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Original Article

Positive correlation of serum leptin levels with obesity and metabolic syndrome in patients with type 2 diabetes mellitus

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Abstract: Leptin is mainly produced in the adipose tissue and is considered to play an important role in appetite control, fat metabolism, and body weight regulation. The aim of this study was to evaluate the relationship between serum leptin concentration and metabolic syndrome (MetS) and obesity in type 2 diabetes mellitus (DM) patients. Fasting blood samples were obtained from 140 type 2 DM volunteers. MetS and its components were defined according to diagnostic criteria from the International Diabetes Federation. Among 140 type 2 DM patients, 95 (67.9%) had MetS and 66 (47.1%) had obesity. We found that female gender ($P = 0.001$), hypertension ($P = 0.005$), body weight ($P < 0.001$), body mass index (BMI, $P < 0.001$), body fat mass ($P < 0.001$), waist circumference ($P < 0.001$), systolic blood pressure ($P < 0.001$), diastolic blood pressure ($P < 0.001$), triglyceride level ($P = 0.001$), high-sensitivity C-reactive protein (hs-CRP, $P = 0.001$), fasting glucose level ($P = 0.022$), glycated hemoglobin level (HbA1c, $P = 0.012$), insulin level ($P < 0.001$), homeostasis model assessment of insulin resistance (HOMA-IR, $P < 0.001$), and leptin level ($P < 0.001$) were higher in DM patients who had MetS, while high-density lipoprotein cholesterol (HDL-C) levels ($P = 0.004$) were lower. Moreover, higher serum leptin levels were significantly ($P < 0.001$) correlated with BMI levels in our DM patients. Multivariate forward stepwise linear regression analysis revealed that body fat mass ($P < 0.001$), logarithmically transformed hs-CRP (log-hs-CRP, $P = 0.005$), and log-insulin ($P = 0.019$) were positively correlated with serum leptin levels in type 2 DM patients. In this study, a higher serum leptin level was found to be positively associated with MetS in type 2 DM patients.

Keywords: Metabolic syndrome, obesity, diabetes mellitus, leptin

Introduction

In 2011, there were 366 million people with diabetes, and this is expected to rise to 552 million in 2030, as per the International Diabetes Federation's definition [1]. Metabolic syndrome (MetS) is a disorder characterized by obesity, atherogenic dyslipidemia, elevated blood pressure (BP), high blood glucose level, and insulin resistance. MetS is considered to be an important risk factor for cardiovascular disease [2]. There is a high prevalence of MetS in type 2 diabetes mellitus (DM) patients, from 68.5% to 78.6%, and MetS is associated with a residual risk of cardiovascular disease [3-5].

Leptin is mainly produced in the adipose tissue and is considered to play an important role in appetite control, fat metabolism, and body weight regulation [6]. However, most obese individuals are hyperleptinemic, and resistance to the central actions of leptin is linked to obesity [7]. Leptin resistance leads to increased triglyceride accumulation in the adipose tissue, muscle, liver, and pancreas, resulting in insulin resistance [8]. Our previous studies have revealed that hyperleptinemia is associated with MetS in renal transplant recipients, hemodialysis patients, and hypertensive patients [9-11]. The aim of this study was to investigate the relationship between fasting serum leptin levels and MetS among type 2 DM patients.

Materials and methods

Patients

This was a prospective cross-sectional study conducted at a medical center in Hualien,

Table 1. Clinical variables of 140 diabetic patients with or without metabolic syndrome

Items	All participants (n = 140)	No metabolic syndrome (n = 45)	Metabolic syndrome (n = 95)	*P* value
Age (years)	63.04 ± 9.07	61.84 ± 9.27	63.60 ± 8.97	0.287
Height (cm)	161.55 ± 8.47	163.22 ± 8.19	160.75 ± 8.53	0.108
Body weight (kg)	70.33 ± 12.36	63.39 ± 9.02	73.62 ± 12.41	< 0.001*
Body mass index (kg/m^2)	26.86 ± 3.68	23.73 ± 2.37	28.34 ± 3.24	< 0.001*
Body fat mass (%)	31.08 ± 7.83	24.79 ± 5.62	34.06 ± 6.92	< 0.001*
Waist circumference (cm)	90.58 ± 8.82	83.49 ± 7.10	93.95 ± 7.48	< 0.001*
Systolic blood pressure (mmHg)	142.81 ± 19.94	130.35 ± 15.03	148.73 ± 19.29	< 0.001*
Diastolic blood pressure (mmHg)	82.88 ± 11.22	76.98 ± 9.05	85.67 ± 11.11	< 0.001*
Albumin (mg/dl)	4.30 ± 0.26	4.28 ± 0.21	4.31 ± 0.28	0.542
Total cholesterol (mg/dl)	161.17 ± 30.40	162.38 ± 28.91	160.00 ± 31.22	0.748
Triglyceride (mg/dl)	115.00 (84.25-170.50)	94.00 (61.50-129.00)	127.00 (91.00-190.00)	0.001*
HDL-C (mg/dl)	47.21 ± 12.56	51.56 ± 14.19	45.15 ± 11.21	0.004*
LDL-C (mg/dl)	98.26 ± 26.66	97.31 ± 23.97	98.71 ± 27.96	0.744
Fasting glucose (mg/dl)	139.00 (121.00-176.00)	125.00 (117.00-162.00)	145.00 (126.00-188.00)	0.022*
Glycated hemoglobin (%)	7.40 (6.60-8.78)	7.00 (6.20-8.05)	7.80 (6.60-9.20)	0.012*
Blood urea nitrogen (mg/dl)	16.00 (12.25-18.00)	15.00 (12.00-18.00)	16.00 (13.00-19.00)	0.080
Creatinine (mg/dl)	0.80 (0.70-1.00)	0.90 (0.70-1.00)	0.80 (0.70-1.00)	0.685
Hs-CRP (mg/dl)	0.09 (0.05-0.25)	0.05 (0.05-0.11)	0.12 (0.05-0.33)	0.001*
Insulin (uIU/ml)	6.55 (3.64-13.90)	4.25 (2.22-6.20)	9.39 (5.20-18.52)	< 0.001*
HOMA-IR	2.34 (1.32-5.39)	1.31 (0.77-2.12)	3.20 (1.90-7.02)	< 0.001*
Leptin (ng/ml)	20.74 (12.98-30.94)	15.08 (8.99-21.46)	23.39 (14.82-32.97)	< 0.001*
Female (n, %)	60 (42.9)	10 (22.2)	50 (52.6)	0.001*
Hypertension (n, %)	74 (52.9)	16 (35.6)	58 (61.1)	0.005*

Values for continuous variables given as means ± standard deviation and are tested by Student's *t*-test; variables not normally distributed given as medians and interquartile range and are tested by Mann-Whitney U test; for values presented as numbers (%), analysis was conducted using the chi-square test. HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; hs-CRP, high-sensitivity C-reactive protein. *$P < 0.05$ was considered statistically significant after Student's *t*-test or Mann-Whitney U test.

Taiwan, from November 2014 through March 2015. In total, 140 type 2 DM patients were enrolled in this study. Type 2 DM was determined according to the World Health Organization criteria [12]. The study was approved by the Protection of Human Subjects Institutional Review Board of Tzu-Chi University and Hospital and was conducted in accordance with the Declaration of Helsinki. All patients provided informed consent before participating in this study. BP was measured by trained staff in the morning using standard mercury sphygmomanometers with appropriate cuff sizes, after patients had been sitting for at least 10 min. Systolic BP (SBP) and diastolic BP (DBP) were measured 3 times at 5-min intervals and were averaged for analysis. Patients were classified as having hypertension if SBP was ≥ 140 mmHg and/or DBP was ≥ 90 mmHg or if they had taken any antihypertensive medication in the past 2 weeks. Patients were excluded if they had an acute infection, acute myocardial infarction, heart failure, or malignancy at the time of blood sampling or if they refused to provide informed consent for the study.

Anthropometric analysis

Body weight of the participants was measured in light clothing and without shoes to the nearest 0.5 kg, and body height was measured to the nearest 0.5 cm. Body mass index (BMI) was calculated as weight in kilograms divided by the square of height in meters. A single-frequency (50-kHz) bioimpedance analyzer (Biodynamic-450, Biodynamics Corporation, Seattle, USA) was used by an experienced operator, according to a standardized, tetrapolar, whole-body (hand-foot) technique and using a specific formula specified by the manufacturer to calculate and analyze the body fat mass. Waist circumference was measured using a tape measurement around the waist from the point between the lowest ribs and the hip bones with the hands on the hips. Measurements were performed by the same operator [3, 9-11, 13].

Table 2. Clinical variables of 140 diabetic patients with different body mass index values

Items	Normal (n = 30) BMI < 24	Overweight (n = 44) 24 ≤ BMI < 27	Obesity (n = 66) BMI > 27	*P* value
Age (years)	62.50 ± 8.50	64.84 ± 9.37	62.08 ± 9.08	0.276
Height (cm)	160.60 ± 9.93	161.61 ± 7.54	161.93 ± 8.45	0.775
Body weight (kg)	57.16 ± 7.61	66.73 ± 7.15	78.73 ± 10.33	< 0.001*
Body mass index (kg/m^2)	22.11 ± 1.67	25.48 ± 0.94	29.94 ± 2.41	< 0.001*
Body fat mass (%)	25.43 ± 6.53	29.68 ± 6.34	34.66 ± 7.48	< 0.001*
Waist circumference (cm)	81.83 ± 6.93	87.64 ± 5.58	96.53 ± 6.87	< 0.001*
Systolic blood pressure (mmHg)	137.47 ± 21.22	138.61 ± 17.48	148.05 ± 19.85	0.012*
Diastolic blood pressure (mmHg)	79.17 ± 9.78	79.43 ± 9.91	86.86 ± 11.46	< 0.001*
Albumin (mg/dl)	4.31 ± 0.20	4.26 ± 0.25	4.33 ± 0.28	0.390
Total cholesterol (mg/dl)	161.33 ± 26.00	160.09 ± 32.48	161.82 ± 31.24	0.958
Triglyceride (mg/dl)	92.50 (57.75-139.25)	113.50 (91.25-151.25)	129.00 (87.50-193.75)	0.015*
HDL-C (mg/dl)	52.87 ± 11.76	46.61 ± 13.37	45.03 ± 11.73	0.016*
LDL-C (mg/dl)	92.30 ± 22.31	99.27 ± 25.44	100.29 ± 29.13	0.381
Fasting glucose (mg/dl)	134.50 (113.00-189.75)	130.00 (118.15-169.50)	144.00 (126.00-185.50)	0.287
Glycated hemoglobin (%)	7.70 (6.43-8.90)	6.95 (6.53-8.10)	7.65 (6.60-9.40)	0.342
Blood urea nitrogen (mg/dl)	15.00 (12.00-19.75)	15.00 (12.00-18.75)	16.00 (14.00-18.00)	0.255
Creatinine (mg/dl)	0.80 (0.70-0.93)	0.80 (0.70-1.00)	0.90 (0.78-1.10)	0.434
Hs-CRP (mg/dl)	0.05 (0.05-0.13)	0.09 (0.05-0.17)	0.15 (0.05-0.36)	0.027*
Insulin (uIU/ml)	3.66 (1.96-6.74)	5.86 (3.37-8.52)	10.33 (5.78-21.74)	< 0.001*
HOMA-IR	1.33 (0.63-2.74)	2.01 (1.04-2.78)	3.65 (1.98-8.25)	< 0.001*
Leptin (ng/ml)	13.13 (8.39-21.55)	20.33 (12.24-29.58)	24.53 (17.19-33.07)	< 0.001*
Female (n, %)	15 (50.0)	18 (40.9)	27 (40.9)	0.672
Hypertension (n, %)	18 (60.0)	17 (38.6)	39 (59.1)	0.074

Values for continuous variables given as means ± standard deviation and are tested by 1-way analysis of variance; variables not normally distributed are given as medians and interquartile range and are tested by Kruskal-Wallis analysis; for values presented as numbers (%), analysis was conducted using the chi-square test. HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; hs-CRP, high-sensitivity C-reactive protein. *P < 0.05 was considered statistically significant after 1-way analysis of variance or Kruskal-Wallis analysis.

Biochemical investigations

Fasting blood samples (approximately 5 ml) from all the participants were immediately centrifuged at 3,000×g for 10 min after collection. Serum levels of albumin, blood urea nitrogen (BUN), creatinine, fasting glucose, glycated hemoglobin (HbA1c), total cholesterol (TCH), triglyceride (TG), high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), and high-sensitivity C-reactive protein (hs-CRP) were measured using an autoanalyzer (Siemens Advia 1800, Siemens Healthcare GmbH, Henkestr, Germany) [6-8]. Serum leptin concentrations were determined using a commercially available enzyme immunoassay (EIA) (SPI-BIO, Montigny le Bretonneux, France) [3, 9-11, 13]. Serum insulin levels were measured using a commercially available enzyme-linked immunosorbent assay (ELISA) (Labor Diagnostika Nord, Nordhorn, Germany) [11, 14, 15]. Insulin resistance was evaluated using a homeostasis model assessment of insulin resistance (HOMA-IR) as follows: HOMA-IR = fasting plasma glucose (mg/dl) × fasting serum insulin (μU/ml)/405 [3, 14, 15].

MetS and its components and obesity

In this study, MetS was defined according to the International Diabetes Federation's definition [16]. Participants were classified as having MetS if they had abdominal obesity (defined as waist circumference of > 90 cm for men and > 80 cm for women) and any 2 of the following 4 factors: (1) TG ≥ 150 mg/dl; (2) HDL-C < 40 mg/dl for men and < 50 mg/dl for women; (3) SBP ≥ 130 mmHg or DBP ≥ 85 mmHg or treatment of previously diagnosed hypertension; (4) fasting serum glucose ≥ 110 mg/dl or a previous diagnosis of type 2 DM. Obesity was defined as BMI ≥ 27 kg/m^2 and overweight was defined as a 27 kg/m^2 > BMI ≥ 24 kg/m^2, according to the criteria of the Department of Health in Taiwan [17].

Table 3. Clinical characteristics and fasting serum leptin levels of 140 diabetic patients

Characteristic		Number (%)	Leptin (ng/mL)	*P* value
Gender	Male	80 (57.1)	15.36 (11.41-22.95)	< 0.001*
	Female	60 (42.9)	27.85 (18.86-45.38)	
Hypertension	No	66 (47.1)	20.22 (13.10-26.99)	0.267
	Yes	74 (52.9)	21.71 (12.87-32.39)	
Statin	No	71 (50.7)	20.28 (12.60-28.80)	0.361
	Yes	69 (49.3)	21.21 (13.27-32.79)	
Fibrate	No	133 (95.0)	20.66 (12.90-29.66)	0.109
	Yes	7 (5.0)	46.64 (14.21-50.21)	
Metformin	No	60 (42.9)	20.70 (12.35-30.96)	0.625
	Yes	80 (57.1)	20.74 (13.72-30.68)	
Sulfonylureas	No	63 (45.0)	22.59 (14.25-32.94)	0.085
	Yes	77 (55.0)	18.81 (12.29-29.05)	
DDP-4 inhibitor	No	53 (37.9)	20.69 (14.19-29.17)	0.488
	Yes	87 (62.1)	20.79 (12.29-31.03)	
Thiazolidinediones	No	138 (98.6)	20.74 (12.91-30.77)	0.409
	Yes	2 (1.4)	35.88 (16.64-55.11)	
Insulin	No	105 (75.0)	20.79 (13.39-30.86)	0.670
	Yes	35 (25.0)	20.50 (12.60-31.95)	

Data are expressed as medians and interquartile range. *$P < 0.05$ was considered statistically significant after Mann-Whitney U test. DDP-4, dipeptidyl peptidase 4.

Statistical analysis

Data were tested for normal distribution using the Kolmogorov-Smirnov test. Normally distributed data are expressed as the mean ± standard deviation (SD), and comparisons between patients were performed by Student's independent t-test (2-tailed). Data that are not normally distributed are expressed as medians and interquartile ranges, and comparisons between patients were performed by Mann-Whitney U test (TG, fasting glucose, HbA1c, BUN, creatinine, hs-CRP, insulin, HOMA-IR, and leptin). Data expressed as the number of patients were analyzed by χ^2 test. The significance of differences in the measured values among groups (normal, overweight, and obese) was determined using Kruskal-Wallis analyses for parameters that presented with non-normal distributions or 1-way ANOVA for normally distributed data. TG, fasting glucose, HbA1c, BUN, creatinine, hs-CRP, insulin, HOMA-IR, and leptin were not normally distributed and underwent base 10 logarithmic transformations to achieve normality. Clinical variables that correlated with logarithmically transformed serum leptin (log-leptin) levels in DM patients were evaluated using univariate linear regression analysis. Variables that were significantly correlated with log-leptin levels in DM patients were tested for independence in multivariate forward stepwise regression analysis. Data were analyzed using SPSS for Windows (version 19.0; SPSS Inc., Chicago, IL, USA). A *P*-value of < 0.05 was considered statistically significant.

Results

Clinical characteristics of the 140 type 2 DM patients are presented in **Table 1**. Ninety-five DM patients (67.9%) had MetS and 45 (32.1%) did not. DM patients who had MetS included a higher proportion of females ($P = 0.001$) and, as expected, had more hypertension ($P = 0.005$) and higher body weight ($P < 0.001$), BMI ($P < 0.001$), body fat mass ($P < 0.001$), waist circumference ($P < 0.001$), SBP ($P < 0.001$), DBP ($P < 0.001$), TG level ($P = 0.001$), hs-CRP level ($P = 0.001$), fasting glucose level ($P = 0.022$), HbA1c level ($P = 0.012$), insulin level ($P < 0.001$), and HOMA-IR ($P < 0.001$) and lower HDL-C levels ($P = 0.004$) than DM patients who did not have MetS. Moreover, DM patients who had MetS had significantly higher serum fasting leptin levels than those who did not have MetS ($P < 0.001$).

Among these DM patients, 66 (47.1%) of them were obese and 44 (31.4%) were overweight. The comparisons of demographic, biochemical, anthropometric, and BMI levels in our patients according to obesity classification (normal, overweight, and obese) are shown in **Table 2**. Increased body weight ($P < 0.001$), BMI ($P < 0.001$), body fat mass ($P < 0.001$), waist circumference ($P < 0.001$), SBP ($P = 0.012$), DBP ($P < 0.001$), TG level ($P = 0.015$), hs-CRP level ($P = 0.027$), insulin level ($P < 0.001$), HOMA-IR ($P < 0.001$), and leptin level ($P < 0.001$) and decreased HDL-C levels ($P = 0.016$) were significantly correlated with BMI levels in our DM patients.

Table 4. Correlation of logarithmically transformed fasting serum leptin levels and clinical variables by univariable linear regression analyses among 140 diabetic patients

Items	Beta	*P* value
Age (years)	-0.024	0.779
Height (cm)	-0.295	< 0.001*
Body weight (kg)	0.063	0.457
Body mass index (kg/m^2)	0.309	< 0.001*
Body fat mass (%)	0.590	< 0.001*
Waist circumference (cm)	0.175	0.039*
Systolic blood pressure (mmHg)	0.157	0.065
Diastolic blood pressure (mmHg)	0.122	0.151
Albumin (mg/dl)	-0.010	0.910
Total cholesterol (mg/dl)	0.065	0.449
Log-Triglyceride (mg/dl)	0.123	0.148
HDL-C (mg/dl)	0.024	0.781
LDL-C (mg/dl)	0.081	0.342
Log-Glucose (mg/dl)	0.071	0.403
Log-HbA1c (%)	0.052	0.539
Log-BUN (mg/dl)	0.001	0.994
Log-Creatinine (mg/dl)	0.182	0.031*
Log-hs-CRP (mg/dl)	0.379	< 0.001*
Log-Insulin (uIU/ml)	0.366	< 0.001*
Log-HOMA-IR	0.358	< 0.001*

Data of triglyceride, glucose, HbA1c, BUN, creatinine, insulin, and HOMA-IR levels showed skewed distribution and were therefore log-transformed before analysis. *P < 0.05 was considered statistically significant after univariable linear analyses. HDL-cholesterol, high-density lipoprotein cholesterol; LDL-cholesterol, low-density lipoprotein cholesterol; BUN, blood urea nitrogen; hs-CRP, high-sensitivity C-reactive protein.

Clinical characteristics, drugs used, and serum leptin levels of the 140 DM patients are presented in **Table 3**. Differences in serum leptin levels failed to reach significance by subgroup analysis for gender distribution, hypertension, and metformin, sulfonylurea, dipeptidyl peptidase 4 inhibitors, thiazolidinedione, insulin, statin, or fibrate use.

Univariate linear analysis of clinical variables associated with fasting serum leptin levels in DM patients is presented in **Table 4**. Height (r = -0.295; P < 0.001) was negatively correlated, while BMI (r = 0.309; P < 0.001), body fat mass (r = 0.590; P < 0.001), waist circumference (r = 0.175; P < 0.039), logarithmically transformed creatinine (log-Cre, r = 0.182; P = 0.031), log-hs-CRP (r = 0.379; P < 0.001), log-insulin (r = 0.366; P < 0.001), and log-HOMA-IR (r = 0.358; P < 0.001) were positively correlated with serum leptin levels in type 2 DM patients.

Multivariate forward stepwise linear regression analysis of the variables significantly associated with fasting serum leptin levels revealed that body fat mass (adjusted R^2 change = 0.343; P < 0.001), log-hs-CRP (adjusted R^2 change = 0.032; P = 0.005), and log-insulin (adjusted R^2 change = 0.020; P = 0.019) were independent predictors of leptin levels for type 2 DM patients (**Table 5**).

Discussion

This study showed that fasting leptin levels were higher in type 2 DM patents with obesity and MetS. Body fat mass, log-hs-CRP, and log-insulin were independent predictors of serum leptin levels in type 2 DM patients.

Type 2 DM results from a progressive insulin secretory defect due to underlying insulin resistance and is characterized by hyperglycemia [18]. Obesity is the main risk factor for type 2 DM [19]. MetS is a cluster of cardiometabolic risk factors, including hyperglycemia, visceral obesity, hypertension, elevated TG levels, and low HDL-C levels; it has a major impact on the risk of cardiovascular disease and type 2 DM [2, 20]. In the United States, 70% of type 2 DM risk is attributable to overweight and obesity; each kilogram of weight gain over 10 years increases the risk by 4.5% [21]. In this study, the prevalence of MetS in type 2 DM patients was 67.9%; 31.4% patients were overweight and 47.1% were obese. In our study, type 2 DM patients who had MetS had significantly higher levels of hypertension as well as higher body weight, BMI, body fat mass, waist circumference, SBP, DBP, TG level, fasting glucose level, and HbA1c level, while they had lower HDL-C levels. Females are at a greater risk of central adiposity and favor adipose tissue storage and gain fat [22]. Our results revealed that type 2 diabetic patients who had MetS were more often females. MetS is generally characterized by central obesity accompanied by adipose tissue inflammation and adipose tissue dysfunction [23]. We revealed that diabetic patients who had MetS had significantly higher hs-CRP, insulin level, and HOMA-IR than diabetic patients who did not have MetS. Obesity is associated with the activation of pro-inflammatory pathways, i.e., the generation of systemic

Table 5. Multivariable stepwise linear regression analysis of gender, height, body mass index, body fat mass, waist circumference, log-creatinine, log-hs-CRP, log-insulin, and log-HOMA-IR: correlation with fasting serum log-leptin level among 140 diabetic patients

Items	Beta	Adjusted R square	Adjusted R square change	*P* value
Body fat mass (%)	0.473	0.343	0.343	< 0.001*
Log-hs-CRP (mg/dl)	0.180	0.375	0.032	0.005*
Log-insulin (uIU/ml)	0.167	0.395	0.020	0.019*

*$P < 0.05$ was considered statistically significant after multivariable stepwise linear regression analyses. hs-CRP, high-sensitivity C-reactive protein; HOMA-IR, homeostasis model assessment of insulin resistance.

insulin resistance and hyperglycemia [24]. Our results revealed that diabetic patients who had obesity had higher hs-CRP, insulin level, and HOMA-IR.

Leptin is mainly produced in the adipose tissue and is considered to play an important role in appetite control, fat metabolism, and body weight regulation [6, 7]. However, in obese subjects, elevated leptin levels are not sufficient to prevent body weight increase and dysregulation of energy balance, suggesting that obese people are leptin resistant [25]. Hyperleptinemia has been shown to be an independent risk factor for MetS in diabetic patients [26] and to be associated with MetS in renal transplant recipients, hemodialysis patients, and hypertensive patients [9-16]. We also revealed higher serum leptin levels in type 2 DM patients who had MetS. Serum leptin levels are higher in women than in men [9, 27]. Kidney failure leads to leptin accumulation in the circulation because of decreased leptin clearance [6]. We revealed that serum leptin levels had a positive correlation with serum creatinine levels in type 2 DM patients, and that correlation was higher in females. Leptin resistance is associated with impairment of leptin transport across the blood-brain barrier, reduction of leptin-mediated JAK-STAT signaling, and induction of suppressor of cytokine signaling-3 (SOCS-3) [7]. Leptin resistance is independently associated with insulin resistance, type 2 DM, hypertension, cardiovascular disease, and increased CRP in humans [28]. Serum leptin levels have been found to positively correlate with BMI, waist circumference, body fat mass, insulin, and HOMA-IR in an African population [29]. Our results showed that BMI, body fat mass, waist circumference, log-hs-CRP, log-insulin, and log-HOMA-IR were positively correlated with serum leptin levels in type 2 DM patients. After adjustment for various confounders using multivariable forward stepwise linear regression analysis, body fat mass, log-hs-CRP, and log-insulin remained positively associated with leptin levels in type 2 DM subjects.

There are some limitations to the present study. First, this study had a cross-sectional design without a control group and with a limited number of participants enrolled; thus, the possibility of bias cannot be excluded. Second, pharmacological interventions have been shown to influence serum leptin levels in humans. For example, simvastatin significantly increased plasma leptin levels and telmisartan increased serum leptin levels in hypertensive and type 2 DM patients [30, 31]. Our results did not show a relationship between statins, fibrates, or other antidiabetic drugs and serum leptin levels in the diabetic patients studied. Further studies are required to elucidate the relationship between medication and leptin in type 2 DM patients.

In conclusion, the present study showed that the serum leptin level was positively associated with MetS in type 2 DM patients. In addition, body fat mass, log-hs-CRP, and log-insulin are positively correlated with leptin levels.

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Disclosure of conflict of interest

None.

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