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Biochemical Markers and Cardio-metabolic Risk Factors among Overweight and Obese Egyptian Women

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ABSTRACT

This cross-sectional study was conducted on 350, unrelated young women, aged between 20 and 30 years. They are assembled according to WHO classification into three groups; normal weight (n=100), overweight (n=120) and obese (n=130). Interleukin-6 (IL-6) and C-reactive protein (CRP) were measured using standard methods and ELISA (R&D Systems. Insulin resistance was detected by the Homeostasis Model Assessment of Insulin Resistance (HOMA-IR).

Anthropometric measures of adiposity showed significant positive correlations with inflammatory biomarkers (IL-6 and CRP) and inverse correlations with serum adiponectin levels (p<0.05). Obese and overweight women had significant lower serum adiponectin concentrations than normal weight women. In addition, significant negative correlation between serum adiponectin levels and inflammatory biomarkers was observed. Multivariate logistic regression analysis shows that increased WHR, WC and elevated blood pressure level are predictor's risk factors for IR in obese/overweight women. The study highlights correlation of the obesity parameters to metabolic and biochemical markers in obese and overweight Egyptian women. Central obesity is a risk factor for IR in overweight/obese women. The study observed link between adiposity, IR and lipid metabolism. Dyslipidemia, hypertension and elevated inflammatory markers are the most prevalent metabolic parameters in overweight/obese women. Thus, investigate of anthropometric and biochemical profiles might be clinically important for risk estimation of chronic diseases. Conclusion: Alterations in metabolic profile and inflammatory markers may be due to excess of body fat and this may predispose to increase cardio metabolic risks at this young age Egyptian women.

Keywords: Obesity, Hypertension, Inflammation, Central obesity, Insulin Resistance, Interleukin-6 and C-reactive protein, Cardio-metabolic risks

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INTRODUCTION

Hypertension, dyslipidemia and pro-inflammatory are cardio metabolic risk factors that leading to various cardiac and metabolic disorders. Several studies revealed that cardiovascular and metabolic disorders has risen as a major public health problem in different groups of population worldwide [1,2]. Obesity is becoming one of the most important social problems of communities in the whole world. The prevalence of obesity is increasing rapidly in both developed and developing countries [3]. Because of public health importance; the trends in young adult obesity should be monitored. The metabolic syndrome is defined as a collection of metabolism-related conditions such as insulin resistance, hyperlipidemia and central obesity [4]. It is a resilient factor of metabolic disorders linked to Insulin Resistance (IR) that increase the vascular risk. Fat accumulation may be contributing in the Insulin Resistance (IR) syndrome which is linked to a group of irregularities that increase cardiovascular risk, including impaired glucose tolerance, hypertension, dyslipidemia, low grade inflammation, hepatitis and sleep apnea syndrome [4]. The association of abdominal adiposity with metabolic disorders depends on BMI [5,6]. Obesity is frequently associated with increased inflammatory markers including, C-reactive Protein (CRP) and Interleukin 6 (IL-6) [7]. IL-6 is one of the most important cytokines responsible for the chronic inflammatory process [8]. These inflammatory markers play an important role in obesity, insulin resistance and the risk of cardiovascular disease [9]. CRP is a sensitive marker of inflammation, positively correlated with abdominal fat and closely correlated with increased risk of cardiovascular diseases [10]. Some studies have begun to show a possible correlation between inflammation and the presence of essential hypertension, especially if it is associated with obesity, dyslipidemia, diabetes mellitus [8,11,12]. The relationship between inflammatory markers, obesity indices and metabolic parameters did not reach a full conclusion yet. The aim of the work was to compare inflammatory, biochemical markers and plasma adiponectin levels in obese, overweight and normal weight women, as well as determining the association of these markers with cardio -metabolic risk components.

PATIENTS AND METHODS

The study comprised 350 unrelated young women, their age ranged between 20 and 30 years. They were grouped according to WHO classification into three groups: normal weight (n=100), overweight (n=120) and obese (n=130). All subjects enrolled in this study gave written informed consent and the Ethics Committee of the National Research Centre approved this study. They were recruited from obesity clinic, National Research Centre, Egypt.

Measurement of insulin resistance was obtained using the homeostasis model assessment

[HOMA-IR=fasting glucose (mg/dl) × fasting insulin (µU/ml)/22.5].

CRP was measured using the rocket immune-electrophoresis method with the established reference value of up to 5 mg/l. Quantitative analysis of human IL-6 was conducted with the use of the sandwich ELISA technique (Enzyme-Linked Immunosorbent Assay) with a complete analysis set by R&D Systems with the method sensitivity of 0.70 pg/ml. The test procedure was conducted according to the manufacturer's recommendations [13].

Serum triglyceride (TG), HDL-cholesterol (HDL-c), and plasma glucose (FPG) were manually measured by their respective kits (Human Company, Germany). Insulin was measured by Electrochemiluminescence immunoassay (ECL) on Elecsys autoanalyzer (Roche Diagnostics, Germany). Patients who were considered to have a diagnosis of a dyslipidemia had values of total cholesterol greater than 199 mg/dL, LDL greater than 159 mg/dL, or triglycerides greater than 150 mg/dL and andhigh-density lipoprotein cholesterol (HDL-C) less than 50 mg/dl. Plasma levels of adiponectin were measured by using an enzyme-linked immunosorbent assay following the manufacturer's instructions [14].

The SPSS 12.0 statistical program for Windows (SPSS Inc., Chicago, IL, USA) was used for statistical analyses. The Kolmogorov-Smirnov test was applied to ensure a Gaussian distribution of the data. Kruskal-Wallis tests were used to determine differences between groups for nonparametric data. One-way analysis of variance (ANOVA), and the post-hoc Bonferroni's test was used to identify significant differences indicated by the ANOVA tests.

Logistic forward regression analysis, was used to assess the association between all clinical variables and anthropometric parameters that independently predicted IR development with a $P<0.05$. The associations of serum adiponectin IL-6, CRP with the obesity, biochemical and clinical features were tested by partial correlation analysis after adjustment for BMI.

Risk for IR development was also estimated by odds ratio (OR) with 95% confidence intervals (CIs) that independently predicted the IR. Statistical significance was set at $P<0.05$.

The anthropometric measurements and instruments followed the International Biological Program (IBP). Measurements were taken three times and the mean values used in the analysis included weight, height, waist circumference (WC), and hip circumference (HC), triceps and subscapular skinfold thickness. Body weight was measured to the nearest 0.1 kg and height was measured to the nearest 1 mm. The skin fold thickness was measured to the nearest 1.0 mm. The triceps skinfold was measured parallel to the long axis of the arm midway between the acromion and the olecranon, with the arm slightly flexed, and the subscapular skinfold was measured below the lower angle of the left scapula at a diagonal in the natural cleavage of the skin, using Harpenden skin fold caliper. BMI in kg/m^2, and waist-to-hip ratio (WHR) were calculated. Body composition was carried out using a body composition analyzer TANITA SC–330 (Tanita Corporation, Tokyo, Japan). BF% was estimated to the nearest 0.1%.

RESULTS

Table 1 shows comparison of anthropometric measurements between the three groups classified by WHO. ANOVA analysis showed significance difference between the three groups, normal weight, overweight and obese women in all anthropometric measurements. Obese and overweight women showed significant higher means in waist circumference (WC), Hip circumference (HC), waist to hip ratio (WHR) and skin old thickness as compared to normal weight controls. No significant differences were found between overweight and obese women in all anthropometric parameters.

Table 1: Anthropometric features of women participating in the study

Variables	Normal weight	Overweight	Obese	P
Waist circumference	80.37 ± 8.2	84.97 ± 7.2	99.37 ± 6.5	0.04
Hip (cm)	100.34 ± 2.94	136.01 ± 5.20	150.37 ± 8.2	0.01
Waist/hip	0.74 ± 0.09	0.84 ± 0.06	0.99 ± 0.07	0.03
Triceps SF (mm)	17.78 ± 6.89	19.34 ± 7.81	32.76 ± 5.84	0.01
Subscapular SF (mm)	15.86 ± 6.70	19.78 ± 5.81	34.93 ± 9.16	0.04

Table 2 shows comparison of body composition between the three study groups. Obese and overweight women had significant higher values of body fat mass and body fat% and significant lower values of basal metabolic rate and total body water than normal weight group.

Table 2: Body composition data of the study groups

Variables	Normal weight	Overweight	Obese	P
BMR (K cal)	1776.05 ± 102.32	1462.63 ± 141.73	1486.79 ± 145.10	0.05
Fat mass (kg)	9.56 ± 4.75	23.26 ± 5.65	42.01 ± 12.23	0.02
Body Fat %	18.19 ± 5.65	32.44 ± 3.87	45.32 ± 4.25	0.01
TBW	30.31 ± 11.71	25.96 ± 13.40	24.99 ± 15.23	0.04
Bone mass (kg)	0.94 ± 1.06	1.05 ± 1.19	1.40 ± 1.39	0.09

Table 3 shows clinical and biochemical characteristics of the study groups. Obese and overweight women had significant elevated levels of blood pressure levels, CRP, IL-6 and HOMA-IR and lower adiponect in concentration than normal weight women. Insulin resistance was determined by the Homeostasis Model Assessment of Insulin Resistance (HOMA-IR). It is a method used to measure insulin resistance and beta-cell function from fasting glucose and insulin concentrations. HOMA is a model of the link of glucose and insulin dynamics that predicts fasting steady-state glucose and insulin concentrations for a wide range of possible combinations of insulin resistance and β-cell function. Insulin levels depend on the pancreatic β-cell response to glucose concentrations while, glucose concentrations are regulated by insulin-mediated glucose production via the liver Matthews.

Table 3: Clinical and biochemical characteristics of the study subjects

Variables	Normal weight	Overweight	Obese	P
Systolic PB (mm Hg)	120.11 ± 6.88	130.99 ± 10.77	160.88 ± 11.67	0.04
Diastolic PB (mm Hg)	75.91 ± 7.34	85.19 ± 5.11	99.89 ± 8.11	0.01
Adiponectin (mg/L)	4.66 ± 1.99	3.45 ± 1.11	2.45 ± 2.01	0.01
HsCRP(μg/mL)	1.20 ± 1.12	3.22 ± 1.30	5.20 ± 1.24	0.01
IL-6 (pg/mL	0.92 ± 0.13	1.19 ± 0.25	2.49 ± 0.21	0.02
HOMA-IR	2.44 ± 1.99	4.47 ± 1.12	6.67 ± 1.03	0.03

Table 4 shows factors that associated with IR. The factors which showed a positive association in predicting IR were WHR (> 0.85) of OR=1.62 (95% CI 1.52-168), WC (>88 cm) of OR= 1.72(95% CI 1.58-1.98) and hypertension (>130/>85 m Hg) of OR= 1.52 (95% CI 1.65-1.99).

Table 4: Factors that associated with IR

	Risk factor	OR*	95.0 % CI	P
Insulin Resistance (IR)	W/H ratio >0.85 cm	1.62	1.52-1.68	0.001
	WC ≥ 88 cm	1.72	1.58-1.98	0.001
	High-blood pressure (>130/>85 mm Hg)	1.52	1.65-1.99	0.001

Table 5 shows correlation coefficients and P values between the change in serum adiponectin, IL-6, CRP and obesity, biochemical and clinical features. Strong positive associations were observed between adiponectin and inflammatory markers (IL-6, CRP), obesity measures and metabolic parameters (insulin, HOMA-IR). Adiponectin showed significant inverse correlation with obesity, metabolic and inflammatory markers.

Table 5: correlation coefficients and P values

Variables	IL-6	CRP	Adiponectin	BMI (kg/m^2)	Body Fat %	HOMA-IR	Insulin (μU/mL)
IL-6	1	P=0.02	P=0.03, r=-0.54	P=0.04, r=0.44	P=0.05, r=0.44	P=0.01, r=0.49	P=0.02, r=0.64
CRP	-	1	P=0.04, r=-0.46	P=0.01, r=0.66	P=0.001, r=0.55	P=0.01, r=0.34	P=0.02, r=0.45
Adiponectin	-	-	1	P=0.04, r=-0.56	P=0.01, r=-0.59	P=0.02, r=-0.64	P=0.03, r=-0.44
BMI (kg/m^2)	-	-	-	1	P=0.02, r=0.48	P=0.03, r=0.57	P=0.01, r=0.39
Body Fat %	-	-	-	-	1	P=0.02, r=0.45	P=0.01, r=0.53
HOMA-IR	-	-	-	-	-	1	P=0.01, r=0.44
Insulin (μU/mL)	-	-	-	-	-	-	1

Table 6 shows prevalence of cardio metabolic risks in the studied groups. Dyslipidemia, hypertension and elevated inflammatory markers are more prevalent in obese and in overweight women than normal weight women (p<0.05 for all parameters).

Table 6: Prevalence of cardio-metabolic risks in the studied groups

Risk factors	Normal weight	Overweight	Obese	p
Dyslipidemia	8%	50%	80%	0.03
Hypertension	10%	40%	60%	0.01
Dyslipidemia+hypertension	7%	20%	40%	0.01
Dyslipidemia+IR	6%	30%	50%	0.02
Elevated hsCRP+IL-6	5%	50%	70%	0.01

DISCUSSION

Overweight and obesity are predominant in developing countries and becoming a big problem. In our study, obese and overweight women showed significant higher means in waist circumference (WC), Hip circumference (HC), waist to hip ratio (WHR) and skin old thickness as compared to normal weight controls. Although, the body mass index (BMI) is the most frequently factor used to define obese, overweight, or normal weight subjects. The World Health Organization (WHO) recommended that alternative measures that reflect abdominal obesity such as WC, WHR, and waist-to-height ratio (WHR) have been found to be more important than BMI [15]. A Chinese study confirmed that BMI and WC were the important indices of obesity, while WC was established to be the best measurement of obesity however WHR could be as an alternative indicator for obesity [16].

WC is an important measure of abdominal obesity compared to WHR, which can be low in some obese people because of high hip circumference (in denominator) [17]. WC is the best indicator as compared with WHR for abdominal obesity for Malaysian adults [17]. Low HDL was more common in females than in males according to the study of Acute Coronary Syndrome Patients in the Middle East [18].

Obesity is the main culprit for low HDL and optimizing women's healthy lifestyles (e.g., moderate weight loss combined with exercise and smoking cessation) will significantly increase HDL. In contrast to other adipocytokines adiponectin is reduced in obese patients and those with diabetes mellitus. Consequently, high adiponectin concentrations are associated with cardiovascular outcomes in general populations. According database from the large population study from the Framingham, increment in BMI exponentially increases the risk of dyslipidemia, insulin resistance and subsequently the risk of coronary heart disease, heart failure and ischemic stroke [19].

No significant differences were found between overweight and obese women in all anthropometric parameters. Although, significant differences between the overweight and obese women groups according to body mass index, waist circumference (WC), and body fat percentage were detected by Gülcan et al. [20].

Obese and overweight women had significant higher values of body fat mass and body fat %. This coincides with the findings of Ranasinghe et al. [21]. Who found significant positive correlation between obesity and body fat %. Moreover, significant lower values of basal metabolic rate and total body water were noted in obese women than the normal weight group. Similarly, McMurray et al. [22], reported that BMR was less in overweight than normal weight adults.

Our study delineated significant elevated of the blood pressure, CRP, IL-6 and HOMA-IR and lower adiponectin concentration than normal weight women. Rość et al. [23] documented that the obese individuals had significantly elevated levels of CRP, TNF-α, triglycerides, HOMA-IR and fasting glucose. WHR, WC and hypertension revealed a positive association in predicting IR, this is in agreement with the findings of Bari et al. [24] and Zaki et al. [25], who declared that WC provides a feasible measure for insulin resistance.

Anthropometric measurements have been used to assess metabolic and cardiovascular risk, including body mass index and body fat percentage, as well as site particular dimensions, such as peripheral or central fat and waist circumference. Classical indices such as WC and waist-to-hip ratio can be described central or abdominal obesity [26]. Moreover, waist to height ratio, body adiposity index, and visceral adiposity index were described as newer obesity indices [27].

There is no agreement on the best anthropometric measurement that associated with risk markers of metabolic diseases. Regardless of sex, age, and total adiposity the good indicator of the location of body fat should be associated with risk markers for metabolic diseases. Due to the limitations of central or peripheral body fat other anthropometric measurements are used in epidemiological studies [28]. In this study, all parameters of anthropometric measurements of both peripheral and central obesity groups were used.
Negative associations between adiponectin and inflammatory markers (IL-6, CRP), obesity measures (BMI, WC, WHR, skin-folds thickness, body fat% and metabolic parameters (BP, insulin glucose, HOMA-IR) were described by several investigators [29,30]. The present study showed association between adiponectin and hyper insulinemia in overweight/ obese women. The relationship between insulin resistance and obesity is complex, and previous studies indicated that adipose tissue is a hormonally active system involved in insulin action as well as glucose and lipid metabolism [31,32].

Dyslipidemia and metabolic risk factors are strongly linked to abdominal obesity [33]. Body mass index and waist circumference have been associated with triglycerides and HDL that determined visceral adiposity index [34]. Our in data is in continent with these findings and showing that excess of body fat together with central obesity in present obese women might provoke inflammatory and metabolic markers. Therefore, the specific impact of waist circumference on women's health is needed in population studies. The levels of inflammatory and metabolic markers were highly prevalent among overweight/obese Egyptian women and this may predispose to increasing cardio-metabolic risks.

CONCLUSION

The study confirmed the potential correlations between biochemical parameters, hypertension, inflammatory markers and obesity parameters among Egyptian women. Therefore, obesity prevention among Egyptian women is urgently needed. Abdominal fat accumulation in addition to hypertension are risk factors for IR in overweight/obese. The study suggests that the analysis of body composition and biochemical parameters in obese and overweight women might be clinically important for the estimation of risk factors for chronic diseases. Adiponectin may play a role in regulating inflammatory responses.

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