Cardiovascular risk factors in obese women and their first-degree relatives

Obez kadınlar ve birinci derecedeki yakınlarında kardiyovasküler risk faktörleri

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ABSTRACT

Objective: Evidence for a connection between obesity and cardiovascular disease is derived from epidemiological studies. The aim of this study was to evaluate the cardiovascular risk factors in obese women and their first-degree relatives.

Methods: Fifty-five obese women and their 154 first-degree relatives (daughter, son, sister, brother), 60 non-obese women and their 100 first-degree relatives were enrolled in this cross-sectional controlled study. Blood pressure, heart rate, body mass index (BMI), waist-to-hip ratio (WHpR), waist circumference (WC) and lipid levels were measured in all participants. Serum concentrations of insulin were measured by chemiluminescence method, plasma levels of high sensitive C-reactive protein (hs CRP) by immunoturbimetric assay and fibrinogen by coagulation method. Measurement of insulin resistance was calculated using homeostasis model assessment (HOMA). Statistical analysis was preformed using Chi-square, Student's t and Mann–Whitney U tests. The relationship between obesity indices and cardiovascular risk factors were studied using linear regression analysis.

Results: Mean values of BMI in female and male relatives were found as 25.10±2.5 kg/m^2 and 23.50±4.98 kg/m^2, respectively. In relatives, the frequencies of obesity, overweight and normal weight were found to be 8.9%, 25.8% and 65.1%, respectively. Central obesity was found higher in males than in females in the first-degree relatives, using WC (28.5% vs. 14.3%, p=0.001) or WHpR (30.9% vs. 24.5%, p=0.002). Elevated blood pressure (≥ 140/90 mmHg) was recorded in 23.6% of obese women and in 8.4% of their relatives. Mean HOMA-IR levels of obese women and their relatives were found as 3.26±0.7 and 2.07±1.1, respectively. Mean hs CRP levels of obese women and their relatives were 0.98±0.08 mg/dl and 0.23±0.03 mg/dl, respectively (p=0.002). Mean fibrinogen levels of obese women and their relatives were 443.21±45.9 mg/dl and 321.10±38.23 mg/dl, respectively.

Conclusion: In obese women and their relatives, body mass index and waist circumferences are related with blood pressure, total cholesterol, fibrinogen and insulin resistance. If there are obese women in family, first-degree relatives have 1.8 fold increased obesity frequency. Body mass index increases together with cardiovascular risk factors. In early term, prevention of obesity may decrease developing of cardiovascular risk. *(Anadolu Kardiyol Derg 2007; 7: 371-7)*

Key words: Obesity, cardiovascular risk, first-degree relative

ÖZET

Amaç: Çeşitli epidemiyolojik çalışmalarda, obezite ve kardiyovasküler hastalıklar arasındaki ilişkiye ait çok sayıda kanıt saptanmıştır. Beden kitle indeksi >28 kg/m^2'den itibaren kardiyovasküler sistem hastalıklarında belirginleşme vardır. Çalışmanın amacı, obez kadınlarda ve birinci dereceden yakınlarında kardiyovasküler risk faktörlerinin belirlenmesidir.

Yöntemler: Bu kros-seksiyonel kontrollü çalışmaya 55 obez kadın hasta ve bunların 154 birinci derecede yakını (kızı, oğlu, kız kardeşi, erkek kardeşi), 60 obez olmayan kadın ve bunların 100 birinci derece yakını alındı. Tüm hastalarda ve yakınlarında kan basıncı, kalp hızı, vücut kitle oranı, bel-kalça oranı, bel çevresi ve lipit düzeyleri ölçüldü. Serum insülin konsantrasyonları kemiluminesans yöntemi ile, yüksek duyarlılıkta C –reaktif protein (hsCRP) – immünoturbimetrik yöntemi ile ve fibrinojen koagülasyon yöntemi ile ölçüldü. İnsülin direci ise "homeostasis model assessment" (HOMA) modeli kullanarak belirlendi.İstatistiksel analiz Ki-kare, Student t test ve Mann–Whitney U test kullanılarak yapıldı. Obezite göstergeleri ve kardiyovasküler risk faktörleri arasında ilişki lineer regresyon analiz ile incelendi.

Bulgular: Obez kadınların birinci derecedeki yakınlarında obezite prevalansı %8.9 oranında saptandı. Birinci derecedeki yakınları da; normal kilolu %65.1, hafif kilolu %25.8 oranında bulundu. Erkek yakınlarında, bel çevresi (28.5% vs. 14.3%, p=0.001) ve bel-kalça oranı (30.9%, 24.5%, p=0.002) kadın yakınlardan fazla bulundu. Kan basıncı yüksekliği (≥140/90 mmHg); obez kadınlarda %23.6 bulunurken, birinci derece yakınlarda %8.4 oranında saptandı. Ortalama HOMA düzeyi; obez kadınlarda 3.26±0.7 ve yakınlarında 2.07±1.1 bulundu. Ortalama hsCRP; obez kadınlarda 0.98±0.08 mg/dl ve yakınlarında 0.23±0.03 mg/dl düzeylerinde saptandı (p=0.002). Fibrinojen düzeyi, obez kadınlarda 443.21±45.9 mg/dl saptanırken, yakınlarında 321.10±38.23 mg/dl bulundu (p=0.021).

Sonuç: Obez kadınlarda ve yakınlarında, beden kitle indeksi ve bel çevresi; kan basıncı, total-kolesterol, fibrinojen ve insülin direnci ile yakın ilişkilidir. Ailede obez kadınlar var ise; birinci derece yakınlar 1.8 kat daha fazla yüksek obezite riski taşımaktadır. Beden kitle indeksi artışı, kardiyovasküler risk faktörlerinin artışı ile birliktedir. Erken dönemde obezitenin önlenmesi kardiyovasküler risk gelişimini azaltabilir. *(Anadolu Kardiyol Derg 2007; 7: 371-7)*

Anahtar kelimeler: Obezite, kardiyovasküler risk, birinci derecede yakın

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Introduction

Evidence for a connection between obesity and cardiovascular disease is derived from epidemiological studies (1-9). Large-scale investigations such as the second National Health and Nutrition Examination Survey in the U.S. have identified increasing risk of the development of cardiovascular disorders (CVD), including hypertension, dyslipidemia, glucose intolerance, and insulin resistance, in overweight subjects with body mass index (BMI) >28 kg/m^2 (10, 15). Increased BMI and waist circumference were associated with cardiovascular risk (15-20). In a Turkish adult population study, the prevalence of obesity was 23.5% (29.4% in women and 16.5% in men). The combined prevalence of both overweight and obesity was 60.3%. The prevalence of abdominal obesity was 29.4%: (38.9% among women and 18.1% among men) (11). Recently, some studies have indicated that the presence of increasing trends in overweight and obesity among children and adolescence (12-14). However, there are few studies related to obesity frequency and cardiovascular risk factors in relatives of obese.

The aim of this study was to evaluate the rate of overweight, obesity and other CVD risk factors, namely high blood pressure and dyslipidemia, in obese women and their first-degree relatives. Cardiovascular risk factors for obese women and first-degree relatives were examined and related to three different obesity indices (body mass index, waist circumference, waist-to-hip ratio).

Methods

Fifty-five obese women, (Group 1) and 154 first-degree relatives (brother (18), sister (62), son (24), daughter (50)) (Group 2) of obese women were enrolled in this cross-sectional study. In first-degree relatives, there were 112 female (Group 2a) and 42 male (Group 2b). Sixty non-obese women with (mean age 57.4±8.9 years, BMI - 23.7±2.3 kg/m^2) (Group 3) and their 100 first-degree relatives (Group 4) (60 female (Group 4a), 40 male (Group 4b)) were chosen as control groups. Obese and non-obese women were selected from the Obese Patient Society and outpatients of Department of Endocrinology and Metabolism at Ege University in İzmir City.

The study was conducted from March 2004 through April 2005. Obese women with any underlying disease (cardiovascular, self-reported infectious or rheumatic) or taking medication likely to effect the results (such as; aspirin, estrogens, statins) or pregnant were not eligible for this study. Exclusion criteria for first-degree relatives were: presence of type 2 diabetes or first-degree relatives of type 2 diabetes, presence of thyroid, liver or renal disease and presence of cardiovascular disease.

The study protocol was approved by the Ethics Committee of the Ege University. All subjects gave written informed consent before entering the study.

A brief clinical history, demographic, anthropometric and clinical profiles were recorded. The anthropometric measurements were obtained according to the methods described earlier (1, 15).

Blood pressure, heart rate, weight, height, BMI, and waist-to-hip ratio (WHpR) were measured according to standard methods. For waist circumference (WC), cut-off points of ≥102 cm in men and ≥88 cm in women were used. A WHpR ≥0.9 in men and ≥0.8 in women was considered to represent central obesity (16). A two point bioelectrical impedance apparatus (Tanita TBF 300, TANITA Corp.) validated for adults, was used to measure the percentage of body fat (%BF).

Participants were classified as having elevated blood pressure if they reported taking anti-hypertensive medication or had a systolic blood pressure (SBP) ≥140 mmHg or diastolic blood pressure (DBP) ≥90mmHg. High-normal blood pressure was defined as blood pressure ≥130/85 – <140/90 mmHg (16).

Habitual alcohol consumption for each subject was ascertained based on the following two questions: 'Do you drink alcohol at least once a month? Yes/No'. 'If Yes, how many units do you have average per week?' One unit of alcohol is equivalent to one glass of wine. Alcohol consumption was categorized into 4 groups of monthly alcohol intake for men and women: for men, none (<1), 1–7, 8–21 and 22 units per month. For women these were under 1 unit, 1-7 units, 7-14 units and over 14 units.

Smoking was evaluated based on the following two questions. 'Do you smoke? Yes/No.' If Yes, smokers were classified as those who stated smoking more than one cigarette per day. Smoking status was classified as follows: current smoker was defined as current use, at the time of the survey, of cigarettes. Ever smoker was defined by any history of ever using cigarettes on a daily basis. Ex-smokers were those who smoked cigarettes regularly in the past but did not currently. Non-smoker had never smoked cigarettes regularly. 'Cigarettes per day' was defined as the number of cigarettes currently smoked per day. 'Pack-years' a measure of cumulative smoking exposure, was defined as the product of the number of years of smoking and the number of packs of cigarettes smoked per day (21).

Blood samples were drawn for biochemical screening tests. Serum concentrations of glucose, triglyceride (TG), total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C) and high density lipoprotein cholesterol (HDL-C) were determined by enzymatic procedures. Serum concentration of insulin was measured by chemiluminescence, plasma levels of high sensitive C-reactive protein (hs CRP) by immunoturbimetric assay and fibrinogen by coagulation method. Coefficients of variation for measurements were 4.3% and 12.4% for TC and HDL-C. Dyslipidemia was defined as TC ≥200 mg/dl, TG ≥150 mg/dl, LDL-C ≥130 mg/dl, and HDL-C <40 mg/dl for men, 50 mg/dl for women (24). Insulin sensitivity was estimated with homeostasis model assessment (HOMA-IR). HOMA-IR=(fasting plasma insulin [μU/ml] x fasting plasma glucose [mmol/l])/22.50 (22).

Statistical analysis

All analyses were performed using SPSS for Windows software (Chicago, Il, USA). The significance of univariate differences was assessed by 2 and Student's t tests. Two groups comparisons were performed with Mann–Whitney U test. The relationship between obesity and other cardiovascular risk factor variables were examined with univariate analyses using obesity indices as categorical variables. Linear regression techniques were applied to assess the extent of dependence cardiovascular risk factors on the obesity indices. A level of $p < 0.05$ was used to indicate statistical significance in all analyses.

Results

Among the subjects who applied to our obesity outpatient clinic, 55 women with age ranged between 30- 65 (mean age 53.3±4.7) years had BMI of 34.1±2.11 kg/m^2 (Group 1) (Table 1). Their 154 first-degree relatives (mean age 37.22±6.20 years) were comprised of brothers (18), sisters (62), sons (24), and daughters (50) (Group 2). There were 112 female (Group 2a) and 42 male (Group 2b) among first - degree relatives of obese women.

In relatives, the frequencies of obesity and normal weight and overweight levels were found as 8.9%, 65.1%, and 25.8%, respectively. The obesity rate was 10.0% in female subgroup of relatives (Group 2a), and 7.2% in male subgroup of relatives (Group 2b).

Comparison of demographic characteristics between obese and non-obese women (Table 1) showed that mean levels of SBP and DBP of obese women were significantly higher than in non-obese women (p=0.02 and p=0.004, respectively). Similarly, the BMI and WHpR were significantly higher in Group 1 women than in Group 3 women (p=0.001 and p=0.01, respectively).

Table 1. Demographic characteristics of obese and non-obese women

Parameters	Group 1 (n=55)	Group 3 (n=60)	p*
Age, years	53.3±4.7	55.45±8.90	0.02
Body mass index, kg/m^2	34.1±2.11	23.71±2.34	0.001
Weight, kg	99.1±12.11	60.74±12.11	0.001
Systolic blood pressure, mmHg	133.12±19.1	127.12±17.1	0.02
Diastolic blood pressure, mmHg	65.5±16.40	51.50±16.40	0.004
Waist, cm	102.2±12.4	80.45±12.90	0.004
Hip, cm	108.3±16.50	103.71±2.34	0.03
WHpR	0.82±0.390	0.76±0.490	0.01
Percent body fat	37.8±11.90	25.02±4.10	0.02
Number of cigarettes per day	3.0±0.01	3.5±0.08	0.85
Number of cigarrette pack-years	0.4±0.01	0.6±0.00	0.70

Data are expressed as mean±SD, * - Mann–Whitney U test
Group 1- obese women, Group 3 - non-obese women

Comparison of demographic characteristics between first-degree relatives of obese and non-obese women (Table 2) revealed no significant differences between groups 2 and 4 in terms of blood pressure levels or obesity indices. There was only significant difference in the number of cigarette pack-years, which was markedly higher (p=0.004) in Group 2 than in Group 4.

Central obesity levels were significantly higher in male than in female first-degree relatives of obese women (WC - 28.5% vs. 14.3%, p=0.001 and WHpR - 30.9% vs. 24.5%, p=0.002) (Table 2). Elevated blood pressure (≥140/90 mmHg) was recorded 23.6% in obese women and 8.4% in their relatives. In a group of obese relatives 28.6% of men and 25.6% of women had high blood pressure levels.

Among obese women 30.1% were current smokers, and 29.8% of their relatives were smokers. In obese women, 12.5% of participants described as ex-smokers. Approximately 8.9% of male and 5.1% of female in the first-degree relatives were ex-smokers.

Mean hsCRP and fibrinogen and DBP values were higher among current smokers in obese women. Likewise, mean hsCRP and fibrinogen and HOMA-IR were higher in male first-degree relatives who were current smokers. Alcohol consumption rate was 10% in obese women and 21.4% in their relatives. Male first-degree relatives who consumed >8 units of alcohol per week and female first-degree relatives who consumed >14 units had higher fibrinogen and DBP levels.

Biochemical and hematological parameters of groups are presented in Tables 3 and 4.

The HOMA-IR, fibrinogen and hsCRP levels were significantly higher (p=0.05, p=0.02 and p=0.002, respectively) and HDL-cholesterol levels were lower (p=0.03) in obese women than in non-obese women (Table 3). Similar differences were observed in their first-degree relatives with higher levels of HOMA-IR and fibrinogen (p=0.05, p=0.02) and lower values of HDL-cholesterol (p=0.04) in Group 2 than in Group 4 (Table 4).

Obese women had significantly higher values of HOMA (3.26±0.70 vs 2.07±1.10, p=0.05), triglyceride (145.8±30.4 mg/dl vs 131.9±27.4 mg/dl, p=0004), hs CRP (0.98±0.08 mg/dl vs 0.28±0.03 mg/dl, p=0.0021), fibrinogen (443.2±45.9 mg/dl vs 321.10±38.23 mg/dl, p=0.002) levels and lower values of HDL- C (41.4±9.5 mg/dl vs 52.7±8.7 mg/dl, p=0.04) than their first-degree relatives.

Table 2. Demographic characteristics of first-degree relatives of obese and non-obese women

Parameters	Group 2 (n=154) (Total)	Group 4 (n=100) (Total)	p*	Group 2a (n=112)	Group 2b (n=42)	Group 4a (n=60)	Group 4b (n=40)
Age, years	37.22±6.20	39.01±7.90	0.50	28.24±5.99	29.61±9.89	29.61±9.89	26.60±1.89
Body mass index, kg/m^2	25.1±2.5	24.61±9.89	0.65	26.2±2.5	23.50±4.98	24.50±11.89	24.50±6.89
Weight, kg	74.84±10.30	69.50±11.89	0.20	57.1±7.1	63.50±6.77	65.50±11.89	64.50±9.89
Systolic blood pressure, mmHg	110.12±10.80	108.50±11.89	0.90	108.90±19.13	114.4±11.9	122.0±21.9	118.98±21.00
Diastolic blood pressure, mmHg	53.5±10.3	50.0±21.9	0.23	50.2±13.9	58.4±8.0	57.4±9.9	53.4±9.9
Waist, cm	88.3±7.8	80.4±9.90	0.64	79.1±9.21	98.2±10.1	70.8±12.1	91.7±16.2
Hip, cm	110.0±13.5	105.8±12.1	0.53	95.67±7.30	89.7±14.9	97.8±0.4	86.83±10.40
WHpR	0.76±0.49	0.75±0.40	0.20	0.77±0.30	0.79±0.30	0.79±0.40	0.80±0.40
Percentage of body fat	27.02±4.10	24.02±4.10	0.45	25.02±4.10	24.02±4.10	25.02±4.10	24.02±4.10
Number of cigarettes per day	2.91±0.08	3.01±0.01	0.63	2.01±0.08	3.77±0.03	2.58±0.04	2.90±0.06
Number of cigarette pack-years	0.30±0.00	0.1±0.00	0.004	0.13±0.0	0.6±0.01	0.40±0.04	0.200±0.007

Data are expressed as mean±SD, * - Mann–Whitney U test
Group 2- first- degree relatives of obese women, Group 2a- female first-degree relatives of obese women, Group 2b-male first- degree relatives of obese women, Group 4- first-degree relatives of non-obese women, Group 4a- female first-degree relatives of non-obese women, Group 4b- male first- degree relatives of non-obese women

Table 3. Blood glucose, insulin, HOMA-IR and lipoproteins in obese and non-obese women

Parameters	Group 1 (n=55)	Group 3 (n=60)	p*
Fasting glucose, mg/dl	93.6±9.95	89.7±9.86	0.80
Postprandial glucose, mg/dl	115.7±16.9	111.7±16.9	0.70
Fasting insulin, µU/ml	12.44±4.20	9.33±3.20	0.03
HOMA-IR	3.26±0.70	2.07±1.10	0.05
Total-Cholesterol, mg/dl	202.0±31.7	181.0±11.7	0.06
LDL-Cholesterol, mg/dl	132.6±23.2	131.7±27.9	0.80
HDL-Cholesterol, mg/dl	41.45±9.5	55.7±8.7	0.03
Triglyceride, mg/dl	145.80±30.4	148.90±27.4	0.90
Fibrinogen, mg/dl	443.21±45.90	311.0±32.5	0.021
hs CRP, mg/dl	0.98±0.08	0.29±0.11	0.002

Data are expressed as mean±SD, * - Mann–Whitney U test
HDL- high-density lipoprotein, HOMA-IR- homeostasis model assessment-insulin resistance, hs CRP- high sensitive C-reactive protein, LDL- low-density lipoprotein

A significantly higher percentage of males than females had high triglyceride, LDL- C, or low HDL- C in first-degree relatives of obese women.

The linear regression analyses showed that BMI and WC were associated with higher SBP, DBP, triglycerides, fibrinogen levels and HOMA in obese women. In relatives of obese women BMI and WC were associated with higher diastolic blood pressure, LDL- C, fibrinogen, and HOMA-IR (Table 5).

Using the odds ratios (OR) for the prediction of the presence of cardiovascular risk factors (Table 6), obese women had 2.81 times higher risk for high DBP, 2.62 – 2.76 times higher risk for dyslipidemia, 3.57 and 3.71 times higher risk for elevated fibrinogen and hsCRP, and 2.96 times higher risk for low insulin sensitivity.

Increased hs CRP (OR 2.99) and fibrinogen (OR 4.01) levels were associated with BMI and WC in first-degree relatives of obese women. Female first-degree relatives of obese women had higher risk for high SBP, (OR 2.91), LDL-C (OR 2.55), fibrinogen (OR 2.83), and hs CRP (OR 2.79) levels, and low insulin sensitivity (OR 3.34). Male relatives with high WC had the highest risk for

Table 4. Blood glucose, insulin, HOMA-IR and lipoproteins in first-degree relatives of obese and non-obese women

Parameters	Group 2 (n=154) (Total)	Group 4 (n=100) (Total)	p*	Group 2a (n=112)	Group 2b (n=42)	Group 4a (n=60)	Group 4b (n=40)
Fasting glucose, mg/dl	85.70±9.86	80.70±14.67	0.90	82.4±13.5	92.4±11.5	82.4±11.5	91.4±13.5
Postprandial glucose, mg/dl	111.7±16.9	110.7±25.4	0.89	104.7±18.9	114.7±18.9	114.7±18.9	121.7±15.8
Fasting insulin, µU/ml	9.33±3.20	8.09±2.70	0.67	10.21±5.20	9.21±5.20	9.21±5.2	10.21±4.98
HOMA-IR	2.07±1.10	1.90±0.80	0.05	2.37±0.32	1.89±0.56	1.89±0.56	2.00±0.82
Total-Cholesterol, mg/dl	191.0±11.7	195.0±29.6	0.097	182.0±26.7	200.17±15.3	200.17±26.7	190.0±46.7
LDL-Cholesterol, mg/dl	121.7±27.9	120.9±30.7	0.076	119.25±28.5	123.2±38.5	123.2±38.5	119.12±12.9
HDL-Cholesterol, mg/dl	52.7±8.7	54.3±12.6	0.04	54.05±9.80	50.76±10.1	50.76±10.1	50.05±8.91
Triglyceride, mg/dl	131.90±27.40	135.64±34.30	0004	127.4±42.6	133.4±33.6	123.4±33.6	149.4±21.6
Fibrinogen, mg/dl	388.0±30.3	321.10±38.20	0.021	300.4±42.6	353.4±33.6	308.1±59.1	365.4±67.9
hs CRP, mg/dl	0.28±0.03	0.22±0.67	0.002	0.29±0.10	0.27±0.007	0.24±0.01	0.20±0.00

Data are expressed as mean±SD, * - Mann–Whitney U test
HDL- high-density lipoprotein, HOMA-IR- homeostasis model assessment-insulin resistance, hs CRP- high sensitive C-reactive protein, LDL- low-density lipoprotein

Table 5. Linear regression analysis of obesity indices relationship with clinical and laboratory variables in all subjects

Dependent variable	Obese women (n =55)				First-degree relatives of obese women (n =154) (Total)				First-degree relatives of non-obese women (n =100) (Total)			
	obesity indices	Beta coefficient	t-statistic	p	obesity indices	Beta coefficient	t-statistic	p	obesity indices	Beta coefficient	t- statistic	p
Systolic blood pressure,	BMI	0.001	3.3	0.003	BMI	0.100	4.3	NS	BMI	0.021	3.9	NS
mmHg	WC	0.0002	3.6	0.001	WC		3.4		WC	0.041	4.5	NS
Diastolic blood pressure,	BMI	0.001	3.1	0.002	BMI	0.004	3.1	0.003	BMI			
mmHg	WC	0.045			WC			0.001	WC	0.04	4.9	NS
Fasting glucose, mg/dl	BMI	1.200	4.1	NS	BMI	0.200	4.1	NS	BMI	0.050	4.1	NS
Fibrinogen, mg/dl	WC	0.009	3.7	<0.001	WC	0.002	3.9	<0.001	WC	0.100	4.2	NS
Total-Cholesterol, mg/dl	WC	0.101	3.1	NS	WC	0.03	3.1	NS	WC	0.0004	3.9	0.001
Triglyceride, mg/dl	WC	0.006	3.0	0.002	WC	0.134	3.9	NS	WC	0.2610	3.1	0.003
HDL- Cholesterol, mg/dl	WC	-0.265	4.1	NS	WC	-0.2610	3.9	NS	WC	0.40	4.6	NS
LDL-Cholesterol, mg/dl	BMI	0.243	3.9	NS	BMI	0.240	4.6	<0.001	BMI	0.003	3.4	0.0006
HOMA- IR	WC	0.005	3.2	<0.001	WC	0.013	3.4	<0.001	WC	0.061	4.3	NS
hs CRP, mg/dl	WC	0.06	3.9	NS	WC	0.061	4.3	NS	WC	0.04	4.8	NS

BMI- body mass index, HDL- high-density lipoprotein, HOMA-IR- homeostasis model assessment-insulin resistance, hsCRP- high sensitive C-reactive protein, LDL- low-density lipoprotein, NS- non significant, WC- waist circumference

increased TC (OR 2.31), LDL-C (OR 2.03), fibrinogen (OR 2.06), hs CRP (OR 1.98) and low HDL (OR 2.99). Female relatives with high WC had the highest odds for high diastolic blood pressure (OR 2.52) and TG (OR 2.93) and LDL-C (OR 2.60), and low insulin sensitivity (OR 4.30) (Table 6).

In first-degree relatives of obese women, BMI levels showed linear relationship with fibrinogen, TC, HOMA- IR and hs CRP levels, while WC levels were related to blood pressures, fibrinogen, TC, HOMA-IR and hs CRP (Table 7).

Discussion

Obesity is associated with increased risk of cardiovascular disease in adults (16-17, 25) and adolescents (18, 19). At every level of risk ranging from low to high, the presence of obesity increased the likelihood of mortality. In many studies, increased weight is associated with high levels of triglycerides, LDL- C, and low HDL- C levels. In addition, cardiovascular risk factors related to chronic subclinical inflammation (C-reactive protein), adipocyte dysfunction (adiponectin and leptin) and prothrombotic activity (fibrinogen) may be further contributing to the burden of cardiovascular disease (21, 24-27).

Many studies identified that obesity was an independent risk factor for developing of cardiovascular disease (16-32, 36, 41). Similarly, The Framingham Heart Study showed that association between obesity and risk of cardiovascular disease after the adjustment for age and other known risk factors were cholesterol, blood pressure, cigarette smoking, and glucose intolerance (31). In many studies, glucose metabolism disorders are increased in the first- degree relatives of type 2 diabetic patients (33-35). However, there are not many studies related to obesity frequency and cardiovascular risk factors in relatives of obese.

Obesity indices, such as BMI and WC levels are considered useful, noninvasive anthropometric measurements that provide information on cardiovascular risks, such as hypertension, diabetes and dyslipidemia. Several studies have reported a strong positive association between abdominal adiposity and cardiovascular risk factors (31). In the present study, linear regression analyses showed that BMI and WC were associated with higher systolic blood pressure, diastolic blood pressure, TG,

Table 6. Odds ratios (95% CI) for the presence of cardiovascular risk factors according to the obesity status

	Obese women (n=55)			Female obese first-degree relatives (n=112)			Male obese first-degree relatives (n=42)		
	BMI ≥ 30 kg/m²	WC ≥ 88 cm	WHpR ≥ 0.9	BMI ≥ 30 kg/m²	WC ≥ 88/102 cm	WHpR ≥ 0.9	BMI ≥ 30 kg/m²	WC ≥ 88/102 cm	WHpR ≥ 0.9
Systolic BP, mmHg	2.81 (0.68-5.10)	2.74 (0.69-2.23)	2.62 (0.87-3.02)	2.91 (1.77-3.4)	2.52 (1.78-4.80)	2.58 (0.54-4.12)	0.91 (0.46-1.76)	1.67 (1.04-2.70)	2.05 (0.66-8.42)
Diastolic BP, mmHg	2.71 (1.03-4.59)	1.38 (0.84-2.57)	1.11 (0.66-1.87)	1.46 (0.90-2.3)	1.67 (1.04-2.70)	3.15 (0.8-11.13)	1.67 (1.4-2.9)	1.61 (1.00-2.58)	1.80 (0.83-3.92)
Fasting glucose, mg/dl	2.03 (0.80-4.05)	1.90 (1.19-4.30)	1.70 (1.00-2.84)	2.26 (1.40-3.6)	1.61 (1.00-2.58)	1.34 (0.35-5.16)	2.35 (0.66-3.42)	2.16 (1.38-3.39)	1.67 (1.04-2.70)
Fibrinogen, mg/dl	3.57 (1.30-4.68)	3.40 (1.79-5.52)	2.91 (1.14-3.41)	2.83 (1.1-2.94)	2.66 (1.08-4.39)	2.11(1.38-3.39)	1.80 (0.83-4.89)	1.67 (1.04-2.70)	2.03 (1.23-3.34)
Hs CRP, mg/dl	3.71 (1.64-6.11)	3.01 (0.89-5.14)	2.39 (0.76-5.56)	2.79 (0.94-6.1)	2.33 (0.91-5.14)	2.01 (0.54-3.14)	2.0 9 (0.92-4.13)	1.89 (0.64-3.24)	1.39 (0.91-2.14)
T-Cholesterol, mg/dl	2.46 (0.55-6.04)	1.67 (1.04-2.70)	1.80 (1.09-2.98)	1.38 (0.84-2.2)	1.67 (1.04-2.8)	1.11 (0.84-2.8)	1.83 (1.14-1.94)	1.11 (0.66-1.87)	1.58 (1.69-3.57)
Triglyceride, mg/dl	2.9 (0.94-6.14)	2.81 (1.03-3.58)	2.73 (1.23-3.35)	1.91 (1.18-3.1)	2.36 (0.86-6.47)	1.45 (0.65-4.62)	1.38 (0.84-1.97)	1.70 (1.01-2.84)	1.01 (1.31-2.69)
HDL- C, mg/dl	2.76 (0.86-6.47)	2.80 (1.78-4.99)	2.78 (1.69-4.57)	1.75 (0.90.-2.9)	2.62 (0.80-8.64)	1.79 (1.83-4.51)	1.91 (1.18-3.10)	2.51 (1.11-5.69)	1.80 (1.19-2.91)
LDL- C, mg/dl	2.62 (0.80-8.64)	2.97 (1.04-4.50)	2.71 (1.11-5.69)	2.55 (1.04-2.7)	2.46 (0.75-4.01)	1.37 (0.94-1.60)	1.80 (0.83-3.92)	1.80 (1.09-2.98)	1.61 (0.83-3.92)
HOMA-IR	2.96 (1.55-7.04)	2.91 (1.00-2.58)	1.99 (1.03-3.98)	3.34 (0.8-4.14)	2.26 (1.40-3.67)	2.41 (1.61-4.68)	2.13 (1.69-4.57)	1.67 (1.04-2.70)	1.17 (.0.74-3.75)

BMI- body mass index, BP- blood pressure, CI- confidence interval, HDL-C- high-density lipoprotein cholesterol, HOMA-IR - homeostasis model assessment-insulin resistance, hsCRP- high sensitive C-reactive protein, LDL-C- low-density lipoprotein cholesterol, WC- waist circumference, WHpR- waist-to-hip ratio

Table 7. Relationship between obesity indices and cardiovascular risk factors variables in first-degree relatives of obese women

	Systolic blood pressure, mmHg	Diastolic blood pressure, mmHg	Fasting glucose, mg/dl	Fibrinogen mg/dl	Total-Cholesterol, mg/dl	Triglyceride, mg/dl	HDL-Cholesterol, mg/dl	LDL-Cholesterol, mg/dl	HOMA- IR	CRP, mg/dl
BMI, kg/m²										
<20	103.5±2.7	51.7±9.86	83.7±5.8	245.9±10.0	175.3.±9.7	128.9±27.4	53.6±6.7	110.7±12.1	1.68±0.11	0.18±0.70
20- 24.9	106.1±5.9	55.1±.8.9	81.1±10.0	295.1±12.9	179.6±11.9	127.6.±9.8	54.5±8.1	112.4±11.1	1.99±1.10	0.21±0.50
25- 29.9	127.5±9.7	57.70±10.86	80.3±9.1	311.1±15.4	207.5±5.1	130.7.5±9.7	51.7±9.7	128.1±11.3	2.0±0.98	0.22±0.80
30-<	100.2±25.8	58.17±9.86	85.7±3.4	389.1±20.0	229.8±9.8	139.2±5.8	49.5±3.1	126.5±17.9	2.97±1.10	0.25±0.10
p	NS	NS	NS	0.002	<0.001	NS	NS	NS	0.003	0.008
Waist, cm										
<88 or 102	109.9±16.9	58.0±13.5	81.3±7.5	230.4±30.7	184.7±11.2	140.7±7.2	53.1±3.7	121.5±11.1	2.01±1.1	0.18±0.7
≥90 or 102	141.2±11.8	99.5±21.5	79.7±10.5	408.1±21.9	245.3±8.9	135.1±8.1	44.9±5.1	128.5±12.5	2.85±0.21	0.28±0.5
p*	0.003	0.001	NS	0.002	0.001	NS	NS	NS	0.001	0.005

Data are expressed as mean±SD, * - Mann–Whitney U test
BMI- body mass index, HDL- high-density lipoprotein, HOMA-IR- homeostasis model assessment-insulin resistance, hsCRP- high sensitive C-reactive protein, LDL- low-density lipoprotein, NS- non significant

fibrinogen and HOMA- IR in obese women. The BMI and WC were associated with higher diastolic blood pressure, LDL-cholesterol, fibrinogen, and HOMA in relatives of obese women. Many studies have been suggested insulin sensitivity was decreased with increased values of BMI and WC (26-28, 37). Likewise, in our study, mean levels of HOMA were increased while BMI and waist were increasing in first-degree relatives of obese women.

Central obesity indices were mostly correlated with adverse serum lipids and lipoproteins (16, 17). Also, WC might be a superior index predicting the presence of central adiposity and dyslipidemia (16-18, 25, 27, 30). Similarly, we found that WC levels of first-degree relatives were a strong indicator for blood pressures and TC levels.

Insulin resistance has been described in several diseases, such as obesity (20), hypertension (23, 41) and metabolic syndrome (24). During the past decade, the relation between insulin resistance and cardiovascular risk was exclusively attributed to the development of atherosclerosis (42). In fact, insulin resistance is thought to promote atherosclerosis, in part through associated metabolic abnormalities, hyperglycemia, hyperinsulinemia, and dyslipidemia, which stimulate smooth muscle cell hypertrophy and hyperplasia and increase synthesis of extracellular matrix proteins. Simple reduction of blood pressure or lowering of serum lipids alone may reduce the risk of CVD to some extent. However, in order to prevent the occurrence of CVD more effectively, comprehensive reductions of cardiovascular risks and improvement of insulin resistance should be considered (25).

Several large prospective cohort studies show that higher levels of CRP and fibrinogen are associated with increased risk for cardiovascular disease (37-40). These studies typically reported age-adjusted relative risks for cardiovascular disease in the range of 2.0 to 3.0 for the highest compared with the lowest of CRP (37). It has been reported that C-reactive protein levels are elevated in overweight adults (38). Because, obesity founds a predisposition to hypertension, hyperlipidemia and diabetes mellitus, the relationship between obesity and atherosclerosis seems rather indirect. However, judging from the values of correlation coefficients, hs CRP seems to have a closer correlation with BMI than with blood pressure, plasma glucose or serum lipids (32). However, adipose tissue is known to be the primary stimulant of CRP synthesis. This suggests the existence of direct mechanism by which obesity increases CRP independently of the effects of insulin resistance (31-32, 36-41). In our study, obese women and their first-degree relatives had increased hs CRP and fibrinogen associated with high BMI and WC levels.

Obesity emerged as an independent risk factor in that elevated risk was present for individuals both with and without other major cardiovascular risk factors (i.e, smoking, high blood pressure, and or high serum cholesterol levels in young adulthood and middle age). Simply being obese increased an individual risk of dying from heart disease and/or diabetes. The results further underscore, the fact that obesity is a major public health problem associated with a reduction in life expectancy, similar in magnitude to that associated with smoking (45, 47-49). Overweight or obese smokers have at least two independent risk factors for cardiovascular and there may be synergistic effects between them (46). Obese smokers have about twice the mortality of the obese non-smokers and four times higher than non-smokers of healthy body mass index (44). In the present study, as expected, mean levels of hsCRP and fibrinogen and DBP were higher among current smokers in obese women. Alcohol consumption was found in 10% of obese women and in 21.4% of their relatives. Male first-degree relatives who consumed >8 units of alcohol per week and female first-degree relatives who consumed >14 units had higher fibrinogen and DBP levels.

Yan et al. (47) suggested that multivariate analyses adjusted for systolic blood pressure and total cholesterol levels showed the odds ratio for cardiovascular heart disease death for obese participants compared with those of normal weight in the same risk category. It was 1.43 (95% CI 0.33-6.25) for low risk and 2.07 (95% CI 1.29-3.31) for moderate risk (47). Likewise, our findings suggested that obese women had higher risk for systolic blood pressure (OR 2.81), TG (OR 2.79), LDL- C (OR 2.62), fibrinogen (OR 3.57), and hs CRP (OR 3.71) and low insulin sensitivity (OR 2.96). Similarly, first-degree relatives of obese women had higher risk for systolic blood pressure (OR 2.91), LDL- C (OR 2.55), fibrinogen (OR 2.83), and hs CRP (OR 2.79), and low insulin sensitivity (OR 3.34). Higher BMI and WC were associated with increased fibrinogen and HOMA-IR levels in first-degree relatives of obese women.

Conclusion

In obese women and relatives, body mass index and waist circumferences are related with blood pressure, total cholesterol, fibrinogen and insulin resistance. If there are obese women in family, first-degree relatives have 1.8 fold increase for obesity frequency. Increased body mass index is associated with cardiovascular risk factors. In early term, prevention of obesity may decrease developing of cardiovascular risk.

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