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The Correlation between Cardiovascular Diseases in Obese Men with The Inflammatory Markers: Dyslipidemia, C-Reactive Protein and Tumor Necrosis Factor-α.

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ABSTRACT

Obesity is one of the most serious public health problems. An important risk factor for cardiovascular disease (CVD), is currently viewed as a pro-inflammatory state with an increase in the expression of inflammatory cytokines, including Tumor Necrosis Factor-alpha(TNF-α) and C-Reactive Protein(CRP). Serum Lipid profile, including (total cholesterol, LDL-cholesterol, HDL-cholesterol and Triglyceride), TNF-α and CRP are estimated in(140) CVD patients (aged between 30 - 65 years) , in the different Body Mass Index (BMI) in AL-Sader teaching hospital in AL-Najaf AL-Ashraf and (40)healthy as control, the result showed a significant increase($P<0.05$) in Lipid profile, TNF- α and CRP in CVD patients compared with control. Also the result showed a significant increase($P<0.05$) in individual patients (BMI<25) and overweight individuals (BMI>25) in lipid profile, CRP and TNF-α. It compared with the control group. Further, there was evidence of worsening dyslipidemia with BMI and cardiovascular risks also. The study suggested that inflammatory marker TNF-α and CRP is correlated with cardiovascular risk factors in obesity, rather than just being a manifestation of the inflammatory state.

Keywords: CVD, Obesity, LDL, HDL,TNF-α.

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INTRODUCTION

Obesity is one of the most serious public health problems[1]. It implies excess fat and not merely excess weight, In the world there is 1 billion overweight people, of whom 300 million are obese. Therefore a several chronic disease is being observed in these countries[2]. The body mass index was recommended to determine the obesity by the National Institutes of Health, National Heart, Lung, and Blood Institute ,[3].

In the United States Obesity is considered "as a dangerous risk factor of atherosclerotic cardiovascular disease" which causing a death [4].Many adipokines like C-Reactive Protein, tumor necrosis factor-α (TNF-α), Resistin and adiponectin were reported as a significant factor of "obesity-link metabolic illnesses[5].

The reported for Dehghan et al., [6] and Lopez-Garcia et al., [7] have that patients with an increased level of CRP are at high risk of developing diabetes and cardiovascular diseases, Since CRP is represented as a very stable inflammatory marker, with a semi time of around 19 hours [8] and to have a good prediction of cardiovascular illness, Hs-CRP is usually associated with increased levels of cholesterol, LDL, and Triglycerides [9].

Among many inflammatory markers, TNF-α has emerged as a key cytokine that influences intermediary metabolism and contributes to proatherogenic changes in lipid metabolism [10] that TNF-α may participate in the etiologic and pathologic processes related to future cardiovascular complications, TNF-α is a multifunctional protein that has been implicated in a number of metabolic disorders including obesity, dyslipidemia, insulin resistance, type II diabetes, and atherosclerosis

MATERIALS AND METHODS

Subjects

Inclusion criteria

One hundred thirty eight men (138) patients and (40)control . The samples were collected from Al-Najaf Al-Ashraf /Al- Sader Teaching Hospital.

Body Mass Index

Body mass index values were calculated from the following equation BMI=Weight(Kg)/Height (m^2) [11].

Biomarkers test (Biochemical Parameter)

Lipid Profile

Measurements of total cholesterol (TC): Biochemistry analyzer (CYANStrat Cy004, cypress diagnostics, Langdrop – Belgium,SN:BSIBQ123E) was used to determined by using a total human cholesterol kits (cypress diagnostics, Langdrop - Belgium . Cat. No. HB006)

Measurements of Triglycerides: Biochemistry analyzer (CYANStrat Cy004, cypress diagnostics, Langdrop – Belgium,SN:BSIBQ123E) was used to determine the Triglycerides kit supplied by (cypress diagnostics, Langdrop - Belgium. Cat. No. HB021)

Measurements of HDL-Cholesterol(HDL-C): Biochemistry analyzer (CYANStrat Cy004, cypress diagnostics, Langdrop – Belgium,SN:BSIBQ123E) was used to determine the Serum HDL-Cholesterol level by HDL-Cholesterol phosphotungstic acid (PTA) precipitant kit ,supplied from (cypress diagnostics, Langdrop –Belgium . Cat. No. HB007) .

Calculation of very low density lipoprotein cholesterol[12]

VLDL-C = TG (mg/dl)/5.

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Calculation of low density lipoprotein

LDL-C= TC(mg/dl)- VLDL-C (mg/dl)- HDL-C(mg/dl) .

Determination of serum CRP

This ELISA kit applies to the in vitro quantitative determination of Human CRP concentrations in serum, was supplied by Elabscience Biotechnology Co., Ltd..(Catalog No: E-EL-0043), that depended on the technique of the quantitative sandwich enzyme immunoassay.

Determination of serum Human TNF-α

Human TNF-α concentrations in serum, was supplied by Elabscience Biotechnology Co., Ltd.(Catalog No: E-EL-H0109)

RESULTS

Lipid profile

Comparison between lipid profile of cardiovascular disease (CVD) and healthy group.

There were statistically significant differences in lipid profile between CVD group and healthy group , showed a significant increased ($p<0.05$) in Serum cholesterol, Triglycerides , VLDL and LDL concentration in CVD group in comparison with the healthy group While serum HDL concentration revealed a significant decreased ($p<0.05$) of CVD group when compared with healthy group. The results for Lipid profile are summarized in Table (1)disease (CVD) and control groups.

Table (1): Serum level of lipid profile parameters in cardiovascular disease (CVD) and control groups.

Groups / Lipid profile	Mean ±S.E.	
	HT	CVD
Cholesterol mg/dl	168.00 ± 5.34	242.39 ± 4.88 *
TG mg/dl	82.11 ± 4.96	193.60 ± 7.80 *
VLDL-C mg/dl	16.422 ± 0.992	38.718 ± 1.560 *
HDL-C mg/dl	45.50 ± 0.87	31.67 ± 0.77 *
LDL-C mg/dl	106.078 ± 3.478	172.002 ± 2.55 *

(*)Statistically significant differences ($p<0.05$) between patients and control groups**.**

Comparison of lipid profile among different body mass index (BMI) groups of cardiovascular disease .

Table (2) showed no significant difference ($p>0.05$) in serum concentration of cholesterol , TG ,LDL , VLDL and HDL at different BMI (normal , over , obese and morbid weight) of CVD group

Table (2): Comparison Serum level of lipid profile parameters among different BMI groups of cardiovascular disease

Groups / Lipid profile mg/dl	Mean ±S.E. / CVD			
	normal weight 18.5-24.9	over weight 25-29.9	obese weight 30-39.9	Morbidweight 40&over

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Cholesterol	230.87 ± 11.20 A	237.14 ± 8.37 a	247.12 ±13.63 a	256.50 ± 9.59 a
TG	160.40 ± 7.42 A	180.80 ± 7.96 a	204.24 ± 7.77 a	218.50 ± 7.06 a
VLDL-C	34.08 ± 1.484 A	36.16 ± 1.592 a	40.848 ± 1.554 a	43.7 ± 1.412 a
LDL-C	162.36 ± 1.85 A	168.39 ± 4.798 a	175.382 ± 10.746 a	182.46 ± 6.748 a
HDL-C	34.43 ± 1.93 A	32.59 ±1.98 a	30.89 ±1.33 a	30.34 ± 1.43 a

The different letters refer to significant differences and the same letters refer to no significant differences , between different BMI groups at level (P<0.05).

Comparison between serum level CRP , TNF-α of cardiovascular disease (CVD) and healthy group.

The results of table (3) showed a significant increase (p<0.05) in serum CRP concentration in CVD group in comparison with healthy group. Also in the same table showed a significant increase (p<0.05) in serum TNF-α concentration in CVD group in comparison with healthy group.

Table (3): Serum level of CRP, TNF-α in cardiovascular disease

Criteria / Groups	Mean ±S.E.	
	CRP (ng/ml)	TNF-α (pg/ml)
CVD	9.605 ± 0.3221 *	16.737± 0.433 *
HT	4.378 ± 0.2669	6.388±0.535

(*)Statistically significant differences (p<0.05) between patients and control groups.

Comparison serum level of CRP, TNF-α among different body mass index (BMI) groups of cardiovascular disease .

The serum CRF concentration indicated no significant differences (P>0.05) at normal and overweight , but a significant increase (p<0.05) at the morbid than (normal, over and obese weight) of CVD group , as shown in table(4).

In the same table showed no significant differences (P>0.05) in serum TNF-α concentration at (normal and overweight) and (obese and morbid weight) , but a highly significant increase (p<0.05) at the (obese and morbid weight) than (normal and overweight) of CVD group .

Table (4): Comparison Serum level of CRP, TNF-α among different BMI groups of cardiovascular disease.

Groups / Criteria	Mean ±S.E. / CVD			
	normal weight 18.5-24.9	over weight 25-29.9	obese weight 30-39.9	Morbid weight 40 & over
CRP (ng/ml)	7.652 ± 0.848 a	8.179 ± 0.413 a	10.322 ± 0.449 b	12.280 ± 0.671 C
TNF-α (pg/ml)	14.227 ± 0.738 a	14.515 ± 0.596 a	18.448 ± 0.741 b	19.573 ± 0.905 b

The different letters refer to significant differences and the same letters refer to no significant differences , between different BMI groups at level (P<0.05).

DISCUSSION

The current study reveled high lipid profile level in cardiovascular disease patients compared with control healthy group the elevation in lipid profile indicated in CVD patients than healthy subjects extracted from the low HDL-C and high values of cholesterol, TG, VLDL-C, and LDL-C, Therefore hyper-lipidemia in the present study considered as one of the major determinant and a risk factor for cardiovascular disease. This is characterized by alterations in the lipid profile [13], These findings are in agreement with [14]. Epidemiological studies have also shown that elevated concentrations of total or LDL-C, cholesterol in the blood are powerful risk factors for coronary disease [15] , LDL is normally associated with the apolipoprotein (APO) B-100.

An increase in plasma LDL levels leads to an increased rate of its entry into the intima, and consequently a higher level of LDL is observed in the intimal region, The interaction of positively charged ApoB to negatively charged proteoglycans leads to the retention of ApoB-linked lipoproteins in the vessel wall [16]. These sequestered lipoproteins are susceptible to modification by oxidation[17] Oxidized LDL induces the formation of foam cells and fatty streaks in the vessel wall [18].Results from the transendothelial passage (transcytosis) of cholesterol richatherogenic Apo-B lipoproteins (VLDL, IDL and LDL) from the plasma into the intima indicated achronic inflammation in the vessels[19]. Body composition and the distribution of adipose tissue have now emerged as critical issues in assessing the link between obesity and metabolic adverse outcomes [20] Moreover, the respective contribution of visceral and subcutaneous body fat, and their relative impact on the development of CHD [21].

Were documented also the relationship between the body fat distribution and CAD, this study was designed to investigate the association of different indices of obesity (BMI), fat distribution indicators (visceral and subcutaneous fat)and lipid profile in patients with angina and CHD[22].

The present study reveal that CRP level was highly significant than control group and suggest that High CRP level is a sensitive marker of systemic inflammation that has been related to cardiovascular disease through several plausible pathways, These include the possibility that CRP levels reflect inflammation of coronary vessels related to the formation and severity of the atherogenic plaque or inflammation related to myocardial ischemia or necrosis, There are several mechanisms with elevated CRP levels in IHD ,It has been suggested that plasma CRP levels reflect the amount and activity of pro-inflammatory cytokines such as TNF-α, IL-1 and IL-6 which are implicated in the process of atherosclerotic plaque formation and acute coronary syndrome. In this regard, IL-6, which is induced by both TNF- α ,IL-1, macrophage chemoattractant protein-1 (MCP-1) and transforming growth factor-β (TGF-β) has been proposed to play a central role in the relationship between CRP and cardiovascular disease [23].

The CRP and TNF-α levels were extensively analyzed in our study with respect to its association with Body Mass Index, cardiovascular risk factors and the lipid profile. This was further strengthened by the presence of strong correlation between TNF-α levels and BMI using correlation with a p value < 0.05. The other important predictors of TNF-α level correlation were Triglycerides, LDL-cholesterol and CRP values[9].

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