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Assessment of IL-18 and lipid profile in Sample of Iraqi obese

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Abstract

Obesity increases interleukin-18 due to inflammation in adipose tissue, contributing to lipid profile disturbances and a higher risk of cardiovascular diseases.

This work was aimed to investigate the changes in concentration of IL -18 and levels of lipid profile parameters in Iraqi. obese patients.

Sixty obese patients (35men and 25 women) with ages between 25-50 years and in different classes of obesity and 30 healthy (15 men and 15women) were enrolled in the study during their attendance at Diabetes and Endocrinology center / AL-Kindi Teaching Hospital in Baghdad /Iraq. During the period from November 2024 to February 2025. Blood samples were collected after an overnight fasting from all participants. Serum was separated and stored in a deep freezer at-20°C .The level of IL-18 were measured based on the Sandwich-ELISA technique. Lipid profile also measured and determined by enzymatic colorimetric method.

The result showed a non-significant difference in the age between obese patients (37.25 ±0.93 years) and control (34.67 ±1.39 years) . While the result showed that there was a highly significant (P≤0.01) increase in BMI in obese patients(36.74 ±0.49 kg/m2) as compared with control (21.93 ±0.29 kg/m2).Also there was a highly significant(P≤0.01)increase in WHR in obese patients(0.903 ±0.006 %) as compared with control (0.796 ±0.009 %).There was a highly significant (P≤0.01)increase in the groups of obese class I (40.00%) with BMI (30-35 kg/m2) as compared with group of obese class II (35.00%) with BMI (35-40 kg/m2) and the group of obese class III (25.00%) with BMI(>40 kg/m2).Also there was a highly significant (P ≤ 0, 01) increased in the level of IL-18 in the obese patients (4764.98 ±139.44 pg/L) as compared with control, (1748.10 ±65.25pg/L) .Also the Results of this study revealed that there were a highly significant (P≤0.01)increase in the levels of cholesterol (251.56 ±1.84), triglyceride (229.96 ±4.48), LDL (156.87 ±1.51) and VLDL (45.99 ±0.96) respectively in obese patients in comparison to control groups (191.78 ±0.81), (133.26 ±1.04), (102.56 ±0.87) and (26.65 ±0.21) respectively .On the other hand the result showed a highly significant (P≤0.01) decrease in the level of HDL (49.3± 0.61) in obese patients as compared with control (62.56 ± 0.36).There were a positive significant correlation in the level of IL-18 with cholesterol , triglycerides , LDL, and VLDL .While it shows a negative significant correlation with HDL.

It can be concluded that the changes in IL-18 and other biochemical parameter(lipid profile) may be a good indicator for assessment of obesity.

Key words: Obesity ,Inflammation, IL-18 and lipid profile

تقييم مستوى البين ابيضاض 18- وصورة الدهون في عينة من مرضى السمنة العراقيين

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مستخلص:

السمنة ترفع إنترلوكين-18 بسبب الالتهاب المناعي في الأنسجة الدهنية، ما يساهم في اضطراب ملف الدهون وزيادة خطر الأمراض القلبية

يهدف هذا العمل الى دراسة التغيرات في تركيز احد الحركيات الخلوية الالتهابية البين ابيضاض- 18 ومستويات معايير ملف الدهون لدى مرضى السمنة العراقيين

ستون مريضا يعانون من السمنة (35 رجلا و25 امرأة) تتراوح اعمارهم بين 50-25 عام من فئات مختلفة من السمنة و30 شخص سليم(15 رجل و 15 امرأة) كمجموعة سيطرة . تم تسجيلهم في الدراسة اثناء حضورهم في المركز التخصصي لأمراض الغدد الصم والسكري في مستشفى الكندي التعليمي في بغداد/ العراق للفترة مابين تشرين الثاني 2024 الى شباط 2025

تم قياس مستوى تركيز البين ابيضاض 18 باستخدام تقنية الممتز المناعي المرتبط بالأنزيم(الاليزا)

كما تم قياس وتحديد مستوى الدهون بطريقة قياس اللون الانزيمي باستخدام جهاز خاص

أظهرت النتائج عدم وجود فرق معنوي في العمر بين المرضى المصابين بالسمنة (37.25 ± 0.93 سنة) والمجموعة الضابطة (34.67 ± 1.39 سنة). بينما أظهرت وجود زيادة معنوية عالية (P≤0.01) في مؤشر كتلة الجسم لدى المرضى المصابين بالسمنة (36.74 ± 0.49 كغم/ م²) مقارنةً مع المجموعة الضابطة (21.93 ± 0.29 كغم/ م²). كذلك، وُجدت زيادة معنوية عالية (P≤0.01) في نسبة محيط الخصر إلى محيط الورك لدى المرضى المصابين بالسمنة (0.903 ± 0.006 ٪) مقارنةً مع المجموعة الضابطة (0.796 ± 0.009 ٪).كما لوحظ وجود زيادة معنوية عالية (P≤0.01) في نسبة المرضى المصابين بالسمنة من الفئة الأولى (40.00٪) والذين لديهم مؤشر كتلة جسم بين (35-30 كغم/ م²)، مقارنةً مع الفئة الثانية (35.00٪) التي يتراوح مؤشر كتلة الجسم لديها بين (35-40 كغم/ م²)، والفئة الثالثة (25.00٪) التي يزيد مؤشر كتلة الجسم لديها عن 40 كغم/ م². كذلك، وُجدت زيادة معنوية عالية (P≤0.01) في مستوى البين ابيضاض-18 لدى المرضى المصابين بالسمنة (4764.98 ± 139.44 بيكوغرام/ لتر) مقارنةً مع المجموعة الضابطة (1748.10 ± 65.25 بيكوغرام/ لتر).كما كشفت النتائج وجود زيادة معنوية عالية (P≤0.01) في مستويات الكوليسترول (251.56 ± 1.84)، والدهون الثلاثية (229.96 ± 4.48) وكوليسترول البروتين الدهني منخفض الكثافة(156.87 ± 1.51-وكوليسترول البروتين الدهني منخفض الكثافة جدا(45.99 ± 0.96) لدى المرضى المصابين بالسمنة، مقارنةً مع المجموعات الضابطة التي كانت مستوياتها (191.78 ± 0.81)، (133.26 ± 1.04)، (102.56 ± 0.87)، و(26.65 ± 0.21) على التوالي.من ناحية أخرى، أظهرت النتائج انخفاضًا معنويًا عاليًا (P≤0.01) في مستوى كوليسترول البروتين الدهني عالي الكثافة (49.3 ± 0.61) لدى المرضى المصابين بالسمنة مقارنةً مع المجموعة الضابطة (62.56 ± 0.36).وأخيرًا، وُجدت علاقة ارتباط معنوية موجبة بين مستوى البين ابيضاض 18 وبين كل من الكوليسترول، والدهون الثلاثية وكوليسترول البروتين الدهني منخفض الكثافة وكوليسترول البروتين الدهني مخفض الكثافة جدا بينما وُجدت علاقة ارتباط معنوية سالبة بين البين ابيضاض 18 وبين كوليسترول البروتين الدهني عالي الكثافة.

يمكن الاستنتاج ان التغييرات في البين ابيضاض 18 والمعايير الكيميائية كملف الدهون قد تكون مؤشر جيد لتقييم السمنة .

الكلمات المفتاحية :السمنة والالتهاب المناعي والبين ابيضاض -18 وملف الدهون .

Introduction

Abnormal or excessive adipose accumulation in the body [1].which is influenced by the regional distribution of adipose tissue[2].Also known as ectopic fat throughout the body. It is a chronic, progressive, relapsing condition with multiple factors that lead to adverse metabolic and psychosocial health consequences[3].A body mass index (BMI) over 25 is considered overweight, and over 30 is obese according to the World Health Organization [4]. It is a serious issue for public health, also It contributes directly or indirectly to the expansion of health care resources in addition to being a risk factor for numerous illnesses[5].One of the main causes of obesity is an imbalance between the excess energy stored and the energy utilized by the body, which can disrupt nutrient signals and result in insufficient energy expenditure[6]. Obesity has spread worldwide during the last 20 years, affecting both children and adults. Despite extensive studies into the connection between obesity and cardiovascular diseases(CVD). many unanswered problems still exist [7]. It is associated with various cardiovascular diseases and conditions, including atherosclerosis, atrial fibrillation, symptomatic coronary artery disease and heart failure [8,9]. Obesity leads to adverse effects on health and life expectancy ,so its proposed to associate with high expression of adiponectin[10]. Adipose tissue is one of the important endocrine organs in the body the main function of adipocytes is as energy storage depots and excretion of important hormones such as adiponectin .Obesity represents a major risk factor for several diseases in which inflammation acts as a major driver in pathogenesis, it was suggested that some forms of obesity are associated with chronic mild inflammation [11].Such as IL-18 is a pro inflammatory cytokine [12,13]. This is produced by various cell types and triggers the expression of adhesion molecules and chemokine receptors. Furthermore, this cytokine activates immune response through type 1 and 2 T-helper cells [14]. Besides its inflammatory role, IL-18 also participates in the pathogenesis of visceral obesity[15]. Between subcutaneous fat and

visceral fat, latter is associated with higher risk of cardiometabolic diseases. Serum lipids (triglyceride (TG), total cholesterol (TC)) are markers which are commonly used to estimate the risk of cardiometabolic diseases[16].

Materials and Methods

Ethics and Subject Recruitment

The study was directly achieved after gaining ethical approval from the Scientific Research Committee at the University of Baghdad in Iraq. It was done in the Department of Biology, College of Science, University of Baghdad .Under the reference number (No. CSEC / 0225/0026) at date (2/11/ 2025) .

Study Population

This was a case-control study conducted in Diabetes and Endocrinology /AL-Kindi Teaching Hospital in Baghdad / Iraq. sixty patients (35men and 25 women) with ages between 25-50 years and in different classes of obesity were selected. A total of 30 healthy (15 men and 15 women were taken as control).

Sample Collection and Analysis

Blood samples were collected after an overnight fasting from all participants. Five ml of venous blood samples were collected into disposable plain plastic tubes. To be placed in a gel tube. Then the gel tube allowed to coagulate at room temperature for 10 minutes to be centrifuged at 3000 rpm for 15 min. Serum was separated and stored in a deep freezer at-20°C .The level of IL-18 were measured based on the Sandwich-ELISA technique. The procedure was done according to the direction of manufacture ELK biotechnology company, China (Human Reader HR , Germany).Lipid profile included levels of cholesterol , levels of triglyceride ,HDL and LDL Were also measured and determined by enzymatic colorimetric method .

Statistical Analysis:

The Statistical Packages of Social Sciences-SPSS (2019) program was used to detect the effect of difference groups in study parameters. T-test was used to significant compare between means. Chi-Square test was used to significant compare between percentage. Estimate of Correlation coefficient between difference variables in patient groups in this study.

Result

Table 1 showed that there was a non-significant difference in the age between obese patients (37.25 ±0.93 years) and control (34.67 ±1.39 years) . While the result showed that there was a highly significant (P≤0.01) increase in BMI in obese patients(36.74 ±0.49 kg/m2) as compared with control (21.93 ±0.29 kg/m2).Also there was a highly significant(P≤0.01)increase in WHR in obese patients(0.903 ±0.006 %) as compared with control (0.796 ±0.009 %).)

Table (1): Age, BMI and WHR in obese patients and control

Group	Means ±SE		
	Age (year)	**BMI (kg/m^2)**	**WHR (%)**
Patients	37.25 ±0.93	36.74 ±0.49	0.903 ±0.006
Control	34.67 ±1.39	21.93 ±0.29	0.796 ±0.009
T-test	3.264 NS	1.440 **	0.0231 **
P-value	0.1194	0.0001	0.0001
** (P≤0.01), NS: Non-Significant.			

Table 2 reveled there was a highly significant (P≤0.01)increase in the groups of obese class I (40.00%) with BMI (30-35 kg/m2) as compared with group of obese class II (35.00%) with BMI (35-40 kg/m2) and the group of obese class III (25.00%) with BMI(>40 kg/m2).

Table(2): Distribution of patients according to BMI (Obese class)

Obese class	BMI (kg/m^2)	Patients (No=60)	Percentage (%)	P-value
Obese class I	30-35	24	(40.00%)	0.0001 **
Obese class II	35-40	21	(35.00%)	
Obese class III	>40	15	(25.00%)	
** (P≤0.01)				

Table 3: Interleukin- 18 and Lipid profile in obese patients and control

Group	IL-18 (pg/ml) Mean ±SD	Cholesterol (mg/dl) Mean ±SD	TG (mg/dl) Mean ±SD	(HDL (mg/dl Mean ±SD	(LDL (mg/dl SD± Mean	VLDL (mg/dl) Mean ±SD
Patients	4764.98 ±139.44	251.56 ±1.84	229.96 ±4.48	49.3 ±0.61	156.87 ±1.51	45.99 ±0.96
Control	1748.10 ±65.25	191.78 ±0.81	133.26 ±1.04	62.56 ±0.36	102.56 ±0.87	26.65 ±0.21
T-test	403.45 **	5.306 **	12.729 **	1.795 **	4.431 **	2.739 **
P-value	0.0001**	0.0001**	0.0001**	0.0001**	0.0001**	0.0001**

** (P≤0.01).

Table 3 showed that there was a highly significant (P ≤ 0, 01) increased in the level of IL-18 in the obese patients (4764.98 ±139.44 pg/L) as compared with control, (1748.10 ±65.25pg/L) .Also the Results of this study revealed that there were a highly significant (P≤0.01)increase in the levels of cholesterol (251.56 ±1.84), triglyceride (229.96 ±4.48), LDL (156.87 ±1.51) and VLDL (45.99 ±0.96) respectively in obese patients in comparison to control groups (191.78 ±0.81), (133.26 ±1.04), (102.56 ±0.87) and (26.65 ±0.21) respectively .On the other hand the result showed a highly significant (P≤0.01) decrease in the level of HDL (49.3± 0.61) in obese patients as compared with control (62.56 ± 0.36).

Table 4 showed that there were a positive significant correlation in the level of IL-18 with cholesterol , triglycerides , LDL, and VLDL .While it shows a negative significant correlation with HDL.

Table 4: Correlation coefficient between interleukin-18 and lipid profile in obese patients

Parameters		Correlation coefficient-r	P-value
IL-18	Cholesterol	0.70 **	0.0001
	Triglyceride	0.68 **	0.0001
	LDL	0.67 **	0.0001
	HDL	-0.62 **	0.0001
	VLDL	0.67 **	0.0001
** ($P \leq 0.01$)			

Discussion

This research study revealed that the mean ages for obese patients matched those for control subjects, and this maybe because of the sample selection .Many studies demonstrate that age affects weight gain because of metabolic and hormonal alterations but obesity develops mostly from lifestyle choices and genetic predispositions [17]. Increase BMI correlates well with adiposity at the population level, as well as with cardiometabolic disease including T2D , atherosclerosis, stroke, and coronary artery disease [18].

Numerous studies verify that elevated BMI acts as an obesity marker which directly links to higher metabolic disorder risk and cardiovascular disease risk and insulin resistance[19,20]. The universal acceptance of BMI as an obesity assessment tool exists although it fails to distinguish body composition variables including fat mass versus lean mass thereby affecting its accuracy in measuring health risks [21] .

Many epidemiological studies have demonstrated that different anthropometric measures for abdominal obesity such as the increase waist-hip ratio are strong and consistent predictors for noncommunicable diseases such as type 2 diabetes mellitus and cardio-

vascular disease[22] .Central obesity measurements through Waist-to-Hip Ratio serve as a vital risk predictor of metabolic syndrome and cardiovascular diseases based on [23]. The health impact of central obesity stands higher than general obesity because abdominal fat accumulation leads to insulin resistance and hypertension along with dyslipidemia [24].Obese patients demonstrated a substantially higher WHR reading which implies they are more prone to develop dangerous visceral fat deposits. Research indicates the Waist-to-Hip Ratio should be used instead of BMI to predict cardiometabolic risks especially when obesity affects a large population[25]. And this agree with [26] who reported that body mass index (BMI)is used most widely as a pragmatic indicator of excess weight.

A majority of patients with obesity according to BMI belonged to class I then class II and finally class III followed. The studied population shows a concerning pattern of moderate to severe obesity rates that matches global obesity prevalence studied in epidemiological reports . [27]Most patients fall under obesity class I (BMI 30–35 kg/m²) indicating many people lie at the beginning stages of obesity. Patients in this stage present metabolic dysregulation which includes insulin resistance combined with low-grade inflammation and enhanced cardiovascular dangers [21]. Research findings demonstrate that subjects in this group can dramatically decrease their health dangers through modifications to their eating patterns combined with physical workout routines and behavioral change strategies. [28] .About one-third of the population had Obesity class II with BMI measurements which demonstrated an excessive severity of obesity burden. People who fall within these obesity classifications develop more obesity-related health conditions including type 2 diabetes along with hypertension and non-alcoholic fatty liver disease (NAFLD) [29]People who fall under class II obesity tend to face higher physical obstacles and increased mortality risk compared to class I obesity patients [30]. The high frequency of class III obesity indicating a substantial public health issue with severe obesity. Peo-

ple with class III obesity experience the greatest danger to their life through potential fatal outcomes such as cardiovascular disease, stroke, obstructive sleep apnea and specific forms of cancer [31].Research indicates that people classified in this weight category face reduced life expectancy along with a need for medical care including bariatric surgery to successfully reduce weight and enhance health results[32] . This comprehensive patient analysis demonstrates the necessity of creating specific intervention programs to stop obesity from advancing further among obese populations [34] .[33]who reported that obesity imposes an increasing burden on society through the related diseases . This is especially true of class III obesity due to the diseases it may cause.

Results revealed significant ($P \leq 0.01$) increase of IL-18 in obese participants and the control participants . This result agreement with [35]which demonstrated a progressive increase in IL-18 levels .Since a positive association founded between IL-18 levels and various metabolic parameters, lipid profiles, estimates of insulin sensitivity, and could be used to predict metabolic risk. IL-18 functions as a pro-inflammatory cytokine because it regulates immune responses together with managing chronic inflammation and metabolic disorders [36].

Experimental evidence demonstrates that obesity-related elevation of IL-18 corresponds to metabolic dysfunction and adipose tissue inflammation [37]. Literature has shown that IL-18 drives insulin resistance development during obesity by enabling inflammatory macrophages into fat tissue which enhances inflammatory marker genes TNF-α and IL-6 [38] .Studies show that IL-18 functionally raises the cardiovascular disease and type 2 diabetes risk for obese people because it activates endothelial dysfunction and promotes vascular inflammation [39].There were a highly significant ($P \leq 0.01$)increase in total cholesterol levels , triglycerides , LDL and VLDL in obese patients than control participants .While HDL levels in blood was noticeably lower. This agree with [40] who reported that Obesity impacts negatively the CV system in several ways, and it is recognized that obesity can

have associations with CVD dependent of increasing the fat in body . Also Present finding are agreement with41] [who reported that lipid metabolism demonstrates changes in obese subjects because their elevated total cholesterol and LDL levels possibly stem from excessive body fat and insulin resistance and impaired lipid drainage systems. Also the present result agree with [42]who suggested that excessive triglyceride levels in obese individuals stem from hepatocyte overproduction of triglyceride-rich lipoproteins along with VLDL particle clearance defects which denote obesity-related dyslipidemia .

The increase in triglyceride levels establishes close connections to insulin resistance and heightens cardiovascular disease dangers in people with abdominal obesity [43]. Obesity creates dyslipidemia which stands as a well-recognized cardiovascular disease and metabolic syndrome and atherosclerosis risk factor [44].The main risk factor for atherosclerosis development comes from elevated levels of LDL cholesterol because this lipid substance produces arterial wall lipid accumulation which generates plaques that result in heart disease complications [45]. HDL levels decrease in obese patients which poses medical concerns because HDL acts as the main transporter of excess cholesterol out of bloodstreams [46] .

A low level of HDL cholesterol functions as a fundamental metabolic syndrome pore indicator which matches up with severe cardiovascular threats [47]. The levels of HDL decline due to inhibited hepatic lipase activity combined with elevated triglycerides and decreased cholesterol efflux capabilities of HDL particles according to research from [48].Several mechanisms contribute to obesity-induced dyslipidemia, including increased adipose tissue mass, which leads to higher free fatty acid release and promotes hepatic triglyceride production [49] .Insulin resistance, which impairs the regulation of lipoprotein lipase and hepatic lipase, resulting in altered lipoprotein metabolism [50].The test showed a strong positive relationship between IL-18 levels and lipid profile (cholesterol ,triglycerides , LDL , and VLDL).

Conclusion

It can conclude that the elevation of lipid profile play a major role in pathogenicity of obesity which is heightened cardiovascular risk . also the pro- inflammatory Cytokines (IL-18) play a major role in cause The inflammation statement in obese patients .So this research reported a positive association was found between IL-18 levels and lipid profiles, estimates of insulin sensitivity, and could be used to predict metabolic risk and the potential involvement of IL-18 in the cardio metabolic syndrome.

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