Circulating Retinol Binding Protein-4 and Total Thiols In Generalized and Abdominal Obesity Regarding; Monitors Of Cardiovascular Disease

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ABSTRACT

Background*: Retinol-binding protein 4 (RBP4) is an adipocyte-secreted hormone considered to link obesity with cardiovascular complications. The oxidative stress caused by overproduction of reactive oxygen species (ROS)) has been concerned in the pathophysiology of obesity. We evaluated serum RBP-4 and plasma total thiols (TT) in generalized obesity (GO) and abdominal obesity (AO) as regard to cardiovascular risk factors. Glycated hemoglobin (HbA_{1c}), C- reactive protein (CRP) and lipid profile were also evaluated.* ***Subjects and Methods:*** *Sixty obese* ***subjects*** *were recruited [30 abdominally obese (AO)* ***subjects*** *(15 males and 15 females); their mean± SD of age was 49.5±5.5 years. Their waist circumference (WC) was > 102 cm for men or > 88 cm for women) and waist/hip ratio (WC divided by that of the hips of > 0.9 for men and > 0.85 for women)] and [30 generalized obese (GO)* ***subjects*** *(22 males and 8 females; their mean± SD of age was 42.5± 8 years), their body mass index (BMI) was ≥ 30-34.9 kg/m^2, with normal WC]. Serum levels of RBP-4 were measured by ELISA, serum levels of TT were measured by colorimetric methods, blood HbA_{1c}%, lipid profiles and CRP were also determined. S****ubjects*** *with AO had significantly higher circulating RBP-4 and CRP levels compared to GO ($p< 0.05$ for each). Total thiols levels were significantly lower in AO* ***subjects*** *compared to GO ($p< 0.05$). Total serum cholesterol, triglycerides and HbA_{1c}% increased with BMI, WC and waist/hip ratio (WHR), but the relations were statistically insignificant.* ***Conclusion****: The study revealed that RBP-4 is autonomously related to visceral fat accumulations and cardiovascular diseases. The study also revealed the beneficial effect of TT against obesity and cardiovascular disease and the potential clinical applicability of RBP4 and total thiols in cardiovascular diseases.*
Key words: Retinol binding protein4-abdominal obesity-generalized obesity-cardiovascular disease.

INTRODUCTION

Obesity primarily is considered as an environmental and behavioral problem and now viewed as a complex disorder and a major health risk factor related to increased cardiovascular disease (CVD), stroke, diabetes mellitus, hypertension, cancer and early death [(1)]. Framingham Heart Study showed that obese individuals had an increase in

the risk of heart failure compared to non obese individuals [(2)]. Those with abdominal obesity are at greater risk for diabetes, CVD and all-cause mortality [(3)]. There are cross relations between the CVD risk and increased waist circumference and there is now concept that the accumulated visceral fat depot acts as a large endocrine gland that becomes inflamed, secreting adipokines that may produce an insulin resistance and proinflammatory state that increases cardiovascular disease risk[(4)].

Body weight control is the cornerstone of both primary and secondary prevention of CVD[(5)]. Adipokines such as leptin, adiponectin, resistin and retinol binding protein 4 were reported to have a role in obesity and other cardiovascular disease [(6)]. RBP4 is 21kDa secreted protein, member of lipocalin family[(7)] and is one of fatty acid binding proteins adipokine which has been correlated significantly to both obesity and cardiovascular disease[(8)]. RBP4 dysregulation may be associated with altered hepatic[(9)], and renal function[(10)], lipid metabolism and inflammation [(11)]. Relationships between RBP4 and other traditional and non- traditional risk factors for CVD, such as inflammatory factors and oxidative stress have been reported in larger populations [(12)]. Leptin is a satiety element produced from adipocytes [(13)] and has direct protective actions against obesity and CVD [(14)]. Adiponectin is an adipose tissue specific hormone that has insulin sensitizing properties, anti-inflammatory properties and is protective against obesity related disorders [(13)]. Numerous other non-traditional risk factors are of particular importance in the context of CVD such as thrombotic and inflammatory biomarkers i.e. plasminogen activator inhibitor-1 (PAI-1), IL-6 and TNF-α [(13)]. Oxidative stress appears to play a major role in the development of CVD [(15)]. Oxidative stress which is an imbalance between tissue oxidants (free radicals or reactive oxygen species) and antioxidants has major role in the development of major obesity-related complications such as CVD and diabetes [(16)]. Several inflammatory biomarkers such as homocysteine and CRP are involved in the production of oxygen radicals in vessel wall promoting atherosclerotic disease causing oxidative vascular damage and conversely, antioxidants such as (vitamin C&E, β-carotene and thiol containing compounds) have protective effects against CVD development [(15)]. Glutathione is the most important intracellular thiol that has a role in many cellular functions including the antioxidant defense against CVD and obesity [(17)]. CRP is a downstream marker of inflammation that has multiple effects, including complement binding, augmentation of expression of adhesions molecules, decreased expression of the vasodilator endothelial nitric oxide synthase, may stimulate the expression of the thrombotic factor PAI-1 and may induce oxidative stress[(18).]

The aim of the present study is to show the relation between the levels of serum RBP4 and plasma Total thiols (TT) in generalized obesity (GO) and abdominal obesity (AO) and to study other risk factors such as

levels of HbA_{1c}%), C- reactive protein (CRP) and lipid profile in both AO & GO.

MATERIAL & METHOD

We recruited a cohort of 80 patients. Thirty generalized obese (GO) patients (22 males and 8 females), their BMI was ≥ 30-34.9 kg/m^2, with normal waist circumference (W.C < 102 cm for men or < 88 cm for women), mean age 42.77 ± 8.24 years. Thirty abdominally obese (AO) patients (15 males and 15 females), their waist circumference (W.C) was > 102 cm for men or > 88 cm for women and waist-hip ratio circumference (the circumference of the waist divided by that of the hips of > 0.9 for men and > 0.85 for women) [19] with BMI ≥ 30-34.9 kg/m^2, mean age was 49.63 ± 5.41 years. Twenty healthy subjects (control) (14 males and 6 females) with normal body mass index (≥18.5-24.9 kg/m^2), with normal waist circumference (< 102 cm for men or < 88 cm for women), mean age 36.60 ± 5.97 years. Exclusion criteria were; presence of fluid retention such as ascites and lower limb edema, abdominal organomegally and pregnancy. Generalized obese and abdominally obese groups were compared for the current cardiovascular risk factors (diabetes mellitus (DM), hypertension (HTN), dyslipidemia, smoking, family history of premature coronary artery disease, physical inactivity, peripheral arterial disease (PAD), coronary artery disease (CAD), chronic kidney disease (CKD) and inflammatory markers such as CRP, retinol binding protein4 and total thiol) and were comparable for age (between 30 and 55 years old) and sex (male or female). Thorough history was taken about DM, HTN, CAD, CKD, PAD, physical activity, smoking and family history of premature CAD. Clinical examination of heart rate, blood pressure, peripheral arterial pulsations, cardiac examination and Electrocardiogram (ECG) were done. This work was conducted at Assuit University Hospital, Cardiology and Medical Biochemistry Departments Faculty of Medicine, Assuit University. Patients were recruited from Obesity Clinic, Coronary Care Unit, and Cardiac Department. Study protocol was approved by the ethical committee of the Faculty of Medicine, Assiut University.

Laboratory investigation:

Venous blood samples were collected from each subject after fasting for 12 hours, part of the sample was placed in plane tube (no anticoagulant), centrifuged at 3,000 rpm (1,000 *xg*) for 20 minutes at 4°C and the serum was separated. The other part of blood sample was placed in tube having EDTA, mixed by inversion and part was used for estimation of blood HbA_{1c} and the remaining part of the EDTA sample was centrifuged at 3,000 rpm (1,000*xg*) for 20 minutes at 4°C and the plasma was separated. All aliquots were stored at -70°C up to patch analysis of biomarkers. Serum RBP-4 levels were measured by enzyme-linked immunosorbent assays (ELISA) using commercial kits (e.g. R&D Systems, Abingdon, Oxfordshire, United Kingdom). Plasma levels of TT were measured

by colorimetric methods [20]. The inter- and intra- assay coefficients of variation for all assays were <5% and <10% respectively. Hitachi 911 automated analyzer at Assiut University Hospital Laboratory was used for estimation of fasting blood glucose (FBG) (8-hour fasting), two-hour postprandial blood glucose (2-h PPBS) , HbA_{1C} and serum fasting lipid profile (12-hour fasting) which included LDL-C, HDL-C, total cholesterol and triglyceride. Serum creatinine level was also measured.

Statistical Analysis:

Following application of the Shapiro-Wilkes test to determine a normal distribution, non-categorical data distributed normally are expressed as mean ±standard deviation and data distributed non-normally are expressed as median (inter quartile range). Categorical data are analyzed by the Chi-squared test (χ^2). Continuously variable data are analyzed by ANOVA or the Kruskal-Wallis test. Turkey's post-hoc test was used to determine differences between groups. Correlations were assayed by Spearman's rank method. A probability of less than 0.05 was considered as statistically significant. Analyses were done using SPSS version 16.

RESULTS

Patients with AO showed significantly higher circulating RBP-4, FBG, 2 hours postprandial blood glucose, blood HbA_{1c} and CRP compared to those with GO ($p<0.05$ for each) and to controls, $p<0.05$ for each (Tables 2 &4; Figures 2). Total thiol (TT) levels were significantly lower in obese subjects with AO compared to those with GO ($p<0.05$ for each) and to controls, $p<0.05$ for each (Tables 2 &4; Figures 1). However, the difference in the levels of TT in obese subjects with GO and non-obese control subjects was insignificant.

The levels of total cholesterol, triglyceride and LDL-C showed no significant difference between obese with AO and those with GO, the HDL-c levels were slightly lower in obese with AO than those GO, but the difference was insignificant.

Positive significant correlations (Spearman's rho) were evident between RBP-4 and levels of HbA_{1c}% in AO and GO ($r=0.371$, 0.567 respective, $P<0.05$ for each). No significant correlation between HbA1c and total thiol in AO and GO ($r=0.147$, 0.143 respective, $P>0.05$ for each). No significant correlations between RBP-4 and CRP in AO and GO groups were obtained ($r=0.075$, 0.158 respective, $P>0.05$ for each). There was significant difference between AO and GO for DM, HTN, physical inactivity, weight, height, BMI, WC, hip circumference and waist/hip ratio, $P<0.05$ for each (Table 5).

Table (1): Demographic data of obese subjects with abdominal obesity; obese subjects with generalized obesity and healthy control subjects.

	Abdominal obesity (AO)		Generalized obesity (GO)		Healthy control (HC)		P value
	No. 30	%	No. 30	%	No. 20	%	
Sex:							> 0.05
Male	15	50.0	22	73.3	14	70.0	
Female	15	50.0	8	26.7	6	30.0	
Age: (years)							< 0.05*
Mean ± SD	49.63 ± 5.41		42.77 ± 8.24		36.60 ± 5.97		
Range	35 – 55		30 – 55		30 – 50		
Smoking:							
Smoker	8	26.7	5	16.7	0	0.0	>0.05
Nonsmoker	22	73.3	25	83.3	14	100.0	
Physical activity:							< 0.05*
Active	5	16.7	15	50.0	20	100.0	
Not active	25	83.3	15	50.0	0	0.0	
Family history of premature CAD:							>0.05
Male first degree relative before age 55	5	16.7	6	20.0	0	0.0	
Female first degree relative before age 65	2	6.7	4	13.3	0	0.0	
Both	0	0.0	2	6.7	0	0.0	
Normal	23	76.7	18	60.0	20	100.0	

Data were presented by ANOVA and chi-square test. There was statistical significant difference between 2 study population groups (AO) and (GO) for age and physical activity.

*Significant Statistical dfference between (AO) & (GO).

Table (2): Serum RBBP-4, Plasma TT and blood HbA_{1c} of obese subjects with abdominal obesity; obese subjects with generalized obesity and healthy control subjects(Mean ± SD)..

	Abdominal obesity (AO)	Generalized obese (GO)	Healthy control (HC)	P-value
RBP-4 (µg/ml)	34.08 (7.72)[a]	15.72 (10.89)[b]	3.05(0.63)	<0.05*
TT(mmol/l)	0.56 (0.21)	1.16 (0.29)	1.08 (0.24)	<0.05*
CRP (mg/l)	24.20 (25.48)a	14.00 (14.38)[b]	6.00 (0.20)	<0.05*
HbA_{1c} (%)	8.79 (2.89)	6.27 (2.25)	3.85 (0.73)d	<0.05*

RBP-4: Retinol binding protein-4, TT: Total thiol, CRP: C-reactive protein, HB A1c: Hemoglobin $A1_c$. Kruskal-Wallis test, all P<0.05, AO[a] group has significantly higher levels of RBP4 and CRP compared to GO[b]. AO group has significantly lower serum levels of TT compared to GO (p<0.05). AO has significantly higher levels of HbA1c compared to GO (p<0.05).

*Significant Statistical difference between (AO) & (GO).

Table (3): Anthropometric measurements of obese subjects with abdominal obesity; obese subjects with generalized obesity and healthy control subjects (Mean ± SD)..

	Abdominal obesity (AO)	**Generalized obesity (GO)**	**Healthy control (HC)**	**P-value**
Weight (kg)	88.63(8.26)	82.20 (6.34)	61.05 (6.68)	< 0.05*
Height (cm)	167.67 (6.88)	163.70 (7.11)	168.40 (8.85)	< 0.05*
BMI (kg/m^2)	31.49 (1.38)	30.68 (0.77)	21.49 (1.32)	< 0.05*
Waist circumference (cm)	114.60 (6.04)	93.93 (6.30)	92.50 (5.92)	< 0.05*
Hip circumference (cm)	122.70 (6.52)	110.70 (6.69)	111.00 (4.28)	< 0.05*
Waist/hip ratio				
In male	0.95(0.02)	0.86 (0.02)	0.86 (0.02)	< 0.05*
In female	0.92(0.04)	0.81 (0.03)	0.77 (0.03)	< 0.05*

Data were presented by ANOVA and T-test. There was significant difference between 2 study population groups (AO) and (GO) for weight, height, BMI, waist circumference, hip circumference and waist/hip ratio.

*Significant Statistical difference between (AO) and (GO).

Table (4): Fasting as well as postprandial serum glucose, serum creatinine and lipid profile of obese subjects with abdominal obesity; obese subjects with generalized obesity and healthy control subjects (Mean ± SD).

	Abdominal obesity (AO)	**Generalized obese (GO)**	**Healthy control (HC)**	**P value**
FBG (mg/dl)	130.20 (32.28)	104.17 (34.42)	80.90 (5.57)	< 0.05*
2-HPPBS (mg/dl)	188.10 (45.75)	159.40 (46.91)	121.85 (7.67)	< 0.05*
Total cholesterol (mg/dl)	178.57 (31.28)	176.03 (17.96)	157.20 (21.90)	<0.70
Triglyceride (mg/dl)	128.00 (26.39)	124.90 (21.32)	107.50 (13.27)	<0.61
HDL-C (mg/dl)	58.70 (16.96)	65.87 (10.80)	72.65 (8.15)	<0.1
LDL-C (mg/dl)	96.73 (31.36)	87.40 (25.28)	66.55 (12.34)	<0.20
Serum creatinine (mg/dl)	0.99 (0.74)	0.91 (0.38)	0.81 (0.13)	<0.61

FBG: Fasting blood glucose, 2-HPPBS: 2-hour post prandial blood sugar, HDL: High density lipoprotein-cholesterol, LDL: Low density lipoprotein-cholesterol. Data were presented by ANOVA, Mann-Whitney and T- test. There was statistical significant difference between 2 study population groups (AO) and (GO) for FBG and 2-HPPBG.

*Significant Statistical difference between (AO) and (GO).

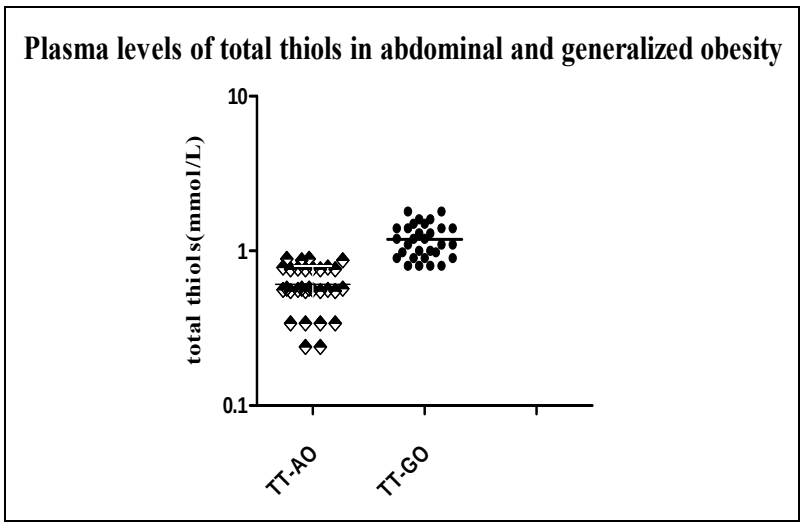
Table (5): Clinical data of obese subjects with abdominal obesity; obese subjects with generalized obesity and healthy control subjects.

	Abdominal obesity (AO)		**Generalized obese (GO)**		**Healthy control (HC)**		**P-value**
	No: 30	**%**	**No: 30**	**%**	**No: 30**	**%**	
DM							
Normal	6	20.0	19	63.3	20	100.0	<0.05*
Type I	5	16.7	2	6.7	0	0.0	
Type II	19	63.3	9	30.0	0	0.0	
HTN							
Yes	10	33.3	4	13.3	0	0.0	<0.05*
No	20	66.7	26	86.7	20	100.0	
CAD							
MI	7	23.3	5	16.7	0	0.0	
Unstable angina	13	43.3	10	33.3	0	0.0	<0.63
MI and Unstable angina	2	6.7	3	10.0	0	0.0	
Normal	8	26.7	12	40.0	20	100.0	
PAD							
Yes	1	3.3	1	3.3	0	0.0	<1.00
No	29	96.7	29	96.7	20	100.0	
CKD							
Normal	26	86.7	30	100.0	20	100.0	<0.11
Proteinuria & hematuria	2	6.7	0	0.0	0	0.0	
Regular dialysis treatment	2	6.7	0	0.0	0	0.0	

DM: Diabetes mellitus, HTN: Hypertension, CAD: Coronary artery disease, MI: Myocardial infarction, PAD: Peripheral arterial disease, CKD: Chronic kidney disease. Data were presented by Chi-square test. There was significant difference between (AO) and (GO) for DM and HTN.

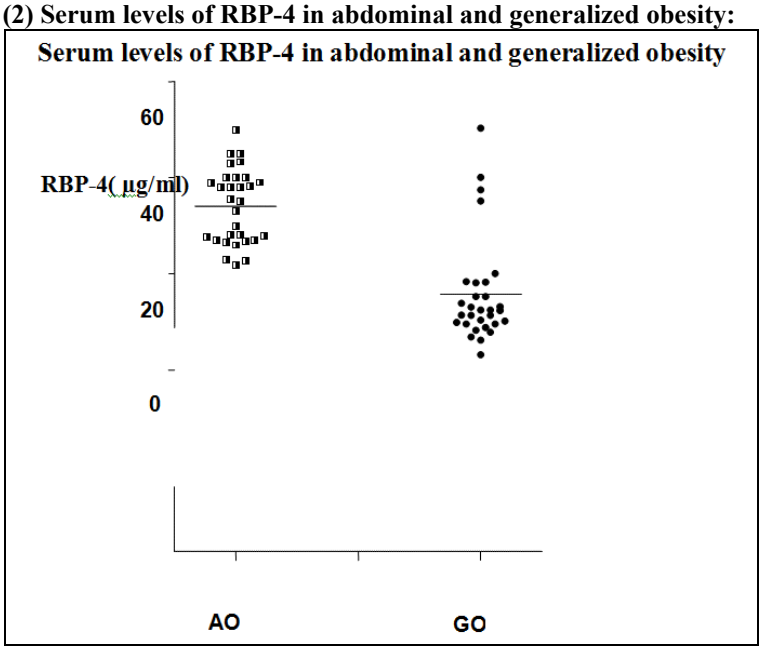
*Significant Statistical difference between (AO) and (GO).

Figure (1) Plasma levels of total thiols in abdominal and generalized obesity:



AO had significantly lower total thiols levels compared to GO ($p < 0.05$).

Figure (2) Serum levels of RBP-4 in abdominal and generalized obesity:



DISCUSSION

The current study investigated the serum levels of RBP4 in obese people with cardiovascular disease. The study demonstrated that obese individuals with AO have elevated concentrations of RBP4 than those with GO and also demonstrated that blood levels of HbA_{1c} were significantly elevated in individuals with higher serum levels of RBP4 compared to individuals with low serum levels of RBP4. This result coincides with what was reported by **Lee et al.**[12] that RBP4 concentrations is linked with distribution of body fat rather than body weight per se since it's more highly correlated with waist/hip ratio or visceral fat than with BMI. In addition **Cho et al.**[21] reported that plasma concentrations of RBP4 were significantly higher in subjects with impaired glucose tolerance (IGT) or Type 2 DM compared to subjects with normal glucose tolerance. **Yang et al.**[7] reported that circulating RBP4 increased in obese subjects with type 2 DM. **Koch et al.**[22] demonstrated that plasma or serum RBP4 concentrations correlated with the severity of insulin resistance in non diabetic participants with family history of type 2DM. So, RBP4 is considered as a convenient marker not only for T2DM but also as an indicator for adiposity.

In the present study, we used BMI, WC and W/H ratio circumference as measures for AO & GO to investigate the relationship between adiposity and cardiovascular risk factors (DM, HTN, physical inactivity, smoking, coronary artery disease, chronic kidney disease, peripheral arterial disease and family history of premature CAD) in both men and women. This coincided with what stated by **Escribano García et al.** [24] that the BMI and WC are the most widely used parameters for determining obesity because they are easily obtained.

Our results showed that HTN and DM are more prevalent among individuals with abdominal obesity highlighting the relationship between abdominal obesity and cardiovascular risk factors and such fact stands in males and females. **Escribano García et al.**[23] verified strong correlations between generalized obesity and either high blood pressure and diabetes mellitus.

There were strong associations between coronary artery disease (CAD) and obesity irrespective to its type and sex difference. Large case-control study demonstrated that WHR was more strongly associated with CAD than with BMI in both men and women[24]. **Rocha et al.**[25] reported that obesity represents a major risk factor for atherosclerosis, in which systemic obesity-related inflammation is believed to be the main culprit.

There were inverse relations between physical activity and both types of obesity either abdominal or generalized in the present study, since physical inactivity was higher among abdominally obese than generalized obese individuals. This finding concurred with what was stated by **Petersen et al.**[26] that decreased physical activity may lead to obesity and obese persons are usually physically less active and with **Donnelly et al.** [27] & **Jakicic et al.** [28] that a large body weight and fat mass

can be reduced by increasing the short term and long term level of physical activity.

Our study also showed that there was no positive relationship between smoking and both types of obesity either abdominal obesity or generalized obesity as non smokers were greater in both groups of obesity than smokers. The results of **Hart et al.**[29] who found that there were negative correlations between obesity and smoking, are confirmed by results of the present study, while **Escribano García et al.**[23] reported that fewer smokers and more ex-smokers were found among obese individuals.

Our results showed that peripheral ischemic arterial disease doesn't affected by the type of obesity. This result coincided with what was reported by **Escribano García et al.**[23] that there was no significant increase in the risk of ischemic vascular disease among obese or overweight individuals, which indicates that the risk of a cardiovascular event may not be associated with high BMI.

Since the lipogram stands to be the molecular evidence for our study, we established that all lipid parameters were abnormally higher (but insignificant) in abdominally obese individuals compared to generalized obese individuals except for HDL-C which was abnormally lower in AO than in GO. Coinciding with these results **, Escribano García et al.**[24] reported that smaller differences in hypercholesterolemia for the different levels of obesity based on BMI and abdominal obesity were found. There were consistent changes in HDL-C and triglycerides with obesity, since obesity seems to be associated with lower HDL-C and increased triglycerides in people of all ethnic groups but less consistent change on LDL-C concentrations has been found [30].

Our study showed that CRP was found to be higher in abdominal obesity group than generalized obesity group in women and men. **Bochud et al.,** [31] reported that CRP gene expression was positively increased with high BMI, WC and fat mass in women, whereas no such evidence was found in men. It is well noted that CRP is an established CV risk marker and carry predictive power for coronary events and patients with elevated basal levels of CRP are at an increased risk of diabetes, hypertension and cardiovascular disease [32]. CRP is associated with insulin resistance and this elevates risk of DM, obesity and cardiovascular risk and possible synergistic effect of obesity, insulin resistance and DM on the chronic low level inflammation may play role in atherosclerosis pathogenesis and so, CRP may be a novel therapeutic target [33].

Our results showed an inverse relation between plasma total thiol (TT) and obesity either abdominal or generalized. Abdominally obese persons had lower concentrations of TT than generalized obese persons. This result concurred with what reported by **Cazzola et al.,**[34] that obesity diminishes antioxidant defense by altering the activity of cytochrome P-450 and reducing the antioxidant enzymes such as catalase, glutathione peroxidase, and glutathione reductase. **Shimizu et**

al.[15] reported that oxidative stress has a key role in cardiovascular disease development. Oxidative stress levels are elevated in human obesity, and these levels are modifiable with various lifestyle modifications and surgical interventions [35].

CONCLUSION: Plasma RBP4 could be considered an important indicator of intra-abdominal adipose mass and insulin-glucose homeostasis regulation. This suggests a potential role for RBP4 as a convenient marker not only for T2DM but also for cardiovascular risk. Public health promotion to maintain appropriate weight should be early in life. Abdominal fat measured by WC or by waist/hip ratio, rather than total fat mass or BMI are the strongest predictors of cardiovascular risk factor levels. Obesity creates the oxidant conditions of for diseases such as diabetes, heart disease, hypertension and CVD. Oxidative stress in obesity is a systemic problem that must be corrected either by improving antioxidant defenses through fat volume reduction, exercise and dietary modification, or a combination of the three.

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مستويات البروتين ٤ المقترن بالريتينول والثيول الكلى بالدم فى البدانة العامة والبدانة الحشوية وما يتعلق بعوامل الخطورة لأمراض القلب و الأوعية الدموية

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البروتين ٤ المقترن بالريتينول يفرز من الأنسجة الدهنية ويرتبط بالبدانة وعوامل الخطورة الأخرى لأمراض القلب و الأوعية الدموية.أيضا الضغط التأكسدى والذى يتميز بزيادة إنتاج طوائف الأكسجين التفاعلية يرتبط بالبدانة.

يهدف هذا البحث إلى دراسة مستويات البروتين ٤ المقترن بالريتينول والثيول الكلى بالدم في البدانة العامة والبدانة الحشوية وما يتعلق بعوامل الخطورة لأمراض القلب و الأوعية الدموية وأيضا عوامل الخطورة الأخرى مثل اضطراب نسبة الدهون ، إرتفاع نسبة السكر وتركيزالهيموجلوبين المسكر، وبروتين سى النشط بالدم.

أجريت الدراسة على ٦٠ بدينا وبدينة، ٣٠ يعانون البدانة الحشوية مقابل٣٠ يعانون البدانة العامة ، بالاضافة الي ٢٠ اصخاء ليس شمنهم بدين أو بدينة [المجموعة الشابطة]. تم قياس تركيزالبروتين ٤ المقترن بالريتينول بمصل الدم بطريقة الإليزا ،وتركيزالثيول الكلى بطريقة التحليل اللونى ،وقياس نسبة الهيموجلوبين المسكر ، الدهون بالدم وبروتين سى النشط بالدم وتم تقييم عوامل الخطورة لأمراض القلب والأوعية الدموية مثل ارتفاع السكر بالدم، إرتفاع ضغط الدم، اضطراب نسبة الدهون بالدم، التدخين، أمراض قصورالشرايين التاجية،التاريخ العائلى المبكر لأمراض الشرايين التاجية للقلب، الخمول البدنى، أمراض الشرايين الطرفية وأمراض الكلى المزمنة.

النتائج: أظهرت الدراسة إرتفاعا ملحوظا بتركيزالبروتين ٤ المقترن بالريتينول ، بمصل الدم ، وبروتين سى النشط ببلازما الدم ، ونسبة الهيموجلوبين المسكربالدم ، وإنخفاضا ملحوظا بتركيز الثيول الكلى ببلازما الدم ، كما لوحظ اضطرابا في تركيز الدهون يالدم فى مرضى البدانة الحشوية عن مرضى البدانة العامة. لوحظ إرتفاع واضطراب بنسبة الدهون بالدم مع زيادة البدانة العامة والحشوية.