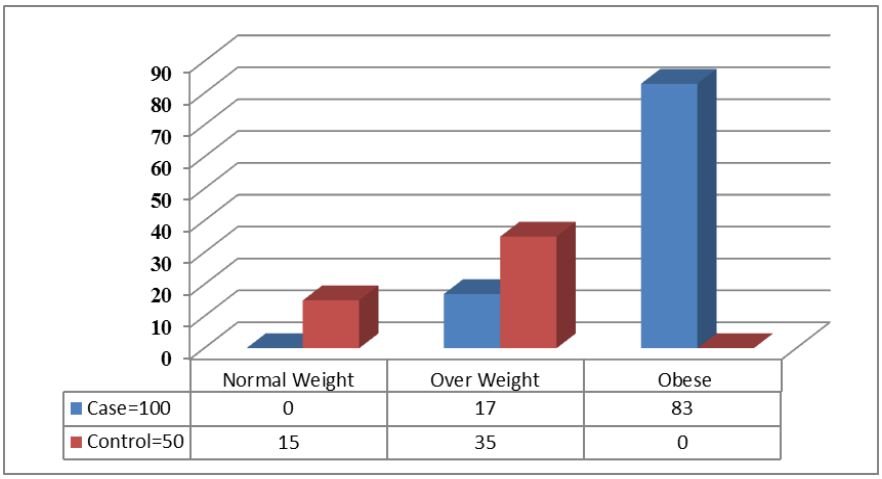

Fig. 5: Percentage of BMI(Kg/m^2) in the studied group (N=150)

Table 3 showed that the levels of total cholesterol, triglycerides (mg/dl), LDL (mg/dl), and VLDL (mg/dl) were higher in concentrations among type-2 diabetic patients (238.19±8.27, 183.48±7.66, 117.20±8.59, 36.69±4.28) versus the concentrations among healthy control groups with mean values (146.03±7.48, 137.54±7.43, 87.55±6.92, 23.6±5.58) respectively this differences statistically were highly significant with (p-value= >0.001). The results of these tables also observed there was a decrease in the levels of good cholesterol HDL (mg/dl) among type- 2 diabetic patients (40.34 ±9.82) versus its level among the healthy control group (52.31±4.94), these differences statistically were highly significant with (p-value= >0.001). The results of this study in Table 3 coincide with *those Made Junior Rina Artha et al.*where it was found that (Total-cholesterol, TG, LDL, VLDL) is high in diabetic patients while HDL is lower and within normal levels [22]. Insulin resistance in adipose tissue results in a reduction in the uptake of circulating free fatty acids and an increase in the hydrolysis of stored triglycerides by lipases. The net result of these actions is an increase in circulating free fatty acids. Also, insulin resistance is associated with increased cholesterol synthesis, decreased cholesterol absorption, and enhanced lipid response to statin therapy and can also alter systemic lipid metabolism which then leads to the development of dyslipidemia and the well-known lipid triad: (1) high levels of plasma triglycerides, (2) low levels of high-density lipoprotein, and (3) the appearance of small dense low-density lipoproteins. Another theory examines the capacity of adipose tissue to store lipids. According to this notion, an individual's ability to store lipids in adipose tissue has a maximum capacity. Excess lipids spill over into plasma when this limit is exceeded, resulting in higher plasma-free fatty acid and triglyceride levels. As a result, non-adipose tissues including skeletal muscle and the liver import and store more of these chemicals. Lipid accumulation in non-adipose tissues may cause metabolic disturbances due to lipid-induced toxicity (lipotoxicity). Lipotoxicity may potentially play a significant role in the degeneration of pancreatic cells that happens when type 2 diabetes progresses. [23, 24].

Table (3): Comparisons between the levels of lipid profile parameters among cases and controls

Parameters	Study Groups	No.	Mean	Std. Deviation	t-test	P-value
Total cholesterol (mg/dl)	Case	100	238.19	8.27	12.2	0.001<(H.S)
	Control	50	146.03	7.43		
TG (mg/dl)	Case	100	183.48	7.66	6.51	0.001<(H.S)
	Control	50	137.54	7.48		

HDL (mg/dl)	Case	100	40.34	9.82	4.38	0.001<(H.S)
	Control	50	52.31	4.94		
LDL (mg/dl)	Case	100	117.20	8.59	6.53	0.001<(H.S)
	Control	50	87.55	6.92		
VLDL (mg/dl)	Case	100	36.692	4.28	6.4	0.001<(H.S)
	Control	50	23.6	5.58		

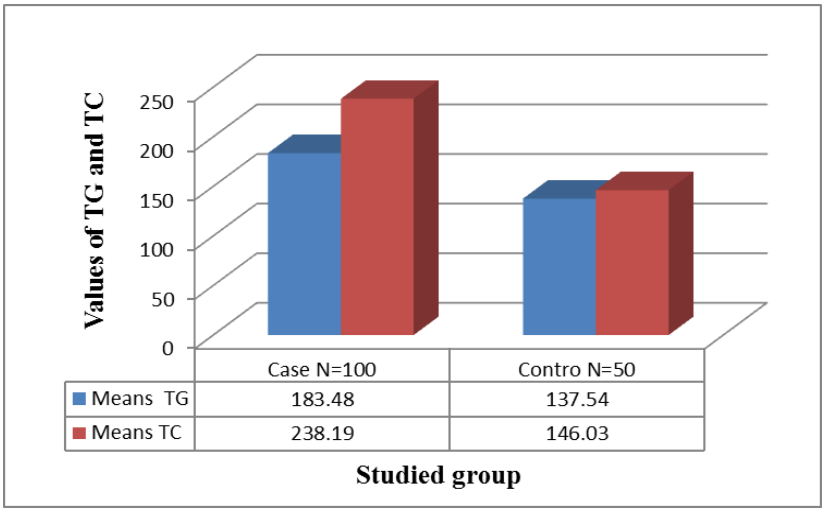

Fig 6. Mean concentrations of TG and TC(mg/dl) for the studied group (case number=100, control number=50), where was the SD of cholesterol for patient and control (8.27, 7.43) respectively, while SD of Triglyceride for patient and control (7.66, 7.48), with P-value <0.001(H.S)

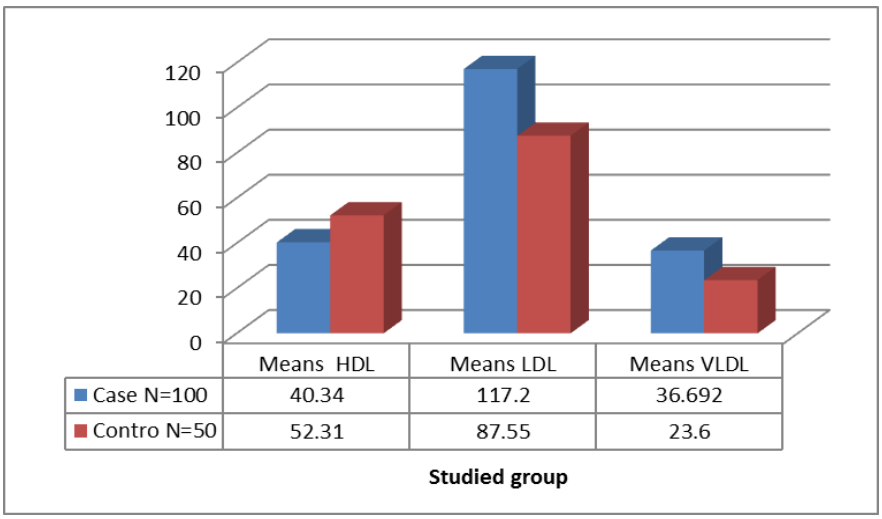

Fig 7. Mean concentrations of HDL, LDL, and VLDL (mg/dl) for the studied group (case number=100, control number=50), where was the SD of HDL for patient and control (9.82, 4.94) respectively, while SD of LDL for patient and control (8.59, 6.92), and SD of VLDL for patient and control (4.28, 5.58), with P-value <0.001 (H.S)

6. Conclusion

In this study, conducted in Iraq, it was observed; that obesity and high BMI, high lipid profiles are risk factors that lead to insulin resistance and the development of type 2 DM. So, Subjects with dyslipidemia had higher TG, TC, and LDL-C levels and lower HDL-C concentrations than those with normal lipid and had higher levels of fasting glucose and fasting insulin and the highest level of HbA1c.

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Ethical approval

Ethical approval for this study was granted by the Ethical Committee of the Iraqi Ministry of Health (no.23187).

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