University of Baghdad
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Assessment of Insulin Resistance and Lipid Profile in Obese Patients.

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بسم الله الرحمن الرحيم

صدق الله العظيم

Dedication

TO our beloved families and friends.

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List of Abbreviations

Abbreviations	
A1C%	**Glycated hemoglobin**
APO-A	**apolipoprotein A**
APO-B	**apolipoprotein B**
BMI	**Body mass index**
CETP	**Cholesteryl ester transfer protein**
CM	**Centimeter**
CVD	**Cardiovascular disease.**
FFA	**Free fatty acids**
FSI	**Fasting serum insulin**
HDL-C	**High density lipoprotein-cholesterol**
HOMA-IR	**Homeostatic model assessment of insulin resistance**
IR	**Insulin resistance**
KG	**Kilogram**
LDL-C	**Low-density lipoprotein-cholesterol**
M	**Meter**
MG/DL	**Milligram/deciliter**
µIU/ML	**Microinternational unit/milliliter**
QUICKI	**Quantitative insulin sensitivity check index**
ORTU	**Obesity Research and Therapy Unit**
SD	**Standard definition**
T2DM	**Type2 Diabetes mellitus**
TG	**Triglyceride**
VLDL-C	**Very low density lipoprotein-cholesterol**
WHO	**World Health Organization**
WHR	**Waist-to-hip ratio**

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Abstract

Background:

Obesity increases the chance of developing insulin resistance. It seems clear that lifestyle changes, including little physical exercise and constant access to food, particularly in developed and economically emergent countries, as well as genetic factors, appear to have triggered the escalating incidence of diseases related to insulin resistance, including type 2 diabetes. Increased adipose tissue has been related to an increased production of pro-inflammatory cytokines which, together with fatty acids, appear to be responsible for development of insulin resistance.

Aims:

The aim of the present study was to evaluate insulin resistance by evaluating Homeostatic Model Assessment for Insulin Resistance (HOMA-IR) in a group of obese patients and compare them to healthy lean subjects and to elucidate the relationship between HOMA-IR, lipid profile; and other parameters.

Methods and materials:

This study was conducted in the Obesity Research and Therapy Unit (ORTU) – Alkindy College of Medicine – University of Baghdad from 1st of December 2022 to February 2023 involved two groups; group 1 involved obese subjects (BMI ≥ 30). Subjects who have malignancy, diabetes, or major renal disease, hepatic, or endocrine and thyroid dysfunction will be excluded. Group 2 involved non- obese patients with (BMI 18.5 - 24.9).

Results:

In group 1 the HOMA-IR was correlated significantly with waist, WHR, Glucose, A1c%, Cholesterol, and LDL. In addition in group 2 the HOMA-IR was correlated significantly with waist, A1c%, cholesterol, and LDL

Conclusion:

In the present study HOMA-IR and lipid profile were associated with obesity.

keywords:

Insulin resistance, Obesity, Dyslipidemia, HOMA-IR, LDL-C, HDL-C.

CHAPTER ONE
(INTRODUCTION)

INTRODUCTION:

1.1 Obesity:

Obesity is an increasing, global public health issue. The prevalence of overweight and obesity is rapidly increasing in developing as well as industrialized countries Patients with obesity are at major risk for developing a range of comorbid conditions, including cardiovascular disease (CVD), gastrointestinal disorders, Insulin resistance, type 2 diabetes (T2D), joint and muscular disorders, respiratory problems, and psychological issues, which may significantly affect their daily lives as well as increasing mortality risks [1].

1.2 The concept of obesity:

The World Health Organization (WHO) defines overweight and obesity as abnormal or excessive fat accumulation that presents a risk to health WHO.A body mass index (BMI) ≥25 kg/m2 is generally considered overweight, while obesity is considered to be a BMI ≥ 30 kg/m2 [2].

1.3 Obesity and insulin resistance:

In individuals who are obese local inflammation that leads to the emergence of insulin resistance, which can be defined as a state of reduced responsiveness to normal circulating levels of insulin, plays a major role in the development of type 2 diabetes [1]. Besides, endoplasmic reticulum stress, adipose tissue hypoxia, oxidative stress, lipodystrophy, and genetic background have a role in insulin resistance. Accumulating evidence suggests that insulin resistance is the most probable link between obesity and obesity-associated metabolic dyslipidemia [3].

Dyslipidemia which is defined as an imbalance of lipids such as cholesterol, low-density lipoprotein cholesterol, (LDL-C), triglycerides, and high-density lipoprotein cholesterol (HDL-C) [4]. This abnormality is very commonly observed in patients who are obese. Approximately 60-70% of patients with obesity are dyslipidemic higher amounts of non-esterified fatty acids, glycerol, hormones, and pro-inflammatory cytokines are released by adipose tissue and could participate in the development of a major health problem is called insulin resistance an extreme adipose tissue expansion due to an increase in nutrients intake and insufficient energetic expenditure is considered as Obesity [3].

On the other hand, insulin resistance can lead to serious health problem called diabetes mellitus which is a complex chronic illness manifested by a high level of blood glucose or hyperglycemia, resulting from deficiencies in insulin secretion, action, or both [5].

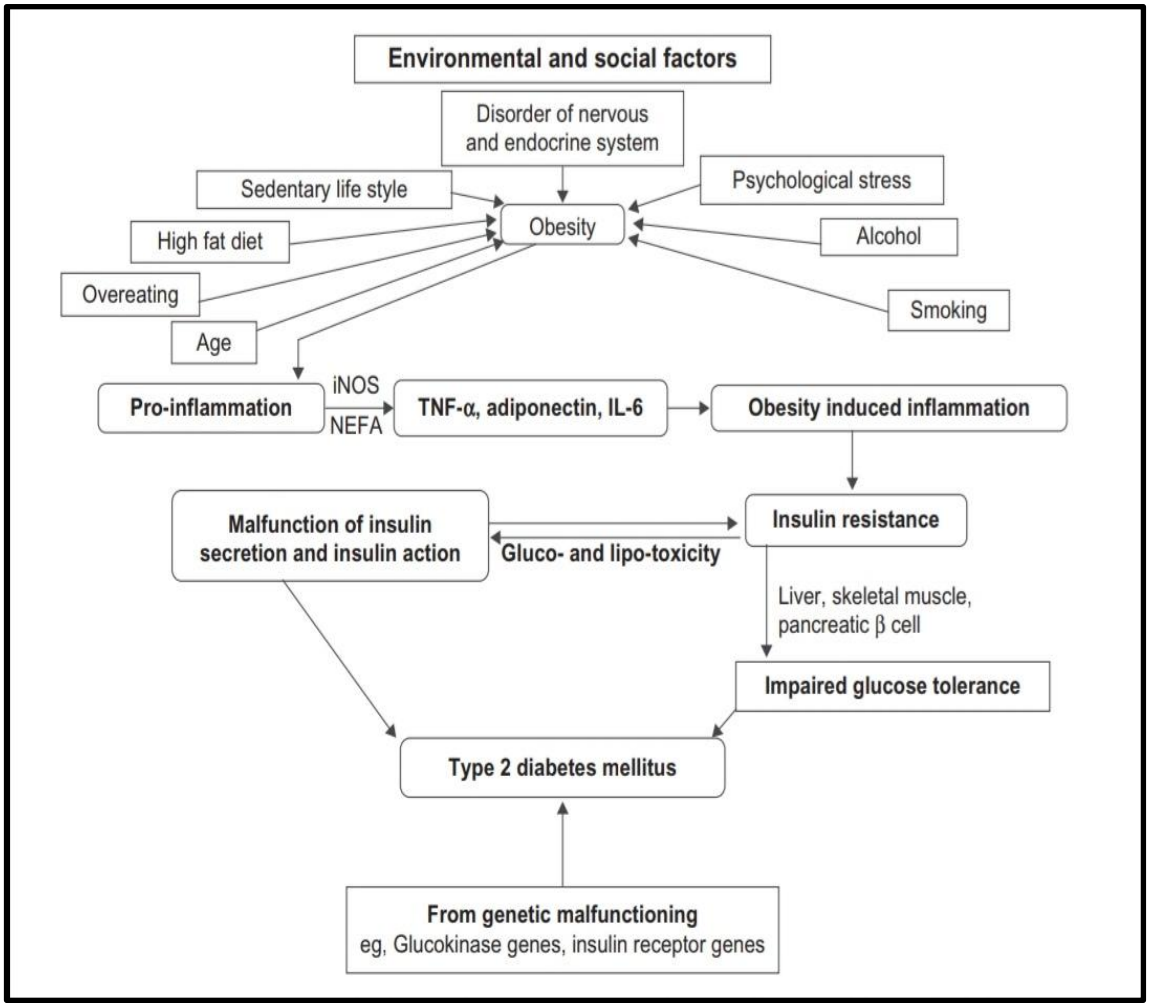

Figure 1. Combined impact of genetic makeup, environmental and social factors in the process of development of type 2 diabetes associated with obesity through impaired insulin secretion and insulin action, explaining the progression from insulin resistance to an impaired glucose tolerance test (IGT) and type 2 diabetes**.**

1.4 Lipid abnormalities in obese patients:

The lipid abnormalities seen in patients who are obese include elevated triglyceride, very low-density lipoprotein (VLDL), Apo B, and non-HDL-C levels, which are all commonly observed. HDL-C and Apo A-I levels are typically low. LDL-C levels are frequently in the normal range, but an increase in small dense LDL is often seen resulting in an increased number of LDL particles [6],[7]. These small dense LDL particles are considered to be more pro-atherogenic than large LDL particles for a number of reasons Small dense LDL-C particles have a decreased affinity for the LDL receptor resulting in a prolonged period of time in the circulation [7].

1.5 Obesity and pathophysiology of insulin resistance:

Although standard definitions of insulin resistance still define it in terms of the effects of insulin on glucose metabolism, the last decade has seen a shift from the traditional "glucocentric" view of diabetes to an increasingly acknowledged "lipocentric" viewpoint. This hypothesis holds that abnormalities in fatty acid metabolism may result in inappropriate accumulation of lipids in muscle, liver, and β-cells. It is further proposed that ectopic lipid accumulation is involved in the development of insulin resistance in muscle and liver as well as impairing β-cell function (so-called "lipotoxicity") [8]. Lipid accumulation within myocytes and hepatocytes is strongly associated with insulin resistance in diabetics, in individuals with impaired glucose tolerance, and obese subjects [9].

1.6 IR and dyslipidemia:

Insulin resistance often occurs with dyslipidemia as part of the metabolic syndrome and the current dominant paradigm is that insulin resistance leads to dyslipidemia. However, dyslipidemia may also cause insulin resistance; this was postulated 30 years ago, but still causes Controversy among the scientific community [10].

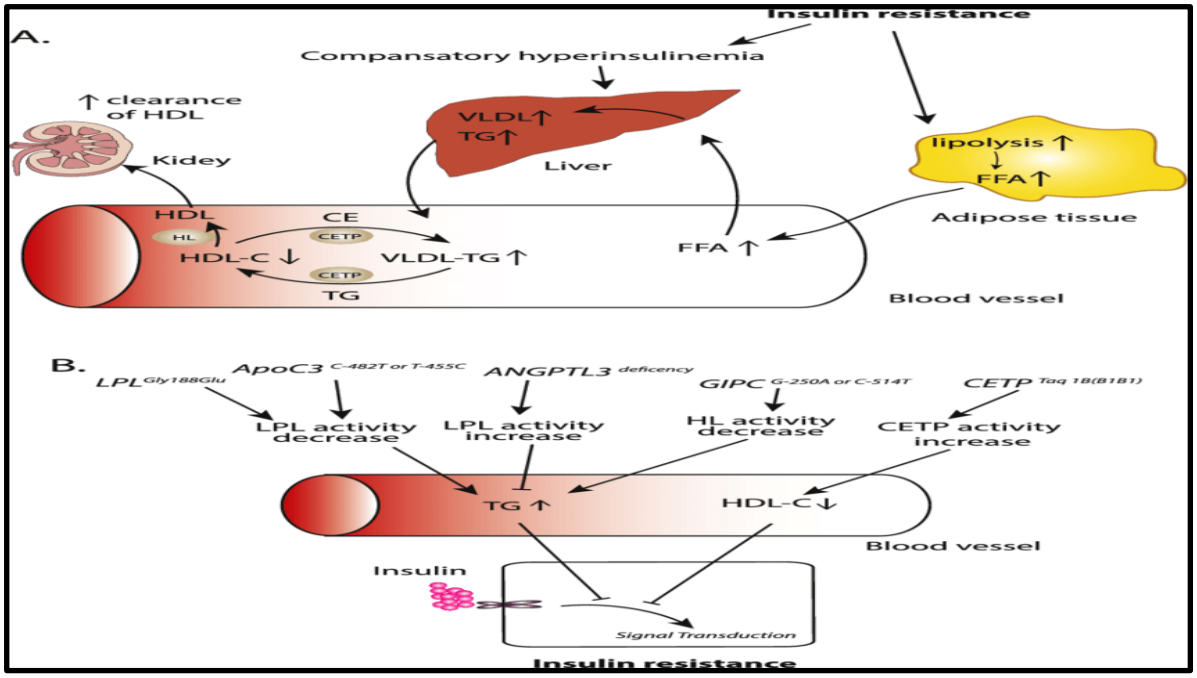

Figure2-Schematic representation of the relationship between insulin resistance, hypertriglyceridemia and low HDL-C**.**

The mechanisms by which insulin resistance leads to hypertriglyceridemia and low HDL-C.

Insulin resistance induces compensatory hyperinsulinemia, causing overproduction and secretion of VLDL in the liver, which leads to increased plasma VLDL-TG [10]. At the same time, insulin resistance activates the process of lipolysis, which is originally inhibited by insulin, so that free fatty acids (FFA) are produced and released to the bloodstream. FFAs also can increase production of triglyceride as a kind of substrate in the liver by entering hepatocytes, which aggravates hypertriglyceridemia. After bidirectional transfer of Cholesteryl ester transfer protein (CETP), the HDL particles without CE are susceptible to be broken down and cleared by the kidney, causing decreased HDL levels [figure 2-A] [11].

The mechanisms leading from dyslipidemia to insulin resistance is mostly supported by genetic variants in lipid genes, depicted on top, leading to increased serum triglycerides or decreased HDL-C. It is therefore likely that lipoproteins can induce insulin resistance. The mechanism for this relationship is not known, but is likely to involve several steps. In addition, it cannot rule out that the genetic variants cause pleiotropic effects leading to insulin resistance, unrelated to the lipoproteins[figure2-B] [10,11].

1.7 Assessment Insulin Resistance:

There are different measuring ways for Assessment IR Including [12]:

1-Hyperinsulinemic-euglycemic clamp:

The gold standard for evaluating insulin sensitivity, this "clamp" technique requires a steady IV infusion of insulin to be administered in one arm. A variation of this technique provides a better measurement of pancreatic beta cell function but is less physiologic than the euglycemic technique.

2-Fasting serum insulin (FSI).

3-Glucose/insulin ratio (G/I ratio).

4-Homeostatic model assessment of insulin resistance (HOMA-IR).

5-Quantitative insulin sensitivity check index (QUICKI): can be applied to normoglycemic and hyperglycemic patients.

1.8 Homeostatic Model Assessment of Insulin resistance (HOMA-IR):

The homeostatic model assessment (HOMA) is a validated method to measure insulin resistance from fasting glucose and insulin. The original model HOMA1-IR, first published by Mattews and cols. in 1985 and has been widely used, especially in epidemiological and clinical studies. Recently, the model was updated with some physiological adjustments to (HOMA2-IR) a computer version providing a more accurate index [13].

It was also demonstrated that insulin resistance, assessed by both HOMA-IR indexes, is associated with an elevated BMI, with a worse lipoprotein profile. Furthermore, it was verified that in the apparently healthy subjects, HOMA-IR indexes were positively associated with BMI and abdominal obesity, and with triglycerides and total cholesterol. (HOMA1-IR), the first described model, is a validated method to evaluate insulin resistance. However, according to Levy and cols, the HOMA2-IR is a more accurate representation of the metabolic process because it models the feedback relationship between insulin and glucose in the various organs in the body on the other hand, the HOMA2-IR has the inconvenience that only a specific range of values are acceptable for calculation. The Homeostasis Model Assessment (HOMA-IR) estimates steady state beta cell function (%B) and insulin sensitivity (%S), as percentages of a normal reference population [14].

Glucose in mass units (mg/dL)

$$\text{HOMA} - \text{IR} = \frac{\text{Glucose x Insulin}}{405}$$

Glucose in molar units (mmol/L)

$$\text{HOMA} - \text{IR} = \frac{\text{Glucose x Insulin}}{22.5}$$

[15].

The constant 405 should be replaced by 22.5 if glucose is expressed in S.I. units. Unlike I0 and the G/I ratio, the HOMA calculation compensates for fasting hyperglycemia. Also keep in mind that HOMA and I0 values increase in the insulin-resistant patient while the G/I ratio decreases [12].

Several studies had suggested that HOMA-IR ranges should be Less than 1.0 for insulin-sensitive which is optimal, while over 1.9 indicates early insulin resistance and over 2.9 indicates significant insulin resistance [16].

Although all methods that can predict insulin resistance where more overweight/obese the person, the more likely they are to be insulin-resistant and at increased risk of cardiovascular disease, but substantial numbers of overweight/obese individuals remain insulin-sensitive, and not all insulin-resistant persons are obese this fact is still a point of study and discussion in researches interested in the field of diabetes and obesity [13].

Aims:

The aim of the present study to evaluate insulin resistance by homeostatic model assessment of insulin resistance (HOMA-IR) in a group of obese patients compared to healthy subject and to elucidate the relationship between HOMA-IR and lipid profile and other parameters.

CHAPTER TWO
(Method and Material)

Method and material:

2.1 Type of study:

Cross – sectional study

2.2 Setting and Duration:

This study was conducted in Obesity Research and Therapy Unit (ORTU) – Alkindy College of Medicine – University of Baghdad from 1st of December 2022 to February 2023. The Study Protocol and Ethical Approval were permitted by Alkindy College of Medicine. Informed consent was obtained from all subjects involved in the study.

2.3 Study Population:

Subjects between (20 to 60) years of age were selected and classified into two main groups according to their Body mass index (BMI - calculated as weight in kilograms divided by height in squared meters). Group1 involved healthy lean volunteers (BMI 18.5 - 24.9); group2 involved obese subjects (BMI ≥ 30). Subjects who had malignancy, diabetes, or major renal disease, hepatic, or endocrine and thyroid dysfunction were excluded.

2.4 Assessment of Anthropometric and Biochemical Parameters:

Blood samples were drawn in the fasting state (for at least 12 hours) and centrifuged. Then serum samples were collected to be stored at -20°C until analytical processing. Patients' health status data were acquired from medical records and augmented with self-reported information from the research participants. Blood pressure and anthropometric measurements; body weight (Kg) and height (m); circumference of waist and hip (cm). In addition, BMI (kg/m^2) and waist to hip ratio (WHR) were estimated according to medical standards in the ORTU.

Serum Glucose (s.Glucose) , cholesterol (chol)triglycerides (TG), high-density lipoproteins and cholesterol (HDL-C). Were measured using diagnostic kits produced by (Human, Germany). Serum insulin levels were estimated by ELISA kits (Demeditec Diagnostics., Germany).

Glycated hemoglobin A1c% was assessed by kits and Huma Meter A1c% system analyzer manufactured by (Human, Germany).

Each biochemical parameter was estimated according to the instructions provided with kits. Low-density lipoprotein cholesterol (LDL-C) was calculated by the Friedewald formula available at:
https://www.mdapp.co/ldl-calculator-96 [17].

$$LDL = CHOL - HDL - \frac{TG}{5}$$

2.5 Estimation of Insulin Resistance Biomarkers:

Fasting glucose and insulin levels were used to calculate the HOMA-IR.
With HOMA2-IR version calculator available at:
http://www.dtu.ox.ac.uk/homacalculator/index.php [16].

2.6 Statistical Analyses:

Data were analyzed with SPSS version 25 software for windows 10 (IBM, NewYork, NY, USA). Parametric Data Are Presented As Mean±Standard Deviation (mean±SD). Independent Student's t-testwas used to compare variables between groups respectively. A p value <0.05 was used as the level of significance. Pearson's correlations were used to determine the relationship between serum omentin level and the other variables. Linear regression analysis was under taken to determin eindependent associations between Omentin and other variables included in study.

CHAPTER THREE
(RESULTS)

Results:

The clinical characteristics and biochemical analytes of participants in the present study are shown in Table 3-1. The obese group has higher HOMA-IR levels when compared to the healthy lean group (3.95 ± 1.929 vs. 1.75 ± 1.2, P <0.001). Moreover, the obese group exhibited significant higher levels of hip, waist circumference (WC), waist to hip ratio (WHR), weight, BMI, glucose, insulin, HOMA2-IR and lipid profile and lower levels of HDL-Cholesterol (p <0.001).

Table 3-1: The anthropometric, biochemical variables of participants enrolled in the present study.

Parameters	Group1 (Obese)	Group2 (Lean)	*P* value
n (%)	53 /115 (46.1%)	62 /115 (53.9)	
Age (year)	43.48 ± 10.42	41.27 ± 11.24	0.243
Waist Circumference (cm)	109.51 ± 13.37	79.76 ± 5.57	0.000**
Hip (cm)	123.41 ± 11.27	97.53 ± 6.06	0.057
Waist to Hip Ratio (WHR)	0.88 ± 0.81	0.80 ± 0.05	0.034*
Weight (Kg)	105.90 ± 21.447	62.92 ± 5.287	0.000**
Height (m)	39.80 ± 7.105	164.10 ± 8.452	0.280
BMI (kg/m^2)	39.80 ± 7.105	23.16 ±1.44	0.000**
Serum Glucose (mg/dl)	105.22 ± 20.13	90.77 ± 7.88	0.000**
Serum Insulin (µIU/ml)	31.56 ± 21.38	17.12 ± 29.15	0.023*
A1c%	5.28 ± 0.70	4.78 ± 0.27	0.000**
HOMA-IR	3.95 ± 1.929	1.75 ± 1.2	0.001**
Triglyceride (mg/dl)	152.72 ± 86.01	79.12 ± 27.63	0.000**
Total Cholesterol (mg/dl)	197.71 ± 39.35	161.81 ± 32.97	0.000**
HDL-C (mg/dl)	37.30 ± 10.24	44.63 ± 8.03	0.001**
LDL-C (mg/dl)	129.80 ± 39.91	101.36 ± 30.40	0.066

Data are represented as (mean ± SD). BMI: body mass index; HOMA-IR: homeostasis model assessment of insulin resistance; HDL–C: high density lipoprotein-cholesterol. LDL–C: Low density lipoprotein-cholesterol. Statistical significance considered at * p <0.05,
** p <0.01, ***p <0.001

Table 3-2 illustrates the correlations between HOMA-IR and the other parameters in group 1 (Obese). HOMA-IR levels were correlated significantly with waist (r =0.458, p =0.008), WHR (r =0.441, p =0.013), Glucose (r = 0.348, p =0.028), A1c% (r = 0.931, p <0.000), Cholesterol (r = 0.506, p <0.001), and LDL (r = 0.361, p =0.022).

Table 3-2: Correlations of Study Analytes with HOMA-IR in Participants enrolled in the Present Study	
Parameters	
Age (year)	**(r = 0.022, p = 0.891)**
Waist Circumference (cm)	**(r = 0.458, p = 0.008)****
Hip (c)	**(r = 0.201, p = 0.278)**
Waist to Hip Ratio (WHR)	**(r = 0.441, p = 0.013)***
BMI (kg/m^2)	**(r = 0.220, p = 0.173)**
Serum Glucose (mg/dl)	**(r = 0.348, p = 0.028)***
Serum Insulin (µIU/ml)	**(r = 0.051, p = 0.754)**
A1c%	**(r = 0.931, p < 0.000)****
Triglyceride (mg/dl)	**(r = 0.156, p = 0.336)**
Total Cholesterol (mg/dl)	**(r = 0.506, p < 0.001)****
HDL-C (mg/dl)	**(r = 0.041, p = 0.800)**
LDL-C (mg/dl)	**(r = 0.361, p = 0.022)***

BMI: body mass index; HOMA-IR: homeostasis model assessment of insulin resistance; HDL-C: high density lipoprotein-cholesterol. LDL– C: Low density lipoprotein-cholesterol. Values with statistical significance at * p <0.05, ** p <0.01, ***p <0.001.

Table 3-3 illustrates the correlations between HOMA-IR and the other parameters in the group 2 (Lean). HOMA-IR levels were correlated significantly with waist (r = 0.401, *P* = 0.047), A1c% (r = 0.956, p < 0.000), cholesterol (r = 0.421, p = 0.008), and LDL (r = 0.338, p = 0.035).

Table 3-3: Correlations of Study Analytes with HOMA-IR in Participants enrolled in the Present Study	
Parameters	
Age (year)	**(r = 0.210, *P* = 0.199)**
Waist Circumference (cm)	**(r = 0.401, *P* = 0.047)***
Hip (cm)	**(r = 0.213, p = 0.307)**
Waist to Hip Ratio (WHR)	**(r = 0.358, p = 0.079)**
BMI (kg/m^2)	**(r = 0.240, p = 0.141)**
Serum Glucose (mg/dl)	**(r = 0.271, p = 0.096)**
Serum Insulin (µIU/ml)	**(r = 0.031, p = 0.850)**
A1c%	**(r = 0.956, p < 0.000)****
Triglyceride (mg/dl)	**(r = 0.055, p = 0.737)**
Total Cholesterol (mg/dl)	**(r = 0.421, p = 0.008)****
HDL-C (mg/dl)	**(r = 0.153, p = 0.351)**
LDL-C (mg/dl)	**(r = 0.338, p = 0.035)***

BMI: body mass index; HOMA-IR: homeostasis model assessment of insulin resistance; HDL-C: high density lipoprotein-cholesterol. LDL– C: Low density lipoprotein-cholesterol. Values with statistical significance at * p <0.05, ** p <0.01, ***p <0.001.

CHAPTER FOUR
(DISCUSSION)

DISCUSSION:

In the present study, study participants were classified according to their BMI into two groups (obese and lean subjects). It was found that group 1 (obese patients) has elevated levels of (WHR, BMI , serum glucose ,serum insulin , A1c% , HOMA2-IR , Triglyceride , LDL total serum cholsterol) in comparison with group 2 (lean). In addition, it was found that HOMA2-IR positively correlated to (waist circumference,WHR , BMI , glucose , insulin , A1c% , LDL ,cholestrol …) .

HOMA2-IR index widely used in researches and clinical practice to evaluate insulin resistance. Several studies had suggested that HOMA-IR ranges should be Less than 1.0 for insulin- sensitive which is optimal,While over 1.9 indicates early insulin resistance and over 2.9 indicates significant insulin resistance [16].

It was confirmed that HOMA2-IR value above 2.5 is taken as indicator in IR estimation. Furthermore other studies that was done in turkey demostrated that the cutoff point for optimal value of HOMA2-IR is 1.40 [18].

This variations of the threshold values of HOMA-IR may depend on population being studied, samples being collected and another factors such as family history, medical history and lab tests should be taken in consideration because they affect HOMA-IR results. This is in agreement with the study demonstrated the finding that (Socio-demographic factors have an effect on IR. Indeed, differing genetic, epigenetic, and sociocultural factors are important determinants of insulin sensitivity [19].

Dietary differences also have an effect on IR; a plant-based, low fat dietary pattern has a protective effect against its development [20].

In the present study, it was found that the HOMA2-IR was elevated in group 1 (obese patients). This is in line with study suggested that a significant differences among the HOMA2-IR values of normal weight, overweight and obese was observed. High values of HOMA-IR in obese subjects compared to normal adolescents has also been validated in large study among adolescents [21].

Commensurate with the rising trend of obesity is the rising prevalence of IR and MS in the population [22]. There are several hypotheses to explain the mechanisms responsable for IR in obese patients such as multifactors including genetic, lifestyle, dietary routine factors have been implicated in obesity Pathogenesis [23].

High HOMA2-IR level in obese patients is a critical risk factor in the progression of type 2 diabetes. This was in link with studies suggested that high HOMA2-IR were individually associated with increased odds of progression of type 2 diabetes compared to the HOMA1-IR. HOMA2-IR had better performance in predicting incident type 2 diabetes [24]. This finding was in similarity to other reports from Iranian (aged 20–86 years, using HOMA2) and Chinese (aged above 40, using HOMA1) cohorts, supporting the important role of IR mediated by obesity and glucolipotoxicity in progression to T2D in both young and older Chinese people [25].

Another hypothesis is that the low-grade inflammation that accompanies obesity leads to impaired peripheral tissue insulin sensitivity. Increased plasma levels of inflammatory mediators, e.g., C-reactive protein, leukocytes or interleukin 6 (IL-6), have been shown to predict the development of insulin resistance and type 2 diabetes [26].

In 2000, Katz et al. developed the quantitative insulin sensitivity check index (QUICKI). It provides an advantage for predicting IR in patients with type 2 diabetes and obesity but is unreliable in patients with type 1 diabetes. In the diagnosis of IR, the McAuley index can also be used, which takes into account fasting insulinemia and TG concentration. According to the authors of a Korean study, the McAuley index best correlates with uncomplicated IR
[27].

HOMA-IR and QUICKI take into account fasting glucose and concentration to estimate the hepatic IR whereas the mastuda index focuses in the dynamic values obtained in oral glucose tolerance test (OGTT) to estimate the peripheral IR. So HOMA2-IR is more accurate to estimate the IR [28].

In this study, HOMA-IR was positively correlated with WHR, and this is confirmed by the study that HOMA-IR has significant correlations with WC and WHR, while the correlation between WHR and HOMA-IR was poor.

Other studies, including one from India [29], also observed the strongest correlation of HOMA-IR with WC. In addition, this finding was confirmed that another parameter has shown a good correlation with HOMA-IR in

our study is WHR. A similar result was reported in a large study from Europe [30,31,32].

All these studies have shown that WC and WHR are good predictors of IR in obese and can be used to identify individuals at risk. A sedentary lifestyle can contribute to an increase in both HOMA-IR and WHR. Lack of physical activity can lead to decreased insulin sensitivity and an increase in adipose tissue, particularly visceral adipose tissue. In addition, sedentary behavior is associated with an increase in central obesity and WHR [33].

Furthermore an unhealthy diet high in processed foods and added sugars, which can contribute to an increase in both HOMA-IR and WHR. Consuming a diet high in calories, sugar, and unhealthy fats can lead to an increase in visceral adipose tissue and insulin resistance, which can contribute to an increase in HOMA-IR and WHR [34].

In our study, HOMA-IR was also positively correlated with BMI, and this was in agreement with a study done by Amruth Raj, which approved that there was a positive correlation of HOMA-IR with BMI [35].

Abtahi et al. observed that the prevalence of prediabetes was higher in obese person having higher range of waist circumference, WHR and BMI. Body weight is determined by many factors, such as genetic, behavioral, cultural, socio-economic, physical inactivity, diet, and psychosocial factors. Excess body weight is a risk factor for a variety of health hazards like diabetes mellitus, prediabetes, and cardiovascular disease. It was concluded that people with lower BMI are less susceptible for development of IR, diabetes mellitus, and obese people have a higher prevalence of abnormal blood glucose levels [36].

The present study found a positive correlation between HOMA-IR and glucose was found. This was explained by the study that demonstrated the genetic factors can play a role in insulin resistance and glucose dysregulation [37]. And by Unhealthy Diet high in processed foods, sugary beverages, refined carbohydrates, and saturated or trans fats can contribute to insulin resistance and elevated glucose levels3. Obesity is strongly associated with insulin resistance and elevated blood glucose levels. Excess body fat, particularly visceral fat (fat around the abdomen), releases chemicals that interfere with insulin action [38].

The positive correlation between HOMA2-IR and insulin was approved by the study confirmed that hyperinsulinemia is significantly correlated with

IR, so it can render more viable way to detect insulin-resistant type 2 diabetics instead of measuring glucose intolerance. This was confirmed by hyperinsulinemia is an effective compensatory mechanism that allows for insulin action in mild to moderate IR [39].
A study reported that genetic, environmental, and dietary factors have been associated with hyperinsulinemia. Air pollution has been associated with adverse lipid changes and higher fasting glucose and insulin [40].
Blacks had higher insulin levels than whites, consistent with impaired insulin clearance in blacks, which could not be explained by differences in BMI, family history, smoking, or other factors [41] and in vitro studies have suggested that hyperinsulinemia is associated with increases in reactive oxygen species [42].

In addition, HOMA-IR was also positively correlated with A1C%, and this is confirmed by the study that glycemia measured by A1C% in the non-diabetic range has been shown to correlate with HOMA-IR [43]. Elevated blood glucose levels, also known as hyperglycemia, can directly contribute to an increase in A1C%. Chronic hyperglycemia leads to the glycation of hemoglobin, which increases the proportion of A1C% in the blood [44].
Both insulin resistance and hyperglycemia can lead to oxidative stress and inflammation, which contribute to the development of type 2 diabetes and cardiovascular disease. These processes can also contribute to an increase in A1C%, as oxidative stress and inflammation can increase the glycation of hemoglobin [45].

High HOMA2-IR was correlated in our study with the elevated levels of (cholesterol, LDL and TG) in obese patients. This is linked to the study that reported the effects of lipid accumulation in tissues are referred to lipotoxicity and indicate systemic inflammation and IR [46]. The excessive lipid accumulation in ectopic tissues leads to local inflammation and IR The ectopic fat accumulation in the pancreas, for example, contributes to β-cell dysfunction, and recent studies in human have proved that the bariatric surgery can improve β-cell function by decreasing pancreatic fat accumulation [39,47]. A marker of ectopic fat accumulation in human is the increased visceral/intra-abdominal fat accumulation, associated with abdominal obesity [48].

Moreover, accumulation of lipids in adipocytes can induce oxidative stress, as evidenced by excess reactive oxygen species (ROS) such as hydrogen peroxide and hydroxyl radical ions by activating NADPH oxidase. Recent studies have shown that ROS-induced damage has lately been recognized as one of the key mechanisms in the pathogenesis of IR [49].
In contrast with the study that discussed the concept that impaired adipose tissue remodeling in obesity is not a homogeneous condition, and obesity does not necessarily translate into IR and increased risk for metabolic comorbidities. Several studies have reported that a subgroup of obese individuals remains insulin-sensitive and metabolically "healthy" and exhibits normal physiology and hormonal profiles [50].

In the present study; it was found that the lipid profile was elevated in obese patients. It was in line with the study reported that the lipid abnormalities seen in patients who are obese include elevated triglyceride, VLDL, Apo B, and non-HDL-C levels, cholestrol, which are all commonly observe. HDL-C and Apo A-I levels are typically low [51]. Studies suggested was approximately 60-70% of patients who are obese are dyslipidemic while 50-60% of patients who are overweight are dyslipidemic [52]. Notably, obesity in children and young adults also leads to an increased prevalence of elevated triglycerides and decreased HDL-C levels [53]. Moreover, these abnormalities are driven by the combination of the greater delivery of free fatty acids to the liver from increased total and visceral adiposity, insulin resistance, and a pro-inflammatory state, induced by macrophages infiltrating fat tissue [54, 52]. In patients with obesity, a decrease in insulin activity due to insulin resistance results in the blunting of the inhibition of triglyceride lipolysis and an increase in triglyceride breakdown in adipose tissue leading to increased fatty acid deliver to the liver [52].

CONCLUSION:

In the present study HOMA-IR and lipid profile were associated with obesity.

LIMITATION:

The study was designed to be cross sectional, thus there were unavoidable limitation.

1- **Limited time.**
2- **sample population was small because it is derived from only ORTU at Al-kindy Collage of Medicine and therefor the sample cannot be generalized to whole people.**

RECOMMENDATION:

We recommend that Evaluation of HOMA-IR and lipid profile to be routinely done for obese individuals.

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APPENDIX

APPENDIX
Study Protocol

- **Name:**

- **Center or Hospital File no.:**

- **Physical Examination:**

Age: Sex: WHR:
BW ; Hgt: BMI:

- **Drugs History and Current Medications:**

- **Social habits:**

Smoking: nonsmoker:
Previous smoker: current smoker:
No. of Cigarette/day:
Alcohol consumption:

- **History of Diseases and Complications**:

- **Routine and Research Laboratory Investigations: -**

i. **Tests of Glycemia:**

1. Fasting Serum Glucose
2. HbA1c%
3. Insulin
4. HOMA-IR

ii. Lipid Profile

1. TG
2. T.chol
3. Hdl-C
4. LDL-C