

Plasma Adiponectin Levels in Elderly Patients with Prediabetes

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Background: The significance of adiponectin levels in elderly individuals with prediabetes has yet to be determined. Thus, the present study was performed to evaluate the relationships between adiponectin levels and anthropometric variables, body composition parameters, insulin sensitivity, and lipid profiles in elderly prediabetic patients.

Methods: The present study included 120 subjects with prediabetes who were >65 years of age and were selected from among 1,993 subjects enrolled in the Korea Rural Genomic Cohort Study. All subjects underwent a 75 g oral glucose tolerance test and tests for measurement of insulin sensitivity. All diagnoses of prediabetes satisfied the criteria of the American Diabetes Association.

Results: Plasma adiponectin levels were lower in elderly prediabetic subjects than elderly subjects with normal glucose tolerance ($P<0.01$) as well as in elderly prediabetic patients with metabolic syndrome (MetS) than in those without MetS ($P<0.02$). When the subjects were categorized into two groups according to plasma adiponectin levels, the waist-to-hip ratio and 2-hour insulin levels were significantly lower in individuals with high plasma adiponectin levels than in those with low plasma adiponectin levels. Additionally, the plasma adiponectin levels of elderly prediabetic subject were inversely correlated with body mass index (BMI), waist circumference (WC), waist-to-hip ratio, visceral fat, visceral fat ratio, and 2-hour insulin levels.

Conclusion: The present findings demonstrated that the major factors correlated with adiponectin levels in elderly prediabetic subjects were BMI, WC, waist-to-hip ratio, visceral fat, visceral fat ratio, and 2-hour insulin levels.

Keywords: Aged; Prediabetic state; Adiponectin; Metabolic syndrome

INTRODUCTION

Type 2 diabetes mellitus (T2DM) and obesity are major public health problems, the incidences of which are rapidly increasing worldwide [1,2]. Furthermore, the global population is aging rapidly, and all countries, including Korea, have undergone a rapid increase in the rates of obesity among the elderly. For example, a recent report from the Korea Centers for Disease Control and Prevention found that the mean prevalence of obesity in

individuals >65 years of age increased from 25.0% in 1998 to 34.2% in 2012 [3] and another study found that aging is associated with an increased body fat mass and insulin resistance [4]. Obesity, particularly central obesity, is associated with insulin resistance, dyslipidemia, and hypertension and is a strong risk factor of cardiovascular disease (CVD) [5,6]. Taken together, these data suggest that obesity, insulin resistance, and aging are closely related.

Adiponectin is an adipose tissue-specific adipokine that plays

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a protective role against insulin resistance and inflammation and also protects the body against metabolic diseases [7,8]. T2DM and the accumulation of visceral fat decrease adiponectin levels [9] via the inhibitory actions of tumor necrosis factor- α on the adiponectin gene [10]. A prospective cohort study that analyzed 372 elderly Korean subjects established a relationship between reduced plasma adiponectin levels and T2DM or metabolic syndrome (MetS) [11]. Additionally, a cross-sectional study of patients with impaired fasting glucose (IFG) revealed that plasma adiponectin levels are associated with the risk of CVD [12]. According to the majority of studies investigating prediabetic patients, adiponectin levels are related to a number of body composition parameters, lipid profiles, insulin resistance factors (such as the homeostasis model assessment of insulin resistance [HOMA-IR] index), and various serum biomarkers of CVD. However, the significance of adiponectin levels in elderly prediabetic individuals has yet to be determined.

Thus, the present study evaluated the relationship between plasma adiponectin levels and clinical factors including anthropometric variables, body composition parameters, insulin sensitivity, and lipid profiles in elderly patients with prediabetes.

METHODS

Subjects

The present study included 120 individuals with prediabetes who were >65 years of age and were selected from among 1993 subjects enrolled in the Korea Rural Genomic Cohort Study (Geumsan County). Institutional Review Board of Chungnam National University Hospital approval was obtained prior to commencement of the study and all participants provided written informed consent prior to participation.

MetS was diagnosed in accordance with the updated International Diabetes Federation guidelines [13] and all diagnoses of prediabetes satisfied the 2014 criteria of the American Diabetes Association [14]. Subjects who were newly diagnosed with diabetes were excluded from the present study. Each subject completed a standardized questionnaire concerning their personal medical history of chronic and acute illnesses and medication use.

Anthropometric and body composition measurements

All subjects underwent measurements of several anthropometric variables including height, body weight, waist circumference (WC), blood pressure (BP), and body mass index (BMI).

A single experimenter performed both the height and weight measurements, WC was measured from the midpoint between the lowest rib and the iliac crest upon expiration, and BP was measured after at least 5 minutes of rest while in a seated position using the right arm of the patients. BMI was calculated as weight (kg) divided by height squared (m^2) and body composition was calculated using a bioelectric impedance analysis (InBody 4.0, Biospace Co., Seoul, Korea) that included fat mass, percent body fat, and lean mass.

Laboratory analysis

After a 12-hour overnight fast, all subjects underwent a 75 g oral glucose tolerance test, blood chemistry analysis, and measurement of their plasma adiponectin levels. Serum insulin levels were measured with the Coat-A-Count radioimmunoassay (RIA, DPC, Los Angeles, CA, USA) and plasma adiponectin levels were measured using a Human Adiponectin RIA kit (Linco Research Inc., Saint Louis, MO, USA). Insulin resistance was estimated using the HOMA-IR index and the quantitative insulin sensitivity check index (QUICKI) using the following formulae: $HOMA-IR = (\text{fasting insulin } [\mu\text{U/mL}] \times \text{fasting plasma glucose } [\text{mmol/L}]) / 405$ and $QUICKI = 1 / (\log \text{fasting insulin } [\mu\text{U/mL}] + \log \text{fasting plasma glucose } [\text{mg/dL}])$.

Pulse-wave velocity

Brachial-ankle pulse-wave velocity (baPWV) was measured using a pulse wave analyzer (BP-203RPE, Colin, Komaki, Japan) and defined as the mean of the left- and right-sided baPWV values. The pulse waves of the brachial and tibial arteries were simultaneously recorded using an oscillometric method.

Statistical analysis

All statistical analyses were conducted using SPSS version 21.0 (IBM Co., Armonk, NY, USA) and all statistical values are presented as mean \pm standard deviations. Student *t* tests were used to compare the baseline characteristics of the normal glucose tolerance (NGT) and prediabetic groups and unpaired *t* tests were used to compare the mean anthropometric variables and clinical parameters of the groups with and without MetS. Pearson's correlation coefficients were calculated to evaluate the relationships between adiponectin levels and blood lipid profiles, anthropometric factors, body composition variables, and surrogate markers of insulin resistance in newly diagnosed elderly prediabetic subjects and elderly subjects with NGT. *P* values <0.05 were considered to indicate statistical significance.

RESULTS

Characteristics of the subjects

The present study included 120 newly diagnosed elderly prediabetic subjects and 100 elderly NGT subjects. The glucose and glycosylated hemoglobin (HbA1c) levels of the elderly prediabetic subjects were higher than those of the elderly NGT subjects. Additionally, the prediabetic subjects had significantly higher

glucose and glycosylated hemoglobin (HbA1c) levels of the elderly prediabetic subjects were higher than those of the elderly NGT subjects. Additionally, the prediabetic subjects had significantly higher

Table 1. Baseline Characteristics of the Study Subjects

Characteristic	NGT	Prediabetes	Male		Female	
			NGT	Prediabetes	NGT	Prediabetes
No. of subjects	100	120	33	55	67	65
Age, yr	67.13±1.69	67.20±1.81	67.09±1.82	67.38±1.94	67.15±1.64	67.05±1.69
BMI, kg/m ²	23.92±3.25	24.30±3.14	24.14±2.37	23.90±3.41	23.82±3.62	24.64±2.88
WC, cm	80.77±8.14	82.42±8.54	82.21±6.94	80.87±8.48	80.05±8.62	83.72±8.43 ^a
HC, cm	91.45±6.23	92.78±6.53	91.11±6.45	91.16±6.69	91.61±6.16	94.14±6.11 ^a
Waist-to-hip ratio	0.88±0.07	0.88±0.05	0.90±0.10	0.88±0.05	0.87±0.05	0.88±0.05
Total body fat, kg	16.68±5.52	17.7±5.86	17.34±3.75	17.54±6.92	16.36±6.21	17.89±4.83
Visceral fat, kg	2.11±0.88	2.36±0.91 ^a	2.14±0.61	2.27±0.97	2.09±0.99	2.44±0.86 ^a
Total body fat ratio	27.59±6.31	28.53±6.99	29.31±5.10	28.71±7.82	26.74±6.70	28.38±6.27 ^a
Visceral fat ratio	10.33±2.95	11.49±2.67 ^b	10.54±2.64	11.50±2.91	10.23±3.10	11.48±2.48 ^a
Total muscle, kg	39.42±6.98	39.90±7.03	37.33±6.21	37.95±5.91	40.45±7.15	41.58±7.52
Fasting glucose, mmol/L	4.91±6.35	5.38±0.55 ^b	4.94±0.36	5.36±0.55 ^b	4.90±0.35	5.39±0.55 ^b
2-Hour glucose, mmol/L	6.13±1.06	8.10±1.74 ^b	6.34±0.84	8.21±1.59 ^b	6.03±1.15	8.01±1.86 ^b
Fasting insulin, pmol/L	52.16±17.15	64.31±36.18 ^b	53.48±11.95	65.84±40.98 ^a	51.46±19.24	62.99±31.81 ^a
2-Hour insulin, pmol/L	281.76±158.00	362.74±300.30 ^b	274.05±132.02	358.29±207.79 ^a	285.51±170.15	366.56±362.95
HbA1c, %	5.25±0.27	5.63±0.36 ^b	5.29±0.19	5.66±0.31 ^b	5.23±0.22	5.60±0.40 ^b
HOMA-IR index	1.65±0.58	2.24±1.40 ^b	1.69±0.42	2.29±1.57 ^a	1.62±0.65	2.21±1.25 ^b
QUICKI	0.35±0.02	0.34±0.02 ^b	0.35±0.01	0.34±0.02 ^b	0.36±0.02	0.34±0.02 ^b
TC, mmol/L	5.30±0.96	5.72±1.00 ^b	5.59±0.88	5.73±1.09	5.15±0.98	5.72±0.92 ^b
TG, mmol/L	1.69±0.97	2.04±1.19 ^a	1.77±0.88	2.14±1.22	1.66±1.02	1.96±1.17
HDL-C, mmol/L	1.18±0.27	1.18±0.30	1.17±0.28	1.20±0.33	1.19±0.26	1.18±0.23
LDL-C, mmol/L	3.14±0.83	3.41±0.83 ^b	3.44±0.76	3.39±0.89	2.99±0.82	3.43±0.78 ^b
Adiponectin, µg/mL	12.71±4.76	10.39±4.56 ^b	14.07±4.68	10.72±4.74 ^a	11.91±4.67	9.86±4.14 ^a
PWV, m/s	15.30±2.70	16.13±3.40 ^a	18.29±2.33	18.86±2.60	13.83±1.28	14.04±1.03
SBP, mm Hg	131.17±15.99	136.87±16.60 ^b	139.58±15.25	145.76±16.43	127.03±14.77	129.34±12.67
DBP, mm Hg	82.66±9.51	85.78±10.14 ^b	86.97±9.28	88.89±10.84	80.54±8.95	83.15±8.77
AST, U/L	27.04±7.82	29.30±10.32	26.51±6.62	30.85±11.56	27.29±8.38	27.98±13.47
ALT, U/L	22.29±12.07	26.49±12.28 ^a	21.78±10.50	26.14±10.81	22.53±12.83	26.78±13.47
γ-GTP, U/L	24.54±23.29	34.21±42.06 ^a	21.42±13.36	32.23±31.80 ^a	26.07±26.83	35.89±49.29
hs-CRP, mg/dL	1.47±2.11	1.98±3.84	1.49±2.13	1.47±2.11	1.45±2.03	2.41±4.83 ^a
Ferritin, µg/L	67.64±50.06	102.31±97.67 ^b	68.87±43.86	102.06±93.80	67.03±53.15	102.53±101.56 ^a

Values are expressed as mean±SD. Two-hour glucose and 2-hour insulin represent glucose and insulin levels at 120 minutes after a glucose challenge. NGT, normal glucose tolerance; BMI, body mass index; WC, waist circumference; HC, hip circumference; HbA1c, glycosylated hemoglobin; HOMA-IR, homeostasis model assessment of insulin resistance; QUICKI, quantitative insulin sensitivity check index; TC, total cholesterol; TG, triglyceride; HDL-C, high density lipoprotein cholesterol; LDL-C, low density lipoprotein cholesterol; PWV, pulse-wave velocity; SBP, systolic blood pressure; DBP, diastolic blood pressure; AST, aspartate aminotransferase; ALT, alanine aminotransferase; γ-GTP, gamma-glutamyl transpeptidase; hs-CRP, high-sensitivity C-reactive protein.

^a*P*<0.05 vs. NGT; ^b*P*<0.01 vs. NGT.

amounts of visceral fat, a higher visceral fat ratio, a higher HOMA-IR index, higher fasting and 2-hour insulin levels, and higher levels of HbA1c, total cholesterol (TC), triglyceride (TG), low density lipoprotein cholesterol (LDL-C), PWV, BP, and ferritin but lower QUICK scores than the elderly NGT subjects. On the other hand, the NGT subjects had significantly higher plasma adiponectin levels than the prediabetic subjects ($12.71 \pm 4.76 \mu\text{g/mL}$ vs. $10.39 \pm 4.56 \mu\text{g/mL}$, respectively; $P < 0.01$). Additionally, the anthropometric variables—WC, hip circumference (HC), visceral fat, the visceral fat ratio, and the total body fat ratio—were significantly higher in prediabetic females, but not males, relative to the NGT subjects (Table 1).

Clinical profiles of the elderly prediabetic subjects according to the presence of MetS

The elderly prediabetic subjects were separated into two groups based on the presence or absence of MetS. There were significant differences between subjects with and without MetS in all of the anthropometric variables and body composition parameters, fasting glucose levels, fasting insulin levels, 2-hour insulin levels, and insulin resistance-related factors, including the HOMA-IR index and QUICK. However, there were no significant differences in high density lipoprotein cholesterol (HDL-C), LDL-C, TC, and BP levels. The subjects without MetS had significantly higher plasma adiponectin levels than did those with MetS ($11.10 \pm 4.62 \mu\text{g/mL}$ vs. $8.61 \pm 3.48 \mu\text{g/mL}$, respectively; $P < 0.02$) (Table 2).

Clinical profiles according to plasma adiponectin levels

When the subjects were categorized into two groups according to plasma adiponectin levels, the high plasma adiponectin group had significantly lower waist-to-hip ratio and 2-hour insulin levels than the low plasma adiponectin group. All of the anthropometric variables, except waist-to-hip ratio, all body composition parameters, and the fasting glucose, 2-hour glucose, TC, LDL-C, and BP levels were higher in the high plasma adiponectin group than in the low plasma adiponectin group; however, there were no significant differences (Table 3).

Correlations between adiponectin levels and clinical profiles

The Pearson's correlation coefficients between the subjects' adiponectin levels and lipid profiles, anthropometric variables, body composition parameters, and surrogate markers of insulin resistance are shown in Table 4. In the elderly prediabetic subjects, adiponectin levels were inversely correlated with BMI ($r = -0.249$,

Table 2. Clinical and Biochemical Characteristics of Elderly Prediabetic Subjects with and without Metabolic Syndrome

Characteristic	Non-MetS	MetS
No. of subjects	85	35
Age, yr	67.33 \pm 1.91	66.89 \pm 1.51
BMI, kg/m ²	23.16 \pm 2.59	27.08 \pm 2.58 ^b
WC, cm	78.61 \pm 6.85	91.67 \pm 3.84 ^b
HC, cm	90.42 \pm 5.68	98.49 \pm 4.69 ^b
Waist-to-hip ratio	0.87 \pm 0.04	0.93 \pm 0.04 ^b
Total body fat, kg	16.01 \pm 5.58	21.91 \pm 4.20 ^b
Visceral fat, kg	1.98 \pm 0.70	3.29 \pm 0.67 ^b
Total body fat ratio	27.43 \pm 6.95	31.20 \pm 6.44 ^b
Visceral fat ratio	10.51 \pm 2.40	13.86 \pm 1.64 ^b
Total muscle, kg	37.87 \pm 5.74	44.84 \pm 7.50 ^b
Fasting glucose, mmol/L	5.30 \pm 0.50	5.56 \pm 0.62 ^a
2-Hour glucose, mmol/L	8.11 \pm 1.66	8.09 \pm 1.94
Fasting insulin, pmol/L	56.39 \pm 27.15	83.62 \pm 47.16 ^b
2-Hour insulin, pmol/L	305.72 \pm 211.27	498.65 \pm 419.96 ^b
HbA1c, %	5.62 \pm 0.36	5.65 \pm 0.37
HOMA-IR index	1.92 \pm 0.96	3.04 \pm 1.91 ^b
QUICKI	0.35 \pm 0.02	0.33 \pm 0.02 ^b
TC, mmol/L	5.70 \pm 1.01	5.76 \pm 1.00
TG, mmol/L	1.89 \pm 1.14	2.41 \pm 1.25 ^a
HDL-C, mmol/L	1.21 \pm 0.31	1.13 \pm 0.20
LDL-C, mmol/L	3.42 \pm 0.83	3.39 \pm 0.85
Adiponectin, $\mu\text{g/mL}$	11.10 \pm 4.62	8.61 \pm 3.48 ^a
PWV, m/sec	16.31 \pm 3.55	15.71 \pm 3.00
SBP, mm Hg	136.20 \pm 17.05	138.49 \pm 15.60
DBP, mm Hg	84.36 \pm 10.15	89.23 \pm 9.40
AST, U/L	28.56 \pm 10.39	31.08 \pm 10.07
ALT, U/L	23.44 \pm 10.15	33.88 \pm 13.91 ^b
γ -GTP, U/L	26.23 \pm 23.25	53.60 \pm 65.65 ^a
hs-CRP, mg/dL	1.82 \pm 3.52	2.37 \pm 4.57
Ferritin, $\mu\text{g/L}$	87.33 \pm 87.53	138.71 \pm 111.95 ^b

Values are expressed as mean \pm SD. Two-hour glucose and 2-hour insulin represent glucose and insulin levels at 120 minutes after a glucose challenge.

MetS, metabolic syndrome; BMI, body mass index; WC, waist circumference; HC, hip circumference; HbA1c, glycated hemoglobin; HOMA-IR, homeostasis model assessment of insulin resistance; QUICKI, quantitative insulin sensitivity check index; TC, total cholesterol; TG, triglyceride; HDL-C, high density lipoprotein cholesterol; LDL-C, low density lipoprotein cholesterol; PWV, pulse-wave velocity; SBP, systolic blood pressure; DBP, diastolic blood pressure; AST, aspartate aminotransferase; ALT, alanine aminotransferase; γ -GTP, gamma-glutamyl transpeptidase; hs-CRP, high-sensitivity C-reactive protein.

^a $P < 0.05$ vs. non-MetS; ^b $P < 0.01$ vs. non-MetS.

Table 3. Clinical and Biochemical Characteristics according to Plasma Adiponectin Level

Characteristic	Plasma adiponectin level	
	Low	High
No. of subjects	36	36
Age, yr	66.94±1.63	67.14±1.80
BMI, kg/m ²	24.88±2.95	24.16±3.31
WC, cm	84.24±8.85	81.40±8.85
HC, cm	92.94±6.15	92.96±7.31
Waist-to-hip ratio	0.90±0.06	0.87±0.05 ^a
Total body fat, kg	18.65±5.08	18.09±7.23
Visceral fat, kg	2.61±0.86	2.33±0.96
Visceral fat ratio	12.13±2.16	11.58±3.11
Total muscle, kg	41.06±7.29	38.59±6.78
Fasting glucose, mmol/L	5.37±0.59	5.30±0.64
2-Hour glucose, mmol/L	8.25±1.74	7.80±1.86
Fasting insulin, pmol/L	72.99±47.85	67.37±36.46
2-Hour insulin, pmol/L	520.94±585.05	337.04±179.88 ^a
HbA1c, %	5.68±0.41	5.70±0.30
HOMA-IR index	2.55±1.89	2.33±1.39
QUICKI	0.34±0.02	0.34±0.02
TC, mmol/L	5.83±0.96	5.77±0.97
TG, mmol/L	2.09±0.91	2.18±1.60
HDL-C, mmol/L	1.22±0.25	1.23±0.36
LDL-C, mmol/L	3.46±0.84	3.34±0.78
PWV, m/sec	16.29±3.55	16.14±4.15
SBP, mm Hg	140.03±18.17	137.47±14.35
DBP, mm Hg	88.28±11.14	86.47±8.19
AST, U/L	29.75±8.23	31.44±12.89
ALT, U/L	29.13±12.77	25.02±10.29
γ-GTP, U/L	38.00±35.40	35.19±59.99
hs-CRP, mg/dL	3.32±6.39	1.72±2.31
Ferritin, μg/L	111.76±95.52	90.74±79.92

Values are expressed as mean±SD. Two-hour glucose and 2-hour insulin represent glucose and insulin levels at 120 minutes after a glucose challenge.

BMI, body mass index; WC, waist circumference; HC, hip circumference; HbA1c, glycated hemoglobin; HOMA-IR, homeostasis model assessment of insulin resistance; QUICKI, quantitative insulin sensitivity check index; TC, total cholesterol; TG, triglyceride; HDL-C, high density lipoprotein cholesterol; LDL-C, low density lipoprotein cholesterol; PWV, pulse-wave velocity; SBP, systolic blood pressure; DBP, diastolic blood pressure; AST, aspartate aminotransferase; ALT, alanine aminotransferase; γ-GTP, gamma-glutamyl transpeptidase; hs-CRP, high-sensitivity C-reactive protein.

^aP<0.05 vs. low.

Table 4. Pearson's Correlation Coefficients for the Relationships between Adiponectin Levels and the Clinical and Biochemical Characteristics of Elderly Prediabetic Patients and Elderly Subjects with Normal Glucose Tolerance

Characteristic	<i>r</i>	
	NGT	Prediabetes
BMI, kg/m ²	-0.164	-0.249 ^a
WC, cm	-0.244	-0.282 ^a
HC, cm	-0.168	-0.132
Waist-to-hip ratio	-0.182	-0.321 ^b
Total body fat, kg	-0.255 ^a	0.046
Visceral fat, kg	-0.309 ^a	-0.306 ^b
Total body fat ratio	-0.110	-0.138
Visceral fat ratio	-0.268 ^a	-0.326 ^b
Total muscle, kg	-0.311 ^a	-0.219
SBP, mm Hg	0.280	0.088
DBP, mm Hg	-0.149	-0.112
Fasting glucose, mmol/L	-0.004	-0.185
2-Hour glucose, mmol/L	0.035	-0.134
Fasting insulin, pmol/L	-0.190	-0.090
2-Hour insulin, pmol/L	-0.009	-0.242 ^a
HbA1c, %	-0.181	-0.015
HOMA-IR index	-0.184	-0.110
QUICKI	0.153	0.175
TC, mmol/L	0.117	-0.080
TG, mmol/L	-0.355 ^b	0.013
HDL-C, mmol/L	0.323 ^a	0.038
LDL-C, mmol/L	0.125	-0.139
AST, U/L	-0.049	0.047
ALT, U/L	-0.308 ^a	-0.158
γ-GTP, U/L	-0.229	-0.154
hs-CRP, mg/dL	-0.211	-0.185
Ferritin, μg/L	0.162	-0.034

Two-hour glucose and 2-hour insulin represent glucose and insulin levels at 120 minutes after a glucose challenge. *r* refers to Pearson's correlation coefficient.

NGT, normal glucose tolerance; BMI, body mass index; WC, waist circumference; HC, hip circumference; SBP, systolic blood pressure; DBP, diastolic blood pressure; HbA1c, glycated hemoglobin; HOMA-IR, homeostasis model assessment of insulin resistance; QUICKI, quantitative insulin sensitivity check index; TC, total cholesterol; TG, triglyceride; HDL-C, high density lipoprotein cholesterol; LDL-C, low density lipoprotein cholesterol; AST, aspartate aminotransferase; ALT, alanine aminotransferase; γ-GTP, gamma-glutamyl transpeptidase; hs-CRP, high-sensitivity C-reactive protein.

^aP<0.05; ^bP<0.01.

$P < 0.05$), WC ($r = -0.282$, $P < 0.05$), waist-to-hip ratio ($r = -0.321$, $P < 0.01$), visceral fat ($r = -0.306$, $P < 0.01$), the visceral fat ratio ($r = -0.326$, $P < 0.01$), and the 2-hour insulin levels ($r = -0.242$, $P < 0.05$). In the elderly NGT subjects, adiponectin levels were inversely correlated with total body fat ($r = -0.255$, $P < 0.05$), visceral fat ($r = -0.309$, $P < 0.05$), the visceral fat ratio ($r = -0.268$, $P < 0.05$), total muscle ($r = -0.311$, $P < 0.05$), alanine aminotransferase levels ($r = -0.308$, $P < 0.05$) but positively correlated with TG ($r = 0.355$, $P < 0.01$) and HDL-C ($r = 0.242$, $P < 0.05$) levels.

DISCUSSION

The findings of the present study clearly demonstrated that increased insulin resistance and MetS were related to low adiponectin levels in elderly prediabetic patients. Additionally, the plasma adiponectin levels of these patients were correlated with the waist-to-hip ratio, visceral fat, and the visceral fat ratio, which are indicators of central obesity.

Many studies have reported that plasma adiponectin levels decrease as insulin resistance increases. For example, diabetic and obese monkeys have decreased adiponectin levels prior to the development of diabetes, and this decrease in adiponectin levels parallels changes in insulin sensitivity [15]. In a study of 376 prediabetic patients, the prediabetic group exhibited a significantly lower mean \pm SD adiponectin level compared to NGT subjects (4.6 ± 2.3 $\mu\text{g/mL}$ vs. 5.0 ± 2.8 $\mu\text{g/mL}$ in males, and 7.1 ± 3.6 $\mu\text{g/mL}$ vs. 8.1 ± 4.6 $\mu\text{g/mL}$ in females, respectively; $P < 0.001$) [16]. Similarly, in the present study elderly prediabetic patients had significantly lower adiponectin levels than elderly individuals with NGT (10.2 ± 4.3 $\mu\text{g/mL}$ vs. 12.7 ± 4.7 $\mu\text{g/mL}$, respectively; $P < 0.001$).

Additionally, there were significant differences between the visceral fat level and visceral fat ratio of elderly prediabetic subjects and elderly NGT subjects. This finding suggests that, similar to the general population, the accumulation of visceral fat was related to insulin resistance in elderly prediabetic patients. Additionally, the BP, baPWV, and lipid profiles of the elderly prediabetic subjects exhibited significant increases compared to those of the elderly NGT subjects. This suggests that a prediabetes status in elderly patients is associated with the risk of CVD and metabolic diseases.

In the present study, all measures of the anthropometric variables and body composition parameters were higher in the prediabetic females than the prediabetic males. Furthermore, compared to the NGT subjects, anthropometric variables—such as WC, HC, visceral fat, the visceral fat ratio, and the total body

fat ratio—were significantly higher in prediabetic females but not males. It is possible that changes in the hormonal status of females during menopause and aging result in increases in measures of central fat distribution and visceral fat accumulation. Previous studies have shown that testosterone decreases adiponectin levels [17] and that the adiponectin levels of males are lower than those of females [16-19]. However, in the present study, the adiponectin levels of males were higher than those of females. It has been demonstrated that effective estradiol treatment decreases adiponectin levels in postmenopausal females [20,21] and the present study indicates that a higher visceral fat ratio and higher BMI, WC, and visceral fat levels in females influence adiponectin levels.

Clinical and experimental studies have indicated that adiponectin directly affects obesity-related disorders, insulin resistance, and atherosclerosis [22-25]. Additionally, it is known that adiponectin plays an essential role in the development of MetS because there is a general correlation between MetS and plasma adiponectin levels in normal healthy subjects [26]. Furthermore, large population-based studies have shown that adiponectin levels in individuals with IFG and MetS are significantly lower than those of subjects with IFG but without MetS [12]. Similarly, the present study found that elderly prediabetic subjects with MetS had lower levels of adiponectin than the prediabetic subjects without MetS (11.10 ± 4.62 $\mu\text{g/mL}$ vs. 8.61 ± 3.48 $\mu\text{g/mL}$, respectively; $P < 0.02$). Additionally, the associations between the metabolic parameters and plasma adiponectin levels of IFG and NGT subjects in the present study were similar to those reported in previous studies [12,20]

Low adiponectin levels likely play a major role in the development of MetS [27,28]. A prospective cohort study that analyzed 372 elderly subjects divided into tertiles based on adiponectin levels found that individuals in the lowest tertile were 3.2-fold more likely to develop T2DM (95% confidence interval [CI], 1.415 to 7.295; $P = 0.005$) and 2.7-fold more likely to develop MetS (95% CI, 0.94 to 6.70; $P = 0.031$) than subjects in the highest tertile [11]. A study of 661 Japanese individuals reported that the components of MetS increased as adiponectin levels decrease [29] and a study of 596 healthy Korean subjects observed an association between low adiponectin levels and MetS [26]. However, in the present study, the elderly subjects with low adiponectin levels only showed significant increases in their waist-to-hip ratio and 2-hour insulin levels.

Many studies have found a correlation between plasma adiponectin levels and the metabolic profiles of various populations, including normal healthy adults, adults with central obesi-

ty, individuals with IFG, and T2DM patients [11,12,30-34]. In a majority of these studies, adiponectin levels were found to be correlated with metabolic parameters and serum biomarkers of insulin resistance or the risk of CVD. However, in the present study, adiponectin levels were negatively correlated with BMI, WC, the waist-to-hip ratio, visceral fat, the visceral fat ratio, and 2-hour insulin levels. Therefore, central obesity, particularly in conjunction with the accumulation of visceral fat, had the highest correlation with adiponectin levels in elderly prediabetic patients.

The present study has several limitations. First, the cross-sectional design and small sample size of this study meant that data regarding the exact predictive values of adiponectin levels in terms of the risks of T2DM and CVD or changes in adiponectin within specific individuals could not be obtained. Second, the present study was unable to adjust for MetS-related lifestyle factors. Nevertheless, this study is the first to investigate the relationships between various metabolic parameters and adiponectin levels in elderly prediabetic subjects.

In conclusion, the present study found that the clinical and biochemical characteristics associated with adiponectin levels in elderly prediabetic subjects were similar to those of prediabetic subjects of all ages, with only a few exceptions. Large-scale longitudinal prospective studies are needed to clarify the role of adiponectin in the development of T2DM and CVD.

CONFLICTS OF INTEREST

No potential conflict of interest relevant to this article was reported.

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