

Original Article

Investigation of relationship of visceral body fat and inflammatory markers with metabolic syndrome and its components among apparently healthy individuals

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Abstract: Metabolic syndrome is a cluster of disorders and great risk for cardiovascular diseases. We aimed to investigate association between severity of metabolic syndrome (MetS) and anthropometric measurements, and to evaluate correlation of MetS and its components with metabolic deterioration and inflammatory indexes. The cross-sectional study enrolled 1474 patients with obesity and overweight. The patients were grouped as MetS and Non-MetS, and were sub-grouped as group 1 (three criteria), 2 (four criteria) and 3 (\geq five criteria) according to NCEP ATP III. Mean age was 38.7 ± 11.9 years and BMI was 35.1 ± 6.3 kg/m². Lipid profile, anthropometric and blood pressure measurements, liver function tests, bioelectric impedance body fat compositions, insulin resistance and HbA1c, and spot urinary albumin-creatinine ratio were significantly different between groups of MetS and Non-MetS. Age, lipid profile, bioelectric impedance fat analyses, BMI, blood pressure values, glucose, insulin resistance, uric acid and hs-CRP levels were significantly different between groups of MetS component groups. ROC analysis revealed that hs-CRP was found to be more predictive for severity of metabolic syndrome components 3 and 4 ($P=0.030$); uric acid and visceral fat were more actual to predict severity of metabolic syndrome between 3 and 5 MetS components, ($P=0.006$) and uric acid was detected as more actual to predict severity of MetS between 4 and 5 components ($P=0.023$). In conclusion, uric acid, hs-CRP and visceral body fat composition were useful to predict to severity of MetS in primary care.

Keywords: Metabolic syndrome, primary care, uric acid, Hs-CRP, bioelectric impedance fat analysis

Introduction

The prevalence of obesity and Metabolic syndrome (MetS) has reached epidemic levels worldwide and related health risk is increased throughout the last decade. Obesity is a chronic metabolic and inflammatory state associated with many cardiovascular and diabetogenic disorders [1, 2]. MetS is a clinical entity characterized by the cluster of insulin resistance, glucose intolerance, atherogenic lipid profile, hypertension, abdominal obesity, and physical inactivity. It had been shown that each of condition which was associated with development of cardiovascular disease (CVD), hypertension and type 2 diabetes mellitus (T2DM) [3-5]. These conditions are interrelated and share similar under-

lying mediators, mechanisms and pathways [6-8]. Several recent studies reported that there was a correlation between inflammatory state and components of MetS. Components of the MetS are associated with incident cardiovascular disease [9]. Substantial high risk of CVD mortality was appeared in those with 3, 4, or 5 components, compared with those with no component [10, 11].

Based on reviewing the literature, relation of metabolic syndrome and its components with body fat composition, and anthropometric measurements such as BMI and waist-hip ratio (WHR) and albumin-to-creatinine ratio (ACR) and high sensitive C reactive protein (hs-CRP) of endothelial dysfunction markers, and uric acid were not sufficiently investigated in the pri-

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mary care settings in Turkey. In the present study, we aimed to investigate association between severity of MetS and anthropometric measurements, and to evaluate correlation of MetS and its components with metabolic deterioration and inflammatory indexes among individuals with obesity and overweight.

Methods and procedures

The study design and data collection

The cross-sectional and population based study was conducted by Family Medicine Department, School of Medicine, Duzce University between September 2012 and Augustus 2013. We invited family physicians working at primary care settings in Duzce Province to refer the patients with obesity and overweight. A total of 1632 consecutive patients who recruited from 103 family health centers were admitted to obesity clinic of our clinic. Out of 1632, 158 patients were excluded: 146 patients with DM, 4 patients with HBsAg (+), 2 patients with end-stage renal disease and 6 patients with suspected as Cushing's disease/or Cushing's disorders (serum cortisol level ≥ 25 $\mu\text{g/mL}$ at morning time after overnight fasting), and data of 1474 (1182 obese and 292 overweight) patients were analyzed. The subjects were informed about the study and informed consent was obtained. Ethical approval was obtained by the ethics committee of our institute.

Anthropometric and blood pressure measurements

All measurements were obtained in the morning time and after overnight fasting status according to protocols and recorded. Weight and height measurements of subjects were taken while wearing light clothing and without shoes. Height was measured to the nearest 0.1 cm with a stadiometer in standing position. Weight was recorded to the nearest 0.1 kg with a regularly calibrated and balance-beam scale. Waist circumference (WC) was measured to the nearest 0.1 cm with a tape-measure at the mid-point between the bottom of the rib cage and the top of the iliac crest while exhaling and standing up without clothing covering the waist area. Hip circumference (HC) was measured to the nearest 0.1 cm a tape-measure applied to the subjects standing up and wearing light underwear covering the hip area around the point with maximum circumference over the buttocks. Blood pressure (BP) measurements was performed with a calibrated sphygmoma-

nometer (Erka, Enlargen, Germany) after the subject has rested 10 minutes in seated position, and dominant arm was used, when smoking and drink containing alcohol and caffeine was avoided.

Metabolic syndrome, insulin resistance and body mass index definition

Subjects with MetS were identified when 3 out of the 5 criteria of the National Cholesterol Education Program (NCEP ATP III): waist circumference (WC) >102 cm (male) or >88 cm (female); blood triglyceride (TG) level ≥ 150 mg/dl, high density lipoprotein-cholesterol (HDL-C) <40 mg/dl (male) or <50 mg/dl (female), or under treatment of anti-lipid agents; blood pressure $\geq 130/85$ mm-Hg or under treatment of anti-hypertensive agents; and fasting blood glucose level (FBG) ≥ 110 mg/dl or presence of DM were met NCEP ATP III [12]. Obesity and Overweight was defined as BMI ≥ 30.0 kg/m^2 and between 25.0-29.9 (kg/m^2), respectively by WHO [13]. BMI was calculated with formulation of [weight (kg) / height (m^2)]. IFG was stated if overnight fasting blood glucose FBG level was ≥ 100 mg/dl [14]. HOMA-IR was calculated with formulation of "fasting glucose (mg/dl) \times fasting insulin (mIU/ml)/(405)". Insulin resistance (IR) was stated as positive if HOMA-IR ≥ 2.5 [15].

Bioelectric impedance fat analysis

Bioelectric impedance (BEI) visceral and total body fat composition was measured with biochemical impedance analyzer with 50 kHz bio-impedance meter without shoes in light indoor clothes using a hand-to-foot single frequency (Omron BF 510; Omron Corp. Kyoto, Japan). After entering the patients' data such as height, age and gender in the BEI, electrodes were placed on hand and foot. The subjects were fasting and wearing barefoot and light clothing. All metallic accessories were removed. The subjects with pregnant and cardiac pace-maker were avoided from BEI measurement according to instructions.

Biochemical assays

Approximately 10 milliliters of blood samples were drawn from the antecubital vein of each subject by applying minimal tourniquet force. The first 2 ml of blood, which was used for the full blood count, was drawn into a vacutainer tube containing 0.04 ml of the 7.5% K3 salt of ethylene diamine tetra acetic acid (EDTA). The

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Table 1. Comparisons of socio-demographic features of subjects with and without MetS

Variables	All (n=1474)	MetS (644, 43.7%)	Non-MetS (830, 56.3%)	P*
Gender				<0.001
Male	298 (20.2%)	163 (54.7%)	135 (45.3%)	
Female	1176 (79.8%)	481 (40.9%)	695 (59.1%)	
Smoking Status				0.002
Current	228 (15.5%)	121 (18.8%)	107 (12.9%)	
Former	206 (13.9%)	97 (15.1%)	109 (13.1%)	
Never	1040 (70.6%)	426 (66.1%)	614 (74.0%)	
Age Groups				<0.001
18-29 years	596 (40.4%)	188 (31.5%)	408 (68.5%)	
30-44 years	572 (38.8%)	279 (48.8%)	293 (51.2%)	
45-64 years	277 (18.8%)	161 (58.1%)	116 (41.9%)	
565 years	29 (2.0%)	16 (55.2%)	13 (44.8%)	
BMI Groups				<0.001
25.0-29.9 kg/m ²	292 (19.8%)	35 (5.4%)	257 (30.9%)	
30.0-34.9 kg/m ²	530 (35.9%)	214 (33.3%)	316 (38.1%)	
35.0-39.9 kg/m ²	370 (25.1%)	210 (32.6%)	160 (19.3%)	
≥40.0 kg/m ²	282 (19.2%)	185 (28.7%)	97 (11.7%)	
IFG				<0.001
(FBG level ≥100 mg/dl)	531 (36.0%)	318 (49.4%)	213 (25.7%)	
(FBG level <100 mg/dl)	943 (64.0%)	326 (50.6%)	617 (65.4%)	
Components of MetS				
Three Criteria (Group 1)		373 (57.9%)		
Four Criteria (Group 2)		228 (35.4%)		
Five Criteria (Group 3)		43 (6.7%)		

*Chi-square (BMI groups, age groups, and smoking status between groups of MetS and Non-MetS). *Fisher's exact test (Gender and patients with IFG between groups of MetS and Non-MetS) used.

remaining 8 milliliters of blood samples was drawn into a vacutainer tube without anticoagulant. These blood samples were allowed to clot for 20 minutes prior to centrifugation. The blood tubes were centrifuged for 10 min at 1500 g. All samples were assayed at central laboratory of Duzce University within the same day when taken. Plasma concentrations of cholesterol, fasting triglycerides, HDL-C, glucose, electrolytes, liver function tests and other biochemical variables were measured by a Cobas 6000 auto analyzer using commercially available kits (Roche Diagnostics GmbH, Mannheim, Germany). Low density lipoprotein-cholesterol (LDL-C) was calculated using the Friedewald equation.

The data analysis

The patients were grouped into two as: MetS and Non-MetS according to NCEP ATP III. The subjects were classified into BMI groups as

25.0-29.9, 30.0-34.9, 35.0-39.9 and ≥40 kg/m², and age was categorized as 18-29, 30-44, 45-64, and ≥65 years. Anthropometric measurements, socio-demographic features, lipid profiles, liver function tests, hormones of TSH, prolactin and cortisol, IR, HbA1c, uric acid, FBG, spot urinary ACR, IFG status, body fat compositions, BMI and age groups were compared between two groups of patients with MetS and Non-MetS [20]. The subjects with MetS were grouped according to components of MetS into three groups: Group 1 (3 criteria), group 2 (4 criteria) and group 3 (5 criteria). Lipid profiles, liver function tests, hormones of TSH, prolactin and cortisol, insulin resistance, HbA1c, uric acid, FBG, and spot urinary ACR, status and body fat compositions were also compared between groups of MetS anthropometric, blood pressure measurements, HbA1c, lipid profile; BEI body fat composition, alanine/aspartate aminotransferase, uric acid and hs-

CRP were evaluated. All data were entered and analyzed in SPSS software version 15.0 (Chicago, IL) in PC software. Continuous variables were stated as mean ± standard deviation (SD). Categorical variables were shown as frequency and percentage. Normal distribution of continuous variables were tested with Kolmogorov-Smirnov test. Chi-square or Fisher's exact test was used for categorical variables to determine differences between two groups. Parameters of PRL, cortisol and WHR were normally distributed. Other continuous variables such as age, systolic and diastolic BP, triglyceride, HDL-C, LDL-C, FBG, BMI, BEI measurements, fasting insulin, HOMA-IR, HbA1c, ACR, TSH, WBC, Uric acid, hs-CRP and ALT. Logarithmic transformation was applied for continuous variables which were not normally distributed and logarithmically transferred values were stated as mean ± Standard Error (SE). Student t-test was used two independent

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Table 2. Comparisons of clinical features of subjects with and without MetS

Variables	All Mean ± SD	MetS Mean ± SD/SE	Non-MetS Mean ± SD/SE	P*
Age (years)	38.7 ± 11.9	41.6 ± 11.5	36.3 ± 11.7	<0.001
LogAge		1.60 ± 0.12	1.53 ± 0.14	
WHR	0.86 ± 0.08	0.89 ± 0.1	0.84 ± 0.2	<0.001
BMI (kg/m ²)	35.1 ± 6.3	37.5 ± 6.4	33.4 ± 5.5	<0.001
LogBMI		1.57 ± 0.06	1.51 ± 0.07	
BEI total fat (%)	42.7 ± 7.6	43.6 ± 7.9	42.9 ± 7.9	0.001
LogBEI-BFA		1.63 ± 0.09	1.61 ± 0.08	
BEI-visceral fat (%)	10.7 ± 4.1	12.3 ± 4.3	9.6 ± 3.7	<0.001
LogBEI		1.06 ± 0.14	0.95 ± 0.15	
SBP (mm-Hg)	126.79 ± 18.19	134.3 ± 17.9	120.3 ± 15.3	<0.001
LogSBP		2.12 ± 0.06	2.07 ± 0.05	
DBP (mm-Hg)	82.67 ± 22.35	86.9 ± 12.3	78.9 ± 27.7	<0.001
LogDBP		1.93 ± 0.06	1.88 ± 0.07	

*Student T test was used between Group of MetS and Non-MetS. SD: Standard deviation. SE: Standard error.

Table 3. Comparisons of laboratory values of subjects with and without MetS

Variables	All* Mean ± SD	MetS Mean ± SD/SE	Non-MetS Mean ± SD/SE	P*
TG (mg/dl)	144.19 ± 86.36	195.7 ± 99.4	103.7 ± 42.9	<0.001
LogTG		2.24 ± 0.18	1.98 ± 0.17	
HDL-C (mg/dl)	48.76 ± 86.36	42.3 ± 9.3	53.9 ± 12.8	<0.001
LogHDL-C		1.61 ± 0.91	1.72 ± 0.97	
LDL-C (mg/dl)	119.13 ± 41.67	125.9 ± 51.2	113.8 ± 31.5	<0.001
LogLDL-C		2.07 ± 0.12	2.03 ± 0.13	
FBG (mg/dl)	97.1 ± 9.8	100.2 ± 11.3	94.6 ± 7.7	<0.001
LogFBG		1.99 ± 0.05	1.97 ± 0.03	
Insulin (mIU/ml)	13.06 ± 9.71	15.8 ± 11.8	10.9 ± 7.1	<0.001
LogInsulin		1.09 ± 0.31	0.94 ± 0.30	
HOMA-IR	3.2 ± 2.5	3.9 ± 1.14	2.6 ± 1.7	<0.001
LogHOMA-IR		0.48 ± 0.33	0.31 ± 0.32	
HbA1c (%)	5.4 ± 0.5	5.6 ± 1.1	5.2 ± 0.3	0.001
LogHbA1c (%)		0.74 ± 0.06	0.72 ± 0.03	
ACR (mg/g)	21.08 ± 55.29	26.4 ± 3.8	12.9 ± 1.9	0.005
LogACR		0.82 ± 0.73	0.65 ± 0.62	
ALT (U/mL)	23.7 ± 18.1	26.9 ± 21.4	21.2 ± 14.5	<0.001
LogALT		1.34 ± 0.24	1.25 ± 0.23	
AST (U/L)	22.8 ± 12.9	23.9 ± 14.4	21.6 ± 11.4	0.007
LogAST		1.33 ± 0.18	1.30 ± 0.15	
UA (mg/dl)	4.9 ± 1.2	5.4 ± 13.2	4.6 ± 1.1	<0.001
LogUA		0.72 ± 0.12	0.65 ± 0.11	
Hs-CRP (mg/L)	5.26 ± 4.65	6.4 ± 0.5	3.8 ± 0.3	<0.001
LogHs-CRP		0.59 ± 0.11	0.37 ± 0.45	

*Student T test was used between Group of MetS and Non-MetS.

groups (MetS and Non-MetS groups). One-way ANOVA-Bonferroni test was used for comparisons between more than two groups (Group 1, Group 2 and Group 3). Pearson's or Spearman's correlation analysis was applied for correlation. A 2-tailed *P*-value of less than 0.05 was considered as statistically significant. ROC analysis was used for comparisons for predictive values of visceral fat, uric acid and hs-CRP between severity groups of metabolic syndrome. Values logarithmically transformed of uric acid, visceral fat and hs-CRP were used for ROC analysis.

Results

The percentage of male and female patients was 20.2% (n=298) and 79.8% (n=1176), respectively. Mean age of total subjects was 38.7 ± 11.9 years. Majority of the subjects with MetS were within age group of 45-64 years-old, compared those with non-MetS (58.1% versus 41.9%, *P*<0.001). The percentage of the patients with stage 2 obesity (BMI: 35.0-39.9 kg/m²) and stage 3 obesity (BMI ≥40.0 kg/m²) were higher in MetS group than non-MetS group (61.3% and 31.0%, *P*<0.001). The number of subjects who had FBG level ≥100 was quite higher in MetS group, compared to non-MetS group (49.4% versus 25.7%, *P*<0.001). The frequency of male subjects were more dominant in MetS group (54.1% in MetS group but 45.3% in non-MetS group, *P*<0.001). The ratio of current smokers was significantly higher in MetS than non-MetS (18.8% versus 12.9%, *P*<0.001) (**Table 1**).

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Table 4. Comparison of components of MetS with clinical features of subjects

Variables	Components of MetS			P* (P ₁ , P ₂ , P ₃)
	Group 1 Mean ± SD/SE	Group 2 Mean ± SD/SE	Group 3 Mean ± SD/SE	
Age (years)	39.12 ± 9.18	42.24 ± 9.52	42.50 ± 11.61	<0.001
LogAge (years)	1.59 ± 0.12	1.62 ± 0.11	1.67 ± 0.08	0.014; <0.001; 0.114
WHR	0.85 ± 0.06	0.87 ± 0.07	0.86 ± 0.06	0.067; 0.283; 0.059; 0.283
BMI (kg/m ²)	39.54 ± 8.95	41.22 ± 5.71	41.40 ± 32.88	<0.001
LogBMI	1.57 ± 0.06	1.59 ± 0.07	1.59 ± 0.08	<0.001; <0.001; 0.264
BEI total (%)	43.62 ± 7.31	47.01 ± 6.21	49.95 ± 3.31	0.018
LogBEI total	1.62 ± 0.09	1.63 ± 0.08	1.59 ± 0.09	0.014; 0.951; 0.815
BEI visceral (%)	11.12 ± 9.50	12.82 ± 4.01	12.75 ± 3.59	<0.001
LogBEI visceral	1.09 ± 1.15	1.11 ± 0.14	1.18 ± 0.38	0.032; <0.001; 0.030
SBP (mm-Hg)	128.7 ± 14.4	145.6 ± 16.5	136.3 ± 7.5	0.001
LogSBP	2.10 ± 0.06	2.14 ± 0.05	2.15 ± 0.07	<0.001; <0.001; 0.136
DBP (mm-Hg)	83.9 ± 9.5	95.9 ± 10.8	85.1 ± 4.1	<0.001
LogDBP	1.91 ± 0.06	1.96 ± 0.05	1.97 ± 0.07	<0.001; <0.001; 0.743

*ANOVA-Bonferroni test was used to compare values between groups of MetS components (P₁: between group 1 and group 2; P₂: between group 1 and group 3; P₃: between group 2 and group 3).

Table 5. Comparison of components of MetS with clinical features of subjects

Variables	Components of MetS			P* (P ₁ , P ₂ , P ₃)
	Group 1 Mean ± SD/SE	Group 2 Mean ± SD/E	Group 3 Mean ± SD/SE	
TG (mg/dl)	162.2 ± 49.7	224.4 ± 89.4	241 ± 81.6	<0.001
LogTG	2.19 ± 0.16	2.33 ± 0.18	2.34 ± 0.11	<0.001; <0.001; 0.725
HDL-C (mg/dl)	43.69 ± 8.76	46.05 ± 8.94	44.51 ± 2.64	<0.001
LogHDL-C	1.63 ± 0.09	1.61 ± 0.09	1.57 ± 0.06	0.015; 0.001; 0.842
LDL-C (mg/dl)	125.09 ± 36.03	136.85 ± 40.31	149.81 ± 57.55	0.056
LogLDL-C	2.07 ± 0.13	2.07 ± 0.12	2.12 ± 0.19	0.652; <0.053; 0.071
FBG (mg/dl)	100.92 ± 10.36	102.03 ± 14.98	114.75 ± 7.13	<0.001
LogFBG	1.99 ± 0.04	2.01 ± 0.06	2.05 ± 0.02	0.186; <0.001; <0.001
Insulin (mIU/ml)	12.91 ± 7.98	18.56 ± 8.13	16.71 ± 7.18	0.001
LogInsulin	1.01 ± 0.33	1.13 ± 0.21	1.05 ± 0.36	0.006; 0.025; 0.925
HOMA-IR	3.24 ± 2.42	4.87 ± 4.50	4.74 ± 2.08	<0.0001
LogHOMA-IR	0.41 ± 0.35	0.52 ± 0.34	0.49 ± 0.37	0.004; <0.001; 0.683
HbA1c (%)	5.56 ± 0.35	5.62 ± 0.46	5.85 ± 0.26	0.143
LogHbA1c	0.73 ± 0.03	0.74 ± 0.04	0.75 ± 0.03	0.864; 0.116; 0.173
ACR (mg/g)	10.31 ± 22.48	15.59 ± 28.78	14.92 ± 19.81	0.980
LogACR	0.83 ± 0.65	0.83 ± 0.79	0.80 ± 0.88	0.843; 0.774; 0.694
ALT (U/mL)	31.74 ± 20.70	25.87 ± 19.58	31.25 ± 46.56	0.026
LogALT	1.39 ± 0.25	1.37 ± 0.62	1.52 ± 0.34	0.377; 0.068; 0.001
AST (U/L)	22.71 ± 10.82	23.28 ± 10.78	53.51 ± 69.98	0.007
LogAST	1.32 ± 0.16	1.33 ± 0.20	1.48 ± 0.32	0.557; 0.87; 0.046
UA (mg/dl)	4.91 ± 1.38	5.54 ± 0.97	5.56 ± 1.15	<0.001
LogUA	0.73 ± 0.10	0.74 ± 0.09	0.81 ± 0.52	0.044; 0.001; 0.041
Hs-CRP	5.12 ± 3.68	6.42 ± 5.13	6.11 ± 3.78	0.007
LogHs-CRP	0.51 ± 0.44	0.61 ± 0.40	0.62 ± 0.36	0.008; 0.014; 0.020

*ANOVA-Bonferroni test was used to compare values between groups of MetS components (P₁: between group 1 and group 2; P₂: between group 1 and group 3; P₃: between group 2 and group 3).

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Table 6. Correlation of MetS components with clinical features of patients

Variables	Components of MetS		Variables	Components of MetS	
	r	P*		r	P*
LogWHR	0.099	0.012	Loginsulin	0.154	<0.001
LogBMI	0.198	<0.001	LogHOMA-IR	0.186	<0.001
LogSBP	0.302	<0.001	LogBFA total	0.102	0.055
LogDBP	0.287	<0.001	LogBFA visceral	0.169	<0.001
LogTG	0.390	<0.001	LogA1c	0.134	0.011
LogHDL	-0.180	<0.001	LogALT	0.085	0.032
LogLDL	0.037	0.355	LogAST	0.136	0.005
LogFBG	0.249	<0.001	LogUA	0.188	<0.001
LogACR	0.001	0.988	LogHs-CRP	0.122	0.026

*Spearman's correlation test was used for correlation between MetS components and variables.

Comparison of biochemical parameters and anthropometric measurements was stated in **Tables 2** and **3**. Mean age, Waist to hip ratio (WHR), BMI, BEI total and visceral body fat composition measurements, systolic and diastolic BP measurements, lipid profile values, HOMA-IR, insulin, liver function tests, uric acid level, spot urinary ACR and HbA1c levels were significantly different in subjects with MetS, compared to those with non-MetS ($P < 0.05$).

Comparisons between components of MetS and some basic features, regarding age, WHR, BMI, BEI body fat composition, SBP and DBP were given in **Table 4**. Accordingly, mean age in group 2 and group 3 was significantly higher than group 1 (42.24 ± 9.52 , 42.50 ± 11.61 and 39.12 ± 9.18 , respectively; $P = 0.014$, $P < 0.001$). Mean WHR was similar between groups ($P = 0.067$). In body fat composition analysis, mean BEI visceral measurement between groups of MetS components was significantly different between three groups (11.12 ± 9.5 , 12.82 ± 4.01 and 12.75 ± 3.59 , $P = 0.032$, $P < 0.001$ and $P = 0.030$). Mean BEI total fat composition in group 1 was significantly lower than group 2 and 3 (43.62 ± 7.31 , 47.22 ± 6.21 and 41.40 ± 32.88 , $P = 0.018$). Mean values of systolic and diastolic BP among the subjects in group 1 was significantly lower than the values in group 2 and 3 ($P < 0.001$ and $P < 0.001$, respectively), but there was no significant difference between group 2 and 3 ($P = 0.136$ for systolic and $P = 0.743$ for diastolic BP).

Table 5 demonstrated that comparisons of serum lipid profiles, FBG, insulin, HOMA-IR,

HbA1c, liver functions, uric acid and hs-CRP levels. Mean LDL-C level were slightly higher in group 2 and 3, compared to group 1, but not significant ($P = 0.056$). Mean serum level of HDL-C was significantly lower in group 3 and 2 than group 1 ($P = 0.015$ and $P = 0.001$), but similar between group 2 and 3 ($P = 0.842$). Mean TG levels in group 2 and 3 was significantly higher than group 1 ($P < 0.001$ and $P < 0.001$). FBG level was significantly higher in group 3 than group 1 and 2 (114.75 ± 7.13 versus 100.92 ± 10.36 and 102.03 ± 14.98 ; $P < 0.001$),

and no significant different between group 1 and 2 ($P = 0.186$). It was found that there was significantly different in insulin resistance (HOMA-IR) between group 1 and 2 as well as group 1 and 3 ($P = 0.004$ and $P < 0.001$), but not between group 2 and 3 ($P = 0.683$). Serum alanine transaminase and aspartate transaminase levels in group 3 was significantly higher than group 1 and 2 between groups was not significantly different ($P = 0.026$ and $P = 0.007$, respectively). Mean uric acid level was significantly different between groups ($P = 0.044$, $P = 0.001$ and $P = 0.041$). Similarly, serum hs-CRP level was significantly different between groups ($P = 0.008$, $P = 0.014$ and $P = 0.020$).

When correlation between MetS severity (components of MetS) and biochemical and anthropometric measurements of patients with MetS was analyzed, no significant correlation for ACR, HbA1c and LDL-C was observed. However, significant positive correlation was detected between age, WHR, BMI, TG, BP, IR, BEI body fat composition, liver function tests, uric acid, hs-CRP and components of MetS, and negative correlation with HDL-C (**Table 6**).

With ROC analysis, hs-CRP was found to be more predictive for severity of metabolic syndrome components 3 and 5 than visceral fat and uric acid ($P = 0.030$, 0.108 and 0.224 , respectively) (**Figure 1**). Uric acid and visceral fat were more actual to predict severity of metabolic syndrome between 3 and 5 MetS components, compared to hs-CRP ($P = 0.006$, 0.007 and 0.912 , respectively) (**Figure 2**). Uric acid,

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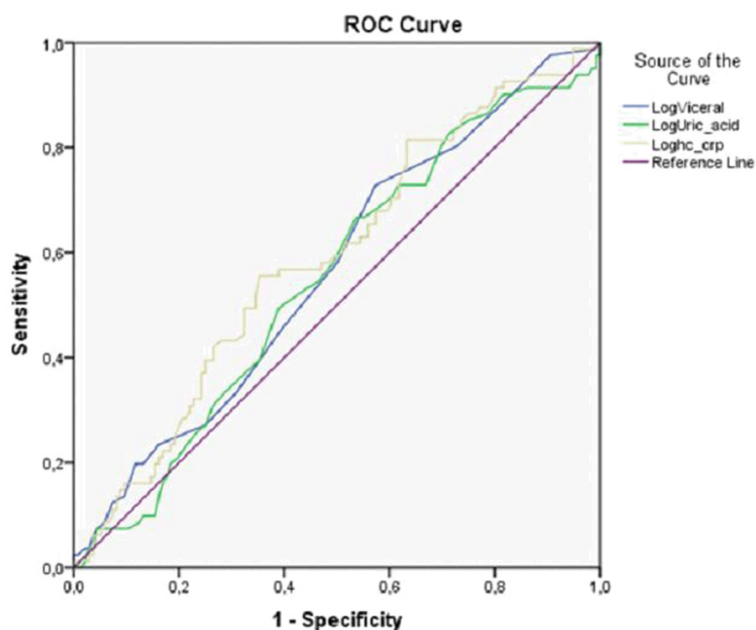


Figure 1. ROC analysis for predictive values of Uric acid, hs-CRP and visceral obesity between severity of metabolic syndrome with 3 and 4 components. Hs-CRP was significantly more predictive for severity of MetS, compared to visceral fat and uric acid (Area \pm SE of predictor variables' curve =0.588, 0.565 and 0.549 and their p values =0.030, 0.108, and 0.224, respectively).

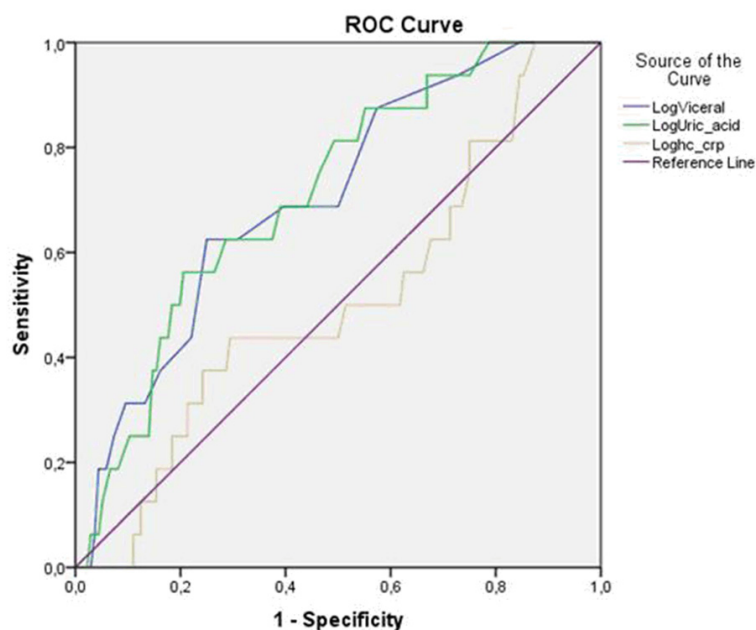


Figure 2. ROC analysis for predictive values of Uric acid, hs-CRP and visceral obesity between severity of metabolic syndrome with 3 and 5 components. Visceral fat and uric acid were significantly more predictive for severity, compared to hs-CRP (Area \pm SE of predictor variables' curve =0.706, 0.711 and 0.509 and their p values =0.007, 0.006, and 0.361, respectively).

compared to visceral fat and hs-CRP, was detected as more actual to predict severity of

MetS between 4 and 5 components ($P=0.023$, 0.065 and 0.305 , respectively) (**Figure 3**).

Discussion

The current study indicated several important points on MetS and severity of MetS in individuals with obesity and overweight. We suggest that male factor, increased BMI, ageing and current smoking are independent risk factor for MetS. We claim that components of MetS are associated with higher inflammatory state and metabolic deterioration. In the literature, a few studies which evaluated correlation of Mets and its components with inflammatory state, body fat composition. Our study investigated the interrelation between the former issues in large sample of obesity. The study is important study conducted in family medicine due to fact that obesity and MetS are epidemic, but preventable, health problem.

Distribution of MetS prevalence was more frequent in female population or similar in both genders. Beigh et al. [16] suggested that MetS was present in both female and male corresponding to 29% and 23%, respectively. Park et al. [17] found similar gender distribution in MetS frequency, reporting 24.6% in men and 24.0 in women. Katulanda et al. [18] also reported that MetS was slightly higher in female but no significant difference in prevalence between males (21.7%) and females (23.9%) according to ATP III criteria. In contrast, we found MetS in male subjects was more frequent than female (54.7%, versus 45.3%).

Our sample was over twenty years-old and obese or overweight. Smoking status was not adjusted for both male and

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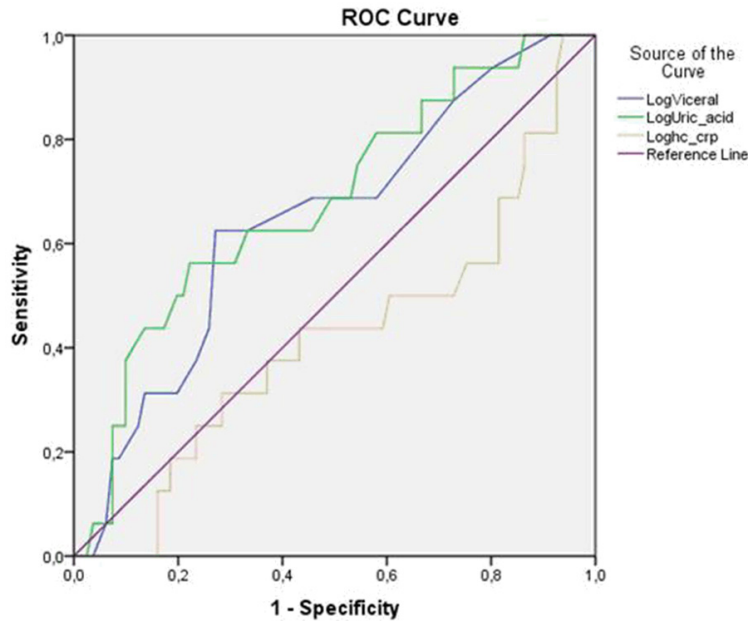


Figure 3. ROC analysis for predictive values of Uric acid, hs-CRP and visceral obesity between severity of metabolic syndrome with 4 and 5 components. Only uric acid was significantly more predictive for severity, compared to visceral fat and hs-CRP (Area \pm SE of predictor variables' curve = 0.646, 0.680 and 0.419 and their p values = 0.023, 0.065, and 0.259, respectively).

female in our study. That was why MetS was more frequent in male subjects.

The positive correlation between smoking, another public health problem, and MetS is significant in studies, but not all, active smoking is associated with development of MetS. However, one study conducted on among Turkish female even found a protective effect of smoking on MetS [19]. Our result was consistent with result of the study by Sun et al. [20]. Smoking has been known to be negative effect on blood pressure and lipid profile. Blood pressure increased and HDL-C level decreased with smoking. Blood pressure and HDL-C are two components of five criteria by ATP III [21]. Thus, smoking would be expected to be risk for development of MetS for both male and female individuals.

We observed that being over age of 30 was great risk for MetS development. In the study, the patients with overweight also had MetS. Therefore, the patients under 30 years-old and with overweight should be taken into consideration for MetS development. With increased BMI, the frequency of MetS was increased. We observed that the subjects whose BMI was between 30-40 kg/m² were at great risk for development of MetS, compared to whose BMI

over 40 kg/m². Consistent with our results, Veronica et al. [22] reported that aging is accelerated when metabolic and cardiovascular diseases (CVD) are present and the risk of these diseases increases with age.

Our results regarding the comparisons of blood pressure, insulin resistance, lipid profile, liver function, fasting glucose and fasting insulin, HbA1c values between obese individuals with MetS and Non-MetS were consistent previous results. Among biomarkers for inflammatory state and endothelial dysfunction in MetS, uric acid level and hs-CRP levels were assayed in the study. The utility of high sensitivity C-reactive protein (hs-CRP) in predicting cardiovascular risk has been demonstrated in many studies.

Some previous studies showed that MetS is also considered a pro-inflammatory state, and measurement of inflammatory markers like hs-CRP might improve the prediction of cardiovascular disease in patients with MetS [23-27]. We suggest that uric acid, hs-CRP, ACR values were strong indicator for detecting inflammatory state and endothelial dysfunction.

Components of MetS are determined by the number criteria of NCEP ATP III. Each of the criteria per se carries risk factor for cardiovascular disorders. The number of the criteria increased, the risk also increased. When looking at comparisons between components of MetS and mean age, anthropometric measurements, lipid profile, blood pressure values, body fat composition, serum uric acid and hs-CRP level, the patients with MetS over three criteria were at great risk for cardiovascular disorders and significant metabolic deterioration, compared to MetS with three criteria. The number of positive MetS components seemed to be not more informative than classifying MetS for CVD risks assessment [24]. We found that hs-CRP level was positively correlated with components of MetS, but there was no significant difference in MetS with more than four criteria. Another study, contrary to our result, revealed no relation between components of

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MetS and body fat composition [26]. We obtained positive correlation between body visceral fat and MetS severity and we can suggest body visceral fat is significant indicator to predict MetS severity, and can suggest that body visceral fat was significant indicator for predicting severity of MetS, compared to total fat composition of body, BMI and WHR.

Although significant differences were observed between patients with MetS and Non-MetS, there were not differences between groups of MetS components, regarding liver functions, LDL-C, HbA1c and ACR level in the study. It means that cardiovascular risk or metabolic deterioration has begun after MetS developed. Those parameters were not good indicator for predicting severity of MetS.

The study weakness and strength

The weaknesses of the study were as follows. First of all, the study was designed as cross-sectional. Secondly, our study focused on MetS prevalence and component distribution in asymptomatic individuals and did not assess prevalence trends in persons with a history of CVD. Mortality and morbidity was not investigated. Thirdly, the majority of the study was middle-aged population. Current smokers were not excluded from the study. Fourthly, current smoker per se has great cardiovascular risk. Fifthly, female to male ratio was quite high. Lastly, the majority of the study subjects were female. We invited to participate in the study. We speculated that male individuals are workman and female ones utilize from health services. That was why female individuals mostly participate in our study. The strengths of the study were sample size and population based study. Subjects who were obese and overweight were referred to our clinics by their family physicians.

Conclusion

Metabolic syndrome can be seen also in individuals with overweight as well as with obesity. Being male, active smoker and over 45 years old carry greater risk for MetS development. Visceral fat accumulation is more associated with metabolic syndrome and its components. Obese individuals with MetS are prone to develop impaired liver function, metabolic deterioration, insulin resistance and albuminuria and cardiovascular events. We suggest that risk for

cardiovascular and steatohepatitis rises as the severity of MetS increases. BMI, age, increased BP, TG, HDL-C, FBG, IR, metabolic and cardiovascular risk. Albuminuria is not correlated with severity of MetS. We can suggest that uric acid and visceral body composition can be used to predict severity of MetS by family physicians in primary care settings, but we need to design several studies on predictive values of uric acid and visceral body fat composition for severity of MetS.

Disclosure of conflict of interest

None.

Abbreviations

MetS, Metabolic Syndrome; IFG, Impaired Fasting Glucose; WHR, Waist-Hip Ratio; BMI, Body Mass Index (kg/m^2); SBP, Systolic Blood Pressure (mm-Hg); DBP, Diastolic Blood Pressure (mm-Hg); BIE, Bioelectric impedance; BFA total (%), Total Body Fat Analysis (%); BFA visceral (%), Visceral Body Fat Analysis (%); FBG, Fasting Blood glucose (mg/dL); TG, Triglyceride (mg/dL); HDL-C, High Density Lipoprotein-Cholesterol (mg/dL); LDL-C, Light density lipoprotein-Cholesterol (mg/dL); TSH, Thyroid Stimulating Hormone (uIU/mL); UA, Uric acid (mg/dL); HOMA-IR, Homeostasis Model of Assessment-Insulin Resistance; HbA1c, Glycosylated Hemoglobin (%); hs-CRP, high sensitive C, reactive protein (mg/dL); ACR, albumin-to-creatinine ratio (mg/g).

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