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Full Length Research paper

Influence of waist circumference and body mass index on the levels of adipokines, insulin and lipid parameters in normal overweight young Saudi females

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Abnormal lipid profile, insulin resistance and hypoadiponectinemia are well recognized risk factors for cardiovascular and metabolic diseases. These risk factors are more prevalent among subjects with increased body adiposity. To study the relationships of body mass index (BMI) and waist circumference (WC) with fasting adipokines (leptin and adiponectin), lipid profile, and insulin sensitivity, a cross-sectional study was undertaken on 127 healthy young females randomly recruited from the College of Medicine at KAU in KSA. Anthropometric measurements and biochemical parameters were estimated. Significant increase in insulin, fasting blood glucose (FBG), HOMA-IR, total cholesterol (TC), triglycerides (TG), and LDL-C were found in subjects with WC > 80 cm compared to those with WC ≤ 80 cm. When the mean of the 3rd quartile of WC was taken as a cutoff point, similar increase in all the parameters was also found in addition to a significantly lower adiponectin level at a WC ≥ 74 cm. Similar abnormalities were found at BMI ≥ 23 kg/m^2 (mean of the 2nd quartile). Moreover, WC was a negative predictor of adiponectin and a positive one of insulin and HOMA-IR, while BMI was a positive predictor of FBG, TC, TG and LDL-C. In conclusion, hypoadiponectemia, hyperlipidemia and insulin resistance were observed at WC and BMI that are normal by Western definitions. Our findings suggest the need to establish local WC and BMI cutoff points to identify subjects with hyperlipidemia, hypoadeponectinemia, and insulin resistance that may be missed when the Western and North American criteria are used.

Key words: Lipid profile, insulin, leptin, adiponectin, Saudi female.

INTRODUCTION

The prevalence of obesity has markedly increased in most countries of the world (York et al., 2004). The concerns about the increased risk of cardiovascular and other co-morbidities associated with increased weight gain are well recognized (Goran et al., 2003; Caterson et al., 2004). However, in some populations health risks associated with obesity occur at a lower body mass index, and redefining overweight and obesity had been recommended based on mortality and morbidity risks (Low et al., 2009). Therefore, the use of World Health Organization (WHO, 2004) criteria to define overweight (≥ 25.0 kg/m^2) and obesity (≥ 30.0 kg/m^2) may not be appropriate to all populations and ethnic-specific cut-off points should be established.

Using WHO criteria, overweight and obesity constitute a major health problem in the Saudi female population with an overall prevalence of 28.4 and 23.6%, respectively (Al-Othaimeen et al., 2007). While body mass index (BMI) correlates well with body fat, it is the body fat

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Abbreviations: **ATP** III, The adult treatment panel III; **BMI**, body mass index; **FBG**, fasting blood glucose; **HDL-C**, high density lipoproteins-cholesterol; **HOMA**, homeostasis model assessment index; **KAU**, King Abdulaziz University; **LDL-C**, low density lipoproteins-cholesterol; **NCEP**, the national cholesterol education program; **TC**, total cholesterol; **TG**, triglycerides; **WC**, waist circumference; **WHO**, world health organization; **WHR**, waist: hip ratio.

distribution that determines the risk associated with obesity (Pataky et al., 2009). Visceral fat, estimated clinically by an increased waist circumference (WC) (Balkau et al., 2007), is the form of obesity mostly associated with the metabolic abnormalities that cluster in the metabolic syndrome (Fox et al., 2007).

Adipose tissue is an active endocrine organ secreting several adipokines involved in glucose metabolism (e.g. adiponectin, resistin) (Galic et al., 2010), lipid metabolism (e.g. cholesteryl ester transfer protein, CETP), inflammation (e.g. TNF-α, IL-6) (Weisberg et al., 2003) specially visceral adipose tissue (Cancello et al., 2006; Ye et al., 2007), coagulation (PAI-1) (Yamauchi et al., 2001), blood pressure (e.g. angiotensinogen, angiotensin II) (Ran et al., 2006), and feeding behaviour (leptin) (Chu et al., 2001; Gower et al., 2003). The increase in adipose tissue, particularly visceral, is a risk factor for insulin resistance, and its secretory products (adipokines) are acquiring a recognized role as determinants of insulin resistance (Fruhbeck et al., 2001).

Plasma adipocytokine levels rise with an increase in adipose tissue and adipocyte volume except for plasma adiponectin (Skurk et al., 2007). Adiponectin, in contrast to other adipokines, has insulin-sensitizing, anti-atherogenic, and anti-inflammatory properties (Kadowaki et al., 2006; Karastergiou et al., 2009). The circulating plasma concentration of adiponectin is decreased with visceral fat accumulation and hypoadepinectinemia is now recognized as a strong risk factor for metabolic and cardiovascular diseases (Matsuzawa, 2010). Leptin is another adipocytokine known as an important regulator of food intake and energy expenditure that links peripheral adipose energy stores to the hypothalamic satiety center and serves as a very sensitive marker of the body fat content and metabolic activity. In addition, it has been shown to be a predictor of cardiovascular diseases (Wallace et al., 2001).

The aim of the present study was to determine the possible relationships of BMI and waist circumference with fasting leptin and adiponectin levels, lipid profile, and insulin sensitivity in a group of apparently healthy young females. Our hypothesis is that abnormal levels may be found at lower BMIs and smaller waist circumferences, if this is true, the appropriateness of utilizing the Western cut-off points to define overweight and abdominal obesity in our population should be revisited.

MATERIALS AND METHODS

This was a cross-sectional study in which a total of 127 female medical students were randomly recruited from the college of Medicine at King Abdul Aziz University (KAU) in Jeddah, Saudi Arabia. Informed consent was obtained from all subjects and the study was approved by the Ethics committee of KAUH. Subjects with inflammatory diseases, hepatic and renal diseases, impaired glucose tolerance or diabetes, and obesity secondary to genetic or metabolic disorders were excluded from the study. A self-administered questionnaire was completed by each subject inquiring about age, demographic data, general health, medications use and dietary intake.

Body weight, height, body mass index (BMI), waist circumference (WC), waist: hip ratio (WHR) and blood pressure readings were recorded by the same observer. Subjects were weighed on electrical scale to the nearest half kilogram while wearing light clothes and bare footed (Seca Alpha, GmbH & Co., Igni, France; range 0.1 to 150 kg, precision 100 g). Height was measured using a stadiometer to the nearest half centimeter (Pfifter, Carlstadt, NJ, USA; range 70 to 205 cm, precision 1 mm). Using a tape measure, waist circumference (midway between the lower rib margin and the iliac crest) and hip circumference (the maximal circumference over the buttocks) were measured to the nearest 0.1 cm. The WHR, calculated as waist circumference divided by hip circumference, was used as an indicator of abdominal visceral fat (Schreiner et al., 1996). The clinical guidelines on the identification, evaluation and treatment of overweight and obesity in adults (1998) were used to define overweight (BMI, 25 to 29.9 kg/m^2) and obesity (BMI ≥ 30 kg/m^2).

Blood samples were obtained from all subjects after a 12 h fast. They were centrifuged at 3000 g for 10 min. Plasma was obtained for the analysis of the following biochemical parameters. Fasting lipid profile and fasting blood glucose (FBG) were measured using enzymatic methods (Crescent Diagnostics, KSA). The within batch coefficient of variation was 5.4% whereas the between batch coefficient of variation was 9.8%. Our laboratory reference ranges were according to the latest National Cholesterol Education Program (NCEP's) clinical guidelines for blood lipids (ATP III): serum total cholesterol (TC), < 5.2 mmol/L, triglycerides (TG) 0.3 to 2.3 mmol/L, high density lipoproteins-cholesterol (HDL-C), 0.9 to 1.55 mmol/L and low density lipoproteins-cholesterol (LDL-C), < 3.57 mmol/L (2001). In accordance with the latest American Diabetes Association guidelines, fasting blood glucose levels < 6.1 mmol/L were considered to be normal (Genuth et al., 2003).

Fasting plasma insulin was determined by a sandwich chemiluminescence immunoassay method using commercial kits from DiaSorin (Italy) and the test was performed on the Liaison analyzer. Sensitivity was 1 µU/ml, the intra-assay coefficient of variation was 4.0% and the inter-assay coefficient of variation was 8%. The high and low insulin control results were within the reference range that was provided by the manufacturer.

The homeostasis model assessment index (HOMA), which is based on fasting insulin and glucose measured in a single blood sample, has been used frequently to predict insulin resistance (Mattews et al., 1985). The HOMA yields an equation where insulin resistance = [fasting insulin (µU/ml) × fasting glucose (mmol/L)]/ 22.5.

Serum total circulating levels of adiponectin and leptin were measured using ELISA assay kits (ALPCO Diagnostics) obtained through local agents. The intra-assay and inter-assay coefficients of variation for each variable was found to be < 8 and < 15%, respectively.

Data are presented as means ± standard deviation for normally distributed variables and as median (inter-quartile ranges) for non-normally distributed variables. Categorical variables are expressed as frequency (percentage). Nonparametric tests were used since most of data were not normally distributed.

The study population was stratified by WC and by BMI into quartiles. Study participants were also divided into sub-categories based on the conventional clinical cutoff point for waist circumference and BMI values. Comparison of two groups was performed using the Mann Whitney-U test. Comparison of more than 2 groups was performed using Kruskall-Wallis test.

Spearman's correlation coefficients were used to assess association between continuous variables. Stepwise multiple regression analysis was used to detect independent predictive variables. Significance levels are shown for all comparisons and relationships where $P < 0.05$. Data results were analyzed using SPSS statistical

Table 1. Anthropometric and biochemical characteristics of the study population (n = 127).

Variable	Mean (S.D.)	Median (interquartile range)
Age (year)	-	20.0 (19- 21)
Weight (kg)	-	61.8 (52.2- 73.8)
Height (cm)	158.5 (6.5)	-
BMI (kg/m^2)	-	24.6 (21.2- 28.5)
WC (cm)	-	71.0 (62.0- 79.0)
HC (cm)	-	100 (93 - 109)
WHR	0.71 (0.05)	-
Adiponectin (ng/ml)	-	9.5 (8.3 - 10.9)
Leptin (ng/ml)	-	14.3 (11.7- 17.5)
Insulin (µIU/ml)	-	9.20 (5.48 - 12.40)
FBG (mmol/L)	4.95 (0.64)	-
HOMA	-	2.00 (1.09- 2.90)
TC (mmol/L)	-	5.14 (4.74- 5.42)
TG (mmol/L)	-	1.56 (1.32- 1.71)
HDL-C (mmol/L)	-	1.42 (0.36- 1.68)
LDL-C (mmol/L)	3.53 (0.91)	-

BMI, body mass index; FBG, fasting blood glucose; HOMA, homeostatic model assessment; HDL-C, high density lipoprotein cholesterol; LDL-C, low density lipoprotein cholesterol; TC, total cholesterol; TG, triglycerides; WC, waist circumference; HC, hip circumference; WHR, waist to hip ratio.

package (version 12).

RESULTS

Anthropometric and biochemical characteristics of the study population

Anthropometric and biochemical characteristics of the study population are presented in Table 1. According to WHO, definitions of overweight and obesity, 35 subjects (27.6%) were overweight and 25 subjects (19.7%) were obese. Two subjects (1.6%) had a WHR ≥ 0.85, and 26 (20.5%) had a WC of > 80cm.

According to the Adult Treatment Panel III (ATP III) recommended limits for lipids in adult fasting blood, 37 individuals (29%) and 58 individuals (46%) were shown to have LDL-C > 4.14 mmol/L and HDL-C < 1.04 mmol/L, respectively. However, when the obese and overweight subjects were excluded, abnormal lipid profile was still seen in 25% of cases (LDL-C > 4.14mmol/L) and 49% of cases (HDL-C < 1.04mmol/L).

Changes in biochemical characteristics across quartiles of WC and BMI

Quartiles of WC were calculated and the differences in hormonal and lipid profile among the groups were compared (Table 2). There was a significant decrease in adiponectin with increased WC, while leptin, insulin, FBG, and HOMA increased significantly as WC increased. TC and TG significantly increased as well with increased WC. Borderline high levels of TC and LDL-C were seen in the 3rd quartile where the mean WC for the group was 74 cm. Similar comparisons were done between quartiles of BMI (Table 3), and there was a significant increase in leptin, insulin, FBG, HOMA, TC, TG, HDL-C and LDL-C with increasing BMI.

Comparisons of biochemical characteristics using a WC of 80 cm as a cutoff point

Using the WC cutoff point of 80 cm, derived from studies on Asian population, there was a significant increase in insulin, FBG and HOMA as well as TC, TG, LDL-C in subjects with WC > 80 cm compared to those with WC ≤ 80 cm (Table 4).

These differences persisted even when a smaller WC cutoff point of 74 cm was used (the mean of the 3rd quartile), in addition to a significantly decreased adiponectin in subjects with WC ≥ 74 cm (Table 5).

Comparisons of biochemical characteristics using a BMI of 23 kg/m^2 as a cutoff point

Since the mean for the 3rd and 4th quartiles of BMI were above normal (27 and 35 kg/m^2, respectively), the mean of the 2nd quartile (23 kg/m^2) was used to compare subjects with BMI ≥ 23 kg/m^2 to those with BMI < 23

Table 2. Biochemical characteristics among the study population as classified by quartiles of WC (n = 127). Group 1: WC ≤ 61.9 cm (mean = 59 cm), Group 2: WC 62 to < 70.9 cm (mean = 65 cm), Group 3: WC 71 to ≤ 78.9 cm (mean = 74 cm), Group 4: WC ≥ 79 cm (mean = 88 cm).

Variable	Group 1 N=26	Group 2 N=36	Group 3 N=33	Group 4 N=32	P value
Adiponectin (ng/ml)	10.8 (9.2 - 14.8)	9.5 (8.2 - 15.1)	9.5 (8.4 - 10.5)	9.1 (8.0 - 9.8)	0.017
Leptin (ng/ml)	12.1 (11.3 - 6.1)	12.3 (11.0 - 14.8)	15.5 (13.5 - 17.6)	17.2 (13.5 - 20)	0.005
Insulin (µIU/ml)	7.3 (4.5 - 10.1)	6.1 (4.5 - 10.1)	10.0 (6.0 - 12.3)	14.2 (10.7 - 18.9)	<0.0001
FBG (mmol/L)	4.82 (4.41 - 5.01)	4.61 (4.27 - 4.79)	5.11 (4.63 - 5.52)	5.28 (4.95 - 5.93)	<0.0001
HOMA	1.44 (0.99 - 2.19)	1.09 (0.94 - 2.00)	2.28 (1.33 - 3.01)	3.39 (2.43 - 5.13)	<0.0001
TC (mmol/L)	5.0 (4.1 - 5.2)	4.9 (4.2 - 5.1)	5.2 (4.7 - 5.5)	5.5 (5.3 - 5.6)	<0.0001
TG (mmol/L)	1.5 (1.2 - 1.6)	1.5 (1.2 - 1.6)	1.6 (1.4 - 1.8)	1.8 (1.6 - 1.8)	<0.0001
HDL-C (mmol/L)	1.5 (0.2 - 1.7)	0.77 (0.26 - 1.6)	1.3 (0.4 - 1.8)	1.5 (0.69 - 1.8)	0.211
LDL-C (mmol/L)	3.3 (2.6 - 3.6)	3.3 (2.8 - 4.3)	3.4 (3.1 - 4.2)	3.7 (3.3 - 4.4)	0.06

Data are presented as median (interquartile range). FBG = fasting blood glucose, HOMA = homeostatic model assessment, HDL-C = high density lipoprotein cholesterol, LDL-C = low density lipoprotein cholesterol, TC = total cholesterol, TG = triglycerides.

Table 3. Biochemical characteristics among the study population as classified by quartiles of BMI (n = 127). Group 1: BMI < 21.2 kg/m^2 (mean = 19.5 kg/m^2); Group 2: BMI 21.2 to < 24.6 kg/m^2 (mean = 22.6 kg/m^2); Group 3: BMI 24.6 to < 28.5 (mean = 26.8 kg/m^2) kg/m^2; Group 4: BMI ≥ 28.5 kg/m^2 (mean = 35 kg/m^2).

Variable	Group 1 N=31	Group 2 N=32	Group 3 N=33	Group 4 N=31	P value
Adiponectin (ng/ml)	9.5 (8.4 - 11.4)	9.7 (8.2 - 15.1)	9.5 (8.0 - 10.6)	9.3 (8.2 -10.2)	0.591
Leptin (ng/ml)	11.7 (11.0 - 14.5)	14.0 (12.0 - 17.3)	14.7 (13.0 - 16.9)	17.5 (10.4-19.9)	0.015
Insulin (µIU/ml)	6.5 (4.5 - 9.1)	6.9 (5.5 - 10.4)	10.2 (6.0 - 13.5)	14.2 (10.6-19.4)	< 0.0001
FBG (mmol/L)	4.68 (4.34 - 4.91)	4.59 (4.22 - 4.77)	5.12 (4.80 - 5.47)	5.49 (5.04-6.09)	< 0.0001
HOMA	1.30 (0.94 - 2.02)	1.34 (0.97 - 2.05)	2.41 (1.60 - 3.12)	3.42 (2.42-5.32)	< 0.0001
TC (mmol/L)	4.9 (4.1 - 5.1)	4.8 (4.1 - 5.1)	5.1 (4.7 - 5.3)	5.5 (5.4-5.8)	< 0.0001
TG (mmol/L)	1.5 (1.3 - 1.6)	1.4 (1.2 - 1.6)	1.6 (1.2 - 1.7)	1.8 (1.6-1.8)	< 0.0001
HDL-C (mmol/L)	0.5 (0.2 - 1.5)	1.6 (0.6 - 1.7)	1.0 (0.5 - 1.8)	1.5 (0.6-1.8)	0.048
LDL-C (mmol/L)	3.5 (2.8 - 4.4)	3.1 (2.7 - 3.6)	3.4 (3.0 - 4.1)	3.9 (3.4-4.7)	0.012

Data are presented as median (interquartile range). FBG, fasting blood glucose; HOMA, homeostatic model assessment; HDL-C, high density lipoprotein cholesterol; LDL-C, low density lipoprotein cholesterol; TC, total cholesterol; TG, triglyceride.

Table 4. Biochemical characteristics in subjects with WC ≤ 80 cm as compared to those with WC > 80 cm.

Variable	WC ≤ 80 cm (n = 101)		WC > 80 cm (n = 26)		P value
	Median	Interquartile range	Median	Interquartile range	
Adiponectin (ng/ml)	9.57	8.35 - 11.05	9.15	8.15 - 9.96	0.131
Leptin (ng/ml)	13.85	11.68 - 16.65	16.85	12.01 - 20.29	0.097
Insulin (µIU/ml)	7.70	5.20 - 10.95	15.40	11.65 - 21.45	< 0.0001
FBG (mmol/L)	4.79	4.49 - 5.11	5.38	4.95 - 6.02	< 0.0001
HOMA	1.67	1.02 - 2.41	3.46	2.90 - 5.80	< 0.0001
TC (mmol/L)	5.00	4.47 - 5.24	5.48	5.34 - 5.64	< 0.0001
TG (mmol/L)	1.52	1.26 - 1.64	1.78	1.64 - 1.85	< 0.0001
HDL-C (mmol/L)	1.24	0.33 - 1.70	1.50	0.64 - 1.66	0.401
LDL-C (mmol/L)	3.34	2.85 - 4.18	3.77	3.40 - 4.43	0.010

FBG, Fasting blood glucose; HOMA, homeostatic model assessment; HDL-C, high density lipoprotein cholesterol; LDL-C, low density lipoprotein cholesterol, TC = total cholesterol, TG = triglycerides.

Table 5. Biochemical characteristics in subjects with WC < 74 cm as compared to those with WC ≥ 74 cm.

Variable	WC < 74 cm (n = 77)		WC ≥ 74 cm (n = 50)		P value
	Median	Interquartile range	Median	Interquartile range	
Adiponectin (ng/ml)	9.79	8.58 - 12.00	9.17	8.10 - 10.20	0.017
Leptin (ng/ml)	12.51	11.53- 15.72	16.50	13.16- 19.32	0.006
Insulin (µIU/ml)	6.80	4.65 - 10.15	12.40	9.65 - 16.90	< 0.0001
FBG mmol/L)	4.68	4.43- 5.01	5.28	4.94- 5.64	< 0.0001
HOMA	1.33	0.97- 2.15	3.09	2.19- 4.13	< 0.0001
TC (mmol/L)	4.92	4.46- 5.18	5.43	5.17- 5.56	< 0.0001
TG (mmol/L)	1.50	1.21- 1.63	1.71	1.53- 1.82	< 0.0001
HDL(mmol/L)	1.21	0.26- 1.65	1.50	0.56- 1.77	0.186
LDL(mmol/L)	3.34	2.78- 4.18	3.55	3.28- 4.35	0.023

FBG, Fasting blood glucose; HOMA, homeostatic model assessment; HDL-C, high density lipoprotein cholesterol; LDL-C, low density lipoprotein cholesterol; TC, total cholesterol; TG, triglycerides.

kg/m^2. There was significant increase in leptin, fasting insulin, FBG, HOMA, TC, TG, and HDL-C but not LDL-C in the former group (Table 6).

Correlations between measures of obesity and adipocytokines, FBG, HOMA and lipid profile

Correlations between 2 measures of obesity, namely BMI and WC, and adipocytokines, insulin, FBG, HOMA and lipid profile are presented in Table 7. There was a significant positive correlation between BMI and leptin, insulin, FBG, HOMA, TC and TG. Similar significant positive correlations were found with the same variables and WC, besides a significant negative correlation between WC and adiponectin and a significant positive correlation between WC and LDL-C.

Anthropometric predictor of adiocytokines, lipid profile, FBG, HOMA and insulin

Multiple regression analysis (stepwise method) was performed to find out the explanatory anthropometric variables (predictors) for the adipocytokines (leptin and adiponectin), insulin, FBG, HOMA and lipid profile. Different measures of obesity (BMI and WC) were entered into the regression model (independent variables) (Table 8). All anthropometric measures of obesity were excluded when leptin and HDL-C were the dependent variables.

Variables predicted by waist circumference in multiple regression analysis

WC was the main predictor for adiponectin concentration, insulin concentration and HOMA-IR (Table 8).

Variables predicted by Body Mass Index in multiple regression analysis

BMI was the main predictor for FBG, TC, TG and LDL-C (Table 8).

DISCUSSION

In the present study, an undesirable lipid profile was found in subjects with normal BMI and WC (according to Western criteria). This may entail the need to use lower WC and BMI cutoff points to identify the risks of developing hyperlipidemia, hypoadeponectinemia, hyperinsulinemia, and/or insulin resistance in young Saudi females. Indeed the WHO (2004) has set ethnic-specific BMI and WC cutoff values for East Asians and South Asians.

The present study also showed a significant increase in fasting lipids, fasting insulin, FBG and HOMA-IR at WC cutoff point of 80 cm, which persisted at lower WC of 74 cm. Moreover, adiponectin was significantly decreased only at WC ≥ 74 cm (P = 0.019). This finding indicates that subjects with low levels of adiponectin were among those with WC ≤ 80 cm which made the differences between the two groups not significant, but when these subjects with low levels of adiponectin were included in the group with WC ≥ 74, the difference in adiponectin level between the two groups became significant. In addition, after exclusion of the overweight and obese subjects from the study group lipid profile analysis showed high LDL-c in almost 25%, and low HDL-c in half of cases. These findings suggest that the use of cutoff points (WC > 80 cm) derived from studies on Asian-populations may not be appropriate for our population and the need for a population-specific value should be considered.

Research in East Asian countries consistently demon-strated a need for a lower BMI (e.g. < 25 kg/m^2) and WC

Table 6. Biochemical characteristics in subjects with BMI < 23 kg/m^2 (mean of the 2nd quartile) as compared to those with BMI ≥ 23 kg/m^2.

Variable	BMI < 23 kg/m^2 (n = 50)		BMI ≥ 23 kg/m^2 (n = 77)		P value
	Median	Interquartile range	Median	Interquartile range	
Adiponectin (ng/ml)	9.64	8.30 - 12.88	9.51	8.22 - 10.55	0.315
Leptin (ng/ml)	12.10	11.05 -15.75	15.14	12.43 - 18.51	0.010
Insulin (µIU/ml)	6.60	4.68 - 10.05	10.90	6.85 - 14.45	< 0.0001
FBG (mmol/L)	4.61	4.33 - 4.91	5.12	4.75 - 5.55	< 0.0001
HOMA	1.33	0.95 - 2.15	2.43	1.57 - 3.49	< 0.0001
TC (mmol/L)	4.86	4.14 - 5.14	5.34	5.02 - 5.53	< 0.0001
TG (mmol/L)	1.46	1.22 - 1.60	1.65	1.46 - 1.79	< 0.0001
HDL (mmol/L)	0.73	0.22 - 1.60	1.48	0.53 - 1.78	0.027
LDL (mmol/L)	3.35	2.75 - 4.17	3.45	3.09 - 4.32	0.098

FBG, Fasting blood glucose; HOMA, homeostatic model assessment; HDL-C, high density lipoprotein cholesterol; LDL-C, low density lipoprotein cholesterol; TC, total cholesterol; TG, triglycerides.

Table 7. Correlations between obesity measures with adipocytokines, insulin, FBG, HOMA and lipid profile among the study population (n = 127).

Variable	BMI		WC	
	r	P	r	P
Adiponectin	-0.132	0.138	-0.267	0.002
Leptin	0.296	0.001	0.296	0.001
Insulin	0.505	< 0.0001	0.535	< 0.0001
FBG	0.564	< 0.0001	0.469	< 0.0001
HOMA	0.575	< 0.0001	0.573	< 0.0001
TC	0.604	< 0.0001	0.560	< 0.0001
TG	0.471	< 0.0001	0.436	< 0.0001
HDL-C	0.170	0.056	0.139	0.120
LDL-C	0.218	0.14	0.245	0.005

FBG, Fasting blood glucose; HOMA, homeostatic model assessment; HDL-C, high density lipoprotein cholesterol; LDL-C, low density lipoprotein cholesterol; TC, total cholesterol; TG, triglycerides.

Table 8. Multiple regression analysis with adipocytokines, insulin, FBG, HOMA and lipid profile as dependent variables and measures of obesity (WC and BMI) as independent variables.

Dependant variable	Waist circumference				Body Mass Index			
	R^2	β	SE	P value	R^2	β	SE	P value
Adiponectin	0.067	-0.080	0.027	0.003	-	-	-	-
Leptin	-	-	-	-	-	-	-	-
Insulin	0.263	0.303	0.046	< 0.0001	-	-	-	-
FBG	-	-	-	-	0.291	0.050	0.007	< 0.0001
HOMA-IR	0.318	0.081	0.011	< 0.0001	-	-	-	-
TC	-	-	-	-	0.216	0.052	0.009	< 0.0001
TG	-	-	-	-	0.128	0.019	0.004	< 0.0001
HDL-C	-	-	-	-	-	-	-	-
LDL-C	-	-	-	-	0.072	0.036	0.011	.002

BMI, body mass index; FBG, fasting blood glucose; HOMA, homeostatic model assessment; HDL-C, high density lipoprotein cholesterol; LDL-C, low density lipoprotein cholesterol; TC, total cholesterol; TG, triglycerides; WC, waist circumference.

and WC cutoff points for estimating risk of metabolic abnormalities (Bei-Fan et al., 2002; Lin et al., 2002; Pua et al., 2005; Zhou, 2002; He et al., 2010).

The current study also showed that at the upper WC quartile, the adiponectin was significantly decreased (P = 0.017), and TC, TG, insulin, FBG and HOMA-IR were significantly increased (P < 0.0001 for all comparisons). On the other hand at the upper BMI quartile, the TC, TG, HDL-c, LDL-c, insulin, FBG, and HOMA were significantly increased. Therefore, neither the WC nor the BMI alone could predict all the possible risk factors. These current findings agree with and support the previous studies that showed that there is non-conclusive evidence concerning the main anthropometric predictor of the different risk factors. This may be caused by the confounding factors such as age, sex, race and co-morbid diseases, besides differences in the sample size. Despite the small sample size in our study (n = 127), they were all young and apparently healthy females. Pataky et al. (2009) showed that abdominal fat accumulation causes enlarged WC which induced a less favorable cardio-metabolic profile, even in normal body weight subjects with WC within the normal range. Wang et al. (2009) suggested that BMI and WC are more useful than WHR for predicting two or more non-adipose components of metabolic syndrome. Baral et al. (2006) showed direct association of between BMI and dyslipidemia in hypertensive patients of the Eastern Nepal. Molist-Brunet et al. (2006) claimed that in clinical practice the BMI and the diameter of the waist are very good predictors of IR, whilst the WHR and skin folds do not provide any information of any value.

In the current study, WC was the main predictor of circulating adiponectin level with lower levels as the WC increases. This finding is in agreement with previous studies which showed that visceral obesity (reflected by an increase in WC), contributes to the hypoadiponectinemia, which is a well recognized risk factor for metabolic and CV disease (Karastergiou et al., 2009). A case-control study performed in Japan, demonstrated subjects with hypoadiponectinemia (less than 4 mg/ml) were at increased risk of multiple metabolic risk factors, which indicates that hypoadiponectinemia is a key factor in the metabolic syndrome (Kumada et al., 2003). On the other hand, a prospective study confirmed that high adiponectin concentrations are associated with reduced risk of acute myocardial infarction in men (Pischon et al., 2004). The current study results are partially in accordance with previous studies. Nakamura et al. (1994) found that non-obese men with marked visceral fat accumulation had higher levels of plasma lipids, insulin and glucose when compared to the control group. Other investigators found that greater visceral fat (estimated by measuring WC) is related inversely to plasma adiponectin (Bacha et al., 2004; Cote et al., 2005; Kwon et al., 2005). In other studies, the decreased adiponectin was found to be significantly associated with increased serum lipids, and IR (Cnop et al., 2003; Baratta et al., 2004; Meilleur et al., 2010), while increased adiponectin was found to be related to a desirable blood lipid profile (Tschritter et al., 2003; Baratta et al., 2004). The mechanism by which plasma levels of adiponectin are reduced with increased WC may be explained by the increased cytokine secretion from accumulated visceral fat, which inhibits adiponectin promoter activity (Halleux et al., 2001, Maeda et al., 2001).

The reduced levels of adiponectin removes its antagonizing effect on hepatic lipase, and decreases HDL-C (Schneider et al., 2005). Hepatic lipase hydrolyzes triglyceride and phospholipids in HDL particles which is an important factor to determine the plasma level of HDL-C (Tschritter et al., 2003). The increased leptin level with increasing body adiposity reported in the current study is in agreement with previous studies (Garaulet et al., 2000; Monti et al., 2006; Bahathiq, 2010) suggesting resistance to its effect. Furthermore Previous studies indicate that leptin is directly associated with insulin resistance (Donahue et al., 1999; Liuzzi et al., 1999; Huang et al., 2004) this was not the case in the present study.

Conclusions

Normal subjects who have large WC in addition to high BMI are at high risk of developing hypoadiponectemia, hyperlipidemia and IR. Therefore, the reduction of visceral fat might be, therefore, an essential preventive measure for serious risk factors and their consequences. The estimation of key adipocytokines such as adiponectin might be considered as a marker for optimum visceral fat.

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