

Prevalence of hyperlipidemia and associated risk factors among healthy young Saudi females: relationship with waist Circumference and body Mass Index

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Abstract

Background and Objectives: Hyperlipidemia, insulin resistance and hypo adiponectinemia are well recognized cardiovascular risk factors especially among obese subjects. The aim of the present study was to determine the prevalence of hyperlipidemia and associated risk factors among young Saudi females and their relationship with waist circumference (WC) and body mass index (BMI).

Study Design: Cross-sectional study.

Subjects and Methods: 127 randomly recruited healthy young Saudi females were studied. Anthropometric (WC and BMI) and biochemical parameters (adiponectin, leptin, lipid profile, fasting blood glucose, and insulin), were measured. Prevalence of different risk factors was assessed in all subjects and in those with normal BMI (<25kg/m²). Anthropometric predictors of different risk factors were estimated.

Results: One third of the study subjects were overweight (28%) and 20% were obese. Hyperlipidemia, especially low high density lipoprotein cholesterol (HDL-C), was highly prevalent in the whole population. This had persisted when subjects with BMI ≥ 25 kg/m² and WC ≥ 80 cm were excluded. Deciles of WC, adiponectin, leptin and the homeostasis model assessment index-insulin resistance (HOMA-IR) were calculated in subjects with normal BMI. Prevalence of hyperlipidemia was also high in subjects with WC < 71 cm (upper decile). Regression analysis showed that WC was a negative predictor of adiponectin and a positive one of insulin and HOMA-IR, while BMI was a positive predictor of fasting glucose and lipid profile. Neither WC nor BMI were predictors of HDL-C.

Conclusion: Hyperlipidemia was observed at normal WC and BMI according to international definitions. Low HDL-C was highly prevalent and did not correlate with WC or BMI. Other determinants of HDL-C in Saudi women should be considered. Locally derived cutoff points for different measures of adiposity must be established to identify high risk subjects that may be missed when international criteria are used.

Keywords: Hyperlipidemia; Measures of Adiposity; Adipokines; Saudi Female

Introduction

The prevalence of obesity has markedly increased in most countries of the world [1]. Using World Health Organization (WHO) criteria, the prevalence of overweight in the Saudi female population is 28% and that of obesity is 24%, constituting a major health problem [2]. The concerns about the increased risk of cardiovascular disease (CVD) and other co-morbidities associated with increased weight gain are well recognized [3]. However, in some populations adverse health effects of obesity occur at a body mass index (BMI) that is considered normal by conventional definitions, and redefining overweight and obesity in Asians had been recommended based on mortality and morbidity risks [4]. Therefore, the use of WHO to define overweight (BMI ≥ 25.0 kg/m²) and obesity (BMI ≥ 30.0 kg/m²) may not be appropriate to all populations and establishment of ethnic-specific cut-off points had been urged [5].

However, while BMI correlates well with body fat, it is the distribution of body fat that is the main determinant of the co-morbidities of obesity [6]. In particular, visceral fat, estimated clinically by an increased waist circumference (WC) [7], is the form of obesity mostly associated with the metabolic abnormalities that cluster in the metabolic syndrome [8].

Adipose tissue is an active endocrine organ secreting several adipokines, including leptin and adiponectin that are involved in glucose and lipid metabolism [9]. Leptin plays an important role in

the control of body adipose stores as well as blood glucose levels, [10] while adiponectin has insulin-sensitizing, anti-atherogenic, and anti-inflammatory properties [11].

In obese subjects, high levels of leptin reflect resistance to its weight-reducing effects but its stimulatory effects on the sympathetic nervous system are preserved. This selective leptin resistance contributes to its role in obesity related CVD [12]. On the other hand, circulating plasma concentration of adiponectin is decreased with visceral fat accumulation, and hypo adiponectinemia is now recognized as a strong risk factor for metabolic and CVD in obese subjects [13]. Obesity is associated with adipose tissue inflammation with macrophage infiltration, and the production of a number of pro-inflammatory cytokines, [14] which inhibit adiponectin synthesis and release [15,16].

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Data from a large population-based study on 197,681 Saudi men and women reported a significant increased risk of diabetes and hypertension at BMI values that are lower than that used by the WHO to define obesity [17]. However, in this study no measurements were done to assess the potential risk factors such as abnormal lipid profile, low adiponectin level or insulin resistance. The aim of the present study was to determine the prevalence of hyperlipidemia and associated risk factors among healthy young Saudi females and their relationship with WC and BMI, and to find out if abnormal levels are present at cutoff points that are lower than those derived from studies on Western and North American populations.

Materials and Methods

Study subjects

This cross-sectional study was conducted in the college of Medicine At King Abdulaziz University (KAU) in Jeddah, Saudi Arabia, during the year 2009. The study lasted for 9 months. Medical students were invited to participate in this study through advertisements and fliers around the college on a voluntary basis. A total of 127 female medical students were randomly recruited. Informed consent was obtained from all subjects and the study was approved by KAU hospital Ethics committee. Subjects with impaired glucose tolerance or diabetes, inflammatory, hepatic or renal diseases, 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, and medication use.

Anthropometric measurements

Body weight, height, WC, and hip circumference (HC) were recorded by the same observer. Subjects were weighed on electrical scale (Seca Alpha, GmbH & Co., Igm, France; range 0.1–150 kg, precision 100 g) to the nearest half kilogram while wearing light clothes and bare footed. Height was measured using a stadiometer (Pflüger, Carlstadt, NJ, USA; range 70–205 cm, precision 1 mm) to the nearest half centimeter. Using a tape measure, WC (midway between the lower rib margin and the iliac crest at the end of normal expiration) and HC (the maximal circumference over the buttocks) were measured to the nearest 0.1 cm. BMI was calculated as weight in kg divided by height in meters squared. Waist to hip ratio (WHR) was also calculated as WC divided by HC. The clinical guidelines on the identification, evaluation and treatment of overweight and obesity in adults [18] were used to define overweight (BMI, 25–29.9 kg/m²) and obesity (BMI ≥30 kg/m²). Central obesity was defined as WC ≥ 80cm [19].

Biochemical measurements

Blood samples were obtained from all subjects after a 12 hour fast. They were centrifuged at 3000g for 10 minutes. Plasma was obtained for the analysis of the different 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%. Definition of abnormal lipid profile was according to the latest National Cholesterol Education Program (NCEP) clinical guidelines for blood lipids (Adult Treatment Panel III; ATP III): serum total cholesterol (TC), ≥5.2 mmol/L, triglycerides (TG) ≥1.7 mmol/L, high density lipoproteins cholesterol (HDL-C) <1.29 mmol/L and low density lipoproteins cholesterol (LDL-C) ≥3.36 mmol/L [20]. In accordance with the latest American Diabetes Association guidelines, FBG levels < 5.6 mmol/L were considered to be normal [21].

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-insulin resistance (HOMA-IR), which is based on fasting insulin and glucose measured in a single blood sample, has been used frequently to predict insulin resistance [22]. The HOMA-IR yields an equation where insulin resistance = [fasting insulin (μU/ml) x fasting glucose (mmol/L)]/ 22.5. Abnormal HOMA-IR was defined as that above the upper decile when estimated for subjects with normal BMI (<25 kg/m²).

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. Low adiponectin, was defined as that below the lower decile when estimated for subjects with normal BMI (<25 kg/m²) and high leptin was defined as that above the upper decile when estimated for subjects with normal BMI (<25 kg/m²).

Statistical analysis

Data are presented as means and standard deviation (SD) for normally distributed variables and as median and inter-quartile ranges (IQR) for non-normally distributed variables. Categorical variables are expressed as frequency and percentage. Dichotomous variables were created for different measured parameters. Data was examined for normal distribution by Kolmogorov-Smirnov statistic. Chi-square test of independence was used to examine association between different categorical variables. Stepwise multiple regression analysis was used to detect the independent predictive measure of obesity (BMI or WC) for each estimated parameter (adipokines, lipid profile, FBG, HOMA-IR and insulin level). Significance levels are shown for all comparisons and relationships where P<0.05. The statistical analysis was performed using the Statistical Package for Social Science (SPSS version 12, Chicago, IL, USA).

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 (28%) were overweight and 25 subjects (20%) were obese. Only one subject (0.8%) had a WHR ≥ 0.85, and 26 (21%) had a WC of ≥ 80cm.

Table 2 shows the prevalence of different estimated risk factor in the whole studied group, in those with normal WC (≤80 cm) and in lean subjects (BMI<25kg/m²). Hyperlipidemia was remarkable in the whole study group. According to the ATP III recommended limits for lipids in adult fasting blood, 69 individuals (54%) had LDL-C ≥ 3.36 mmol/L and 61 individuals (48%) had HDL-C<1.29 mmol/L. However, when subjects with WC ≥ 80 cm or BMI ≥25 kg/m² were excluded, abnormal lipid profile was still seen especially for the HDL-C and LDL-C (see Table 2).

Variable	All subjects
Anthropometric	
Age (year)	20.4 (1.6)
Weight (kg)	65.7 (18.3)
Height (cm)	158.5 (6.5)
BMI (kg/m ²)	26.0 (6.8)
WC (cm)	72.0 (12.5)
HC (cm)	101.6 (12.7)
WHR	0.71 (0.05)
Biochemical	
Adiponectin (ng/ml)	9.5 (8.3-10.9)
Leptin (ng/ml)	14.8 (6.2)
Insulin (μIU/ml)	9.20 (5.48-12.40)
FBG (mmol/L)	4.95 (0.64)
HOMA-IR	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)

Continuous variables are presented as mean (standard deviation) for normally distributed variables and as median (inter-quartile ranges) for non-normally distributed variables. BMI= body mass index, WC= waist circumference, HC= hip circumference, WHR= waist to hip ratio, FBG= fasting blood glucose, HOMA-IR= homeostasis model assessment index-insulin resistance, TC= total cholesterol, TG= triglycerides, HDL-C= high density lipoprotein cholesterol, LDL-C= low density lipoprotein cholesterol.

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

Variable	All subjects N(%)	WC ≤ 80 cm N(%)	BMI <25 kg/m ² N(%)
Adiponectin <7.5 ng/ml	12 (9%)	9 (9%)	6 (9%)
Leptin > 20.2 ng/ml	14 (11%)	7 (7%)	6 (9%)
FBG ≥ 5.6mmol/L	17 (14%)	8 (8%)	2 (3%)
HOMA-IR > 2.85	38 (32%)	19 (20%)	6 (9%)
TC ≥ 5.2 mmol/L	53 (42%)	29 (29%)	11 (17%)
TG ≥ 1.7 mmol/L	33 (26%)	14 (14%)	5 (8%)
HDL-C <1.29 mmol/L	61 (48%)	51 (51%)	34 (51%)
LDL-C ≥ 3.36 mmol/L	69 (54%)	49 (49%)	31 (46%)
BMI			
Overweight (25-29.9kg/m ²)	35 (28%)	30 (30%)	-
Obese (≥30kg/m ²)	25 (20%)	4 (4%)	-

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

Table 2: Prevalence of abnormal measured variables in the whole studied group, in those with no central obesity (WC ≤80 cm) n=101 and in lean subjects (BMI <25 kg/m²) n=67.

Deciles of WC were calculated for subjects with normal BMI (<25kg/m²). The upper decile of WC was used as a cutoff value and comparisons of the different estimated risk factors was made between those with WC < 71cm (n=62) and WC ≥ 71 cm (n=65). Even in the group with WC < 71cm, unfavorable lipid profile was prevalent especially for the HDL-C and LDL-C (Table 3). Prevalence of impaired FBG (p<0.01), insulin resistance (p<0.0001), hypercholesteremia (p<0.0001), and hypertriglyceridemia (p<0.0001) was significantly higher in the group with WC> 71 cm.

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

Multiple stepwise regression analysis was performed to find out the explanatory anthropometric variable (predictor) for the adipocytokines, insulin, FBG, HOMA-IR and lipid profile. Different measures of obesity (BMI and WC) were entered into the regression model (independent variables) (Table 4).

WC was the main predictor for adiponectin concentration, insulin concentration, and HOMA-IR, while BMI was the main predictor for FBG, TC, TG and LDL. All anthropometric measures of obesity were removed from the model when leptin and HDL-C were the dependent variables.

Discussion

The main finding in the current study was the high prevalence of unfavorable lipid profiles especially the low HDL-C and high LDL-C, at BMI and WC values that are considered normal by international definitions. Research in East Asian countries consistently demonstrated a need for a lower BMI and WC cutoff points for estimating risk of metabolic abnormalities [23-27]. In Saudi Arabia, there was one study that attempted to establish BMI cutoff points that predict diabetes and hypertension in the Saudi population [17]. They concluded that BMI may be of limited use in the Saudi population because of the shorter

Variable	WC <71 (n = 62)	WC ≥71 (n = 65)	P value
Adiponectin <7.5 ng/ml	5(8%)	7(11%)	0.602
Leptin > 20.2 ng/ml	5(8%)	9(14%)	0.298
FBG ≥ 5.6mmol/L	3(5%)	14(23%)	0.004
HOMA-IR > 2.85	5(8%)	33(56%)	<0.0001
TC ≥ 5.2 mmol/L	9(15%)	44(68%)	<0.0001
TG ≥ 1.7 mmol/L	3(5%)	30(46%)	<0.0001
HDL-C <1.29 mmol/L	33(53%)	28(43%)	0.253
LDL-C ≥ 3.36 mmol/L	29(47%)	40(62%)	0.95

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

Table 3: Prevalence of the different risk factors when women were stratified into two groups according to the upper decile of WC (71cm) in subjects with normal BMI (<25kg/m²).

Dependant Variable	WC				BMI			
	R ²	β	SE	P	R ²	β	SE	P
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	0.002

FBG= fasting blood glucose, HOMA-IR= homeostatic model assessment-insulin resistance, TC= total cholesterol, TG= triglycerides, HDL-C= high density lipoprotein cholesterol, LDL-C= low density lipoprotein cholesterol.

Table 4: Multiple regression models with adipocytokines, insulin, FBG, HOMA-IR and lipid profile as dependent variables and measures of obesity as independent variables among the study population (n=127).

stature of the Saudi women and suggested the use of other measures of obesity such as WC, WHR, or a combination of several measures.

The high prevalence of hyperlipidemia [28] and low HDL-C [29] had been previously reported in the Saudi population. These studies included older people who were not completely healthy. In a large population-based study conducted in Riyadh, the prevalence of low HDL-C was reported as 85% among the age group between 18-29 years (which is the age group that is closest to that in our study) [30]. The cause of this high prevalence is not clear but different determinants of HDL-C had been reported. Higher carbohydrate diet was the only dietary risk factor found for abnormal HDL-C in a large cross-sectional study conducted in Brazil (n=997, mean age 52±10, 67% of which were females) [31]. Higher carbohydrate intake in the Saudi youth had been reported previously [32] and could possibly contribute to the low levels of HDL-C in our population. WC was another determinant of HDL-C in the same Brazilian study; however, this was not the case in our study. The increased prevalence of low HDL at lower BMI and WC, although not significant, was notable and indicates that factors other than adiposity measures affect the HDL-C level at least in our population. This is also evident when both BMI and WC were removed from the regression model when HDL-C was the dependant factor. Other factors (e.g. physical activity level, genetic) not accounted for in the current study must be influencing levels of HDL-C. Therefore, this finding needs more exploration in future studies addressing different determinants of HDL in the Saudi population.

Hyperlipidemia and impaired FBG were more prevalent in the group with WC ≤ 80 cm when compared to that of BMI <25 kg/m², this is probably because 30% of these subjects were overweight and 4% were obese. When deciles of WC were calculated for subjects with normal BMI (<25 kg/m²), the upper decile for WC was 71 cm. This was taken as a cutoff point, and subjects with WC <71 cm included only one overweight and one obese and corresponded to an upper BMI decile of 24 kg/m². This may suggest that 80 cm is quite a high cutoff point in our women, but given the small sample size in our study, this cannot be generalized to the whole Saudi women. However, establishing cutoff values was not one of the objectives of this study and large longitudinal population-based studies should be conducted to assess the different anthropometric measures of obesity cutoff values that are appropriate in predicting cardiovascular risk in our population.

The prevalence of impaired FBG, high TC and high TG was significantly higher in the group with WC ≥71cm than those with WC <71 cm. Higher level of leptin and lower level of adiponectin were found among subjects with higher WC (≥71 cm) which is consistent with the reported association between low adiponectin and high leptin with the risk of metabolic syndrome and CVD [33].

Multiple regression analysis showed that WC and not BMI was a negative predictor of adiponectin which is in agreement of the documented association between visceral obesity (estimated by increased WC) and low adiponectin level [13]. Neither WC nor BMI were found to be independent predictors of leptin which points to other unestimated determinants of leptin level. One of these was found to be sleep duration and quality in adolescent Saudi girls [34] which were not estimated in our study.

The finding that WC was a positive predictor of insulin level and HOMA-IR, while BMI was a positive predictor of FBG, TC, TG and LDL, favors the recommendation of considering more than

one measure of adiposity to predict different cardiovascular and metabolic risk factors [17,35]. Because of the uncertainty regarding which measure of adiposity best predict CVD, [36] future studies utilizing other measures of adiposity such as waist to height ratio, body adiposity index, visceral adiposity index are recommended to find out the optimal measure/measures among the Saudi population.

Study limitations

This study has certain limitations including the cross sectional design, and hence the causative nature of the association between the anthropometric measures and the different risk factors cannot be established. Moreover, the small sample size and the recruitment of young, well educated females may limit the generalizability of our findings. Therefore, larger, longitudinal studies including subjects of both sexes and from all age groups should be conducted.

Conclusions

Young apparently healthy Saudi women with WC and BMI that are considered normal by conventional definitions showed undesirable lipid profile mainly low HDL-C and high LDL-C. These women are probably at higher risk of developing cardiovascular and metabolic diseases. Low levels of HDL-C were not associated with measures of adiposity and studies addressing determinants of HDL-C in the Saudi population are needed. The results of the present study also suggest the need to establish local WC and BMI cutoff values appropriate to identify subjects with abnormal lipid profile and other risk factors that may otherwise be missed if Western or North American derived values are used.

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