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ARTICLE

Serum omentin-1 levels in hypertensive patients

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Abstract

Hypertension (HT) is a disease that can cause death due to multiple target organ damage and eventually related vascular system damage. High blood pressure is known increased inflammatory activity and to cause endothelial dysfunction has been showed in HT patients. Omentin-1 is a glucoprotein of the adiponectin family released from visceral adipose tissue, endothelial cells, and visceral fat stromal–vascular cells. It has anti-inflammatory effect and circulating omentin-1 concentration correlates negatively with waist circumference, insulin resistance, and body-mass index. Serum omentin-1 is used as a biomarker of coronary artery disease, obesity, cancer, metabolic syndrome, inflammatorydisease, atherosclerosis, and diabetes mellitus. The aim of our study is to investigate circulating omentin-1 levels in HT patients compared to healthy normotensive controls. Patients diagnosed with new essential HT ($n = 61$) and healthy normotensive individuals ($n = 60$) were enrolled in this study. The HT group was separated into two subgroups. There were 30 patients in stage 2 HT group and 31 patients in stage 1 HT group. Omentin-1 levels were significantly lower both in stage 1 and 2 HT subgroup as compared with the normotensive controls (72.19 ± 54.33 ng/ml for stage 1 HT subgroup; 62.45 ± 47.01 ng/ml for stage 2 HT subgroup; and, 147.84 ± 58.55 ng/ml for healthy normotensive controls; overall $P < 0.001$). The present study demonstrated that serum Omentin-1 levels decreased in patients with HT compared with normotensive controls. These lower concentrations may be attributed to a combined outcome of endothelial dysfunction, renal injury, and inflammation in the setting of hypertension.

Introduction

Visceral adipose tissue is an ectopic adipose tissue that plays a role in lipid metabolism as well as energy storage. In addition, it is considered an important endocrine organ, as well as secretion of adipokines. Adipokines regulate important biological processes in target organs such as the endocrine pancreas, skeletal muscle, brain, immune and cardiovascular systems, and the liver. This could explain the close link between obesity and the metabolic and cardiovascular complications [1, 2]. The production of many adipokines is deregulated in obesity [3] and could participate into disturbances of appetite and satiety, and into changes in the distribution of adipose tissue, hemostasis, endothelial function, insulin secretion, insulin sensitivity, inflammation energy expenditure, angiogenesis, blood pressure, osteoarticular functions and repro-duction.

Omentin-1 is a glucoprotein of the adiponectin family released from visceral adipose tissue, endothelial cells and visceral fat stromal–vascular cells [4]. It has anti-inflammatory effect and circulating omentin-1 concentration correlates negatively with waist circumference, insulin resistance and body-mass index (BMI). Serum omentin-1 is used as a biomarker of coronary artery disease, obesity, cancer, metabolic syndrome, inflammatory disease, atherosclerosis, and diabetes mellitus [5–8].

Hypertension (HT) is a disease that can cause death due to multiple target organ damage and eventually related vascular system damage [9]. High blood pressure is known increased inflammatory activity and to cause endothelial dysfunction has been showed in HT patients [10, 11].

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According to these results, we can think that omentin-1 may be involved in the inflammatory process of HT.

Relationship between omentin-1 and coronary disease inflammatory diseases, metabolic syndrome have already been demonstrated in previous studies; however, the relationship between omentin-1 and HT has still yet to be comprehensively investigated. The aim of our study is to investigate circulating omentin-1 levels in HT patients compared to healthy normotensive controls.

Methods

Study population

Our study was designed prospectively, single-center and cross-sectional. HT was diagnosed with clinical blood pressure measurements. Patients diagnosed with new essential HT ($n = 61$) and healthy normotensive individuals ($n = 60$) were enrolled in this study. Subject ages were between 18 and 70 years. Newly diagnosed hypertensive patients were examined by the doctor in the outpatient clinic. The number and age range of the young patients in our study were as follows: two patients aged between 18 and 29 years; six patients aged between 30 and 39 years; and, ten patients aged between 40 and 49 years.

Patients with significant valvular disease, diabetes mellitus, systolic heart failure (ejection fraction <45%), coronary artery disease, secondary hypertension, renal insufficiency

(GFR < 60 ml/min/1.73 m^2), cerebrovascular disease, inflammatory diseases, hematological disease, and atrial fibrillation were excluded.

Our study was approved by the local ethics committee of Pamukkale Faculty of Medicine on 22/10/2018. (Approval number: 60116787- 020/75102). Our study was carried out without compromising the Helsinki Declaration principles.

Clinical BP measurements

After patients were rested for 10 min and at the level of their heart with their arms, office blood pressure (BP) measurements were taken for all patients. Mercury sphygmomanometer (Erka Aneroid, Berlin, Germany) was used for BP measurement in quiet environment. BP measurements were performed between 8 and 10 a.m. in the outpatient clinic. A total of three measurements were performed with an interval of 5 min. As a result, the average of these measurements was taken as BP measurement. The cuff of the BP measuring device distal end was 2.5–3 cm above the antecubital fossa and surrounded 80% of the upper arm[12]. The definition of hypertension was made as follows: systolic blood pressure (SBP) ≥ 140 mmHg and/or diastolic blood pressure (DBP) ≥ 90 mmHg. The patients in the HT group were separated into 2 group. Stage1: SBP between 140 and 159 mm Hg and DBP between 90 and 99 mmHg. Stage 2: SBP between 160 and 179 mmHg and DBP between 100 and 109 mmHg. Patients with newly diagnosed stage 3 HT (SBP 180 mm Hg and DBP between 110 mm Hg) were not enrolled in the study due to lack of sufficient patient inclusion within the predefined study period.

Laboratory analysis

Peripheral venous blood samples were collected after at least 12 h fasting period from all the subjects. The samples were centrifuged and the serum was separated from the cells by centrifuging at $3000 \times g$ for 10 min. The serum concentration of omentin was measured using a commercially available enzyme-linked immunosorbent assay kit (Sunred, cat. 201-12-0156, Shanghai Technology Co., China) in accordance with the manufacturer's instructions. The serum was stored at −80 °C until assayed. All samples were assayed in duplicate. The detection limit of the assay was 5.224 ng/ml (range: 6–1500 ng/ml). The absorbance was measured at 450 nm with Biotek Elx800 microplate reader. Omentin results were calculated based on the standard curve generated using a five-parameter curve fitting equation and The data were processed with the Gen5 Data Analysis software (BioTek Instruments Inc., USA)

Statistical analysis

While performing statistical analysis, software for the Statistical Package for Social Sciences for Windows version 21.0 was used (IBM SPSS Statistics for Windows, Armonk, USA). Categorical variables are expressed as percentages, numerical variables are presented as mean values ± standard deviation (SD). Kolmogorov–Smirnov test was used to check the normal distribution of all parameters. For statistical analysis, the background data were analyzed by Anova Test. Independent *t*-test was applied to test whether two independent samples have different averages in terms of a certain variable. Also pearson correlation test was performed among omentin-1 and individual parameters. $P > 0.05$ was considered significant.

Results

Total of 121 participants were included in this study: 60 in the control group, and 61 patients in hypertensive group. The HT group was separated into two subgroups. There were 30 patients in stage 2 HT group and 31 patients in stage 1 HT group). As evident in the tables, there were no significant differences between the groups in terms of

Table-1 Labaratuary and demographic characteristics of the control groups and essential hypertension.

Variables	Controls ($n = 60$)	Stage 1 HT ($n = 30$)	Stage 2 HT ($n = 31$)	P value
Age (years)	46.52 ± 11.82	51.47 ± 7.96	53.77 ± 11.07	0.01
Gender (Female, %)	31 (51%)	15 (50%)	16 (51%)	0.99
Smokers (%)	40 (66%)	21(70%)	20(64%)	0.90
BMI (kg/m^2)	27.11 ± 4.42	29.26 ± 4.56	29.5 ± 5.1	0.03
Height (cm)	167.87 ± 9.7	166.13 ± 8.37	168.61 ± 10.01	0.57
GFR (ml/min/1.73-m^2)	98.18 ± 16.52	91.37 ± 13.67	91.48 ± 13.72	0.06
Glucose (mg/dl)	94.62 ± 14.87	95.87 ± 10.97	97.16 ± 9.68	0.66
CRP (mg/dl)	0.26 ± 0.29	0.41 ± 0.51	0.37 ± 0.27	0.07
Hb (g/dl)	14.5 ± 1.77	15 ± 1.71	14.86 ± 1.86	0.41
WBC (×10^9/l)	7.67 ± 1.88	8.46 ± 2.1	8.03 ± 1.61	0.18
Plt (×10^9/l)	255.33 ± 62.92	276.53 ± 56.81	254.16 ± 57.92	0.24
Triglyceride level (mg/dl)	152 ± 114.06	194.6 ± 146.41	192.06 ± 101.77	0.17
Total cholesterol level (mg/dl)	184.29 ± 35.72	199.58 ± 32.5	196.27 ± 29.31	0.12
LDL-C (mg/dl)	104.98 ± 30.54	119.58 ± 30.36	112.68 ± 26.26	0.13
HDL-C (mg/dl)	49.93 ± 13.23	44.93 ± 12.22	48.9 ± 14.99	0.25
Omentin-1 (ng/ml)	147.84 ± 58.55	72.19 ± 54.33	62.45 ± 47.01	<0.0001

HT hypertension, *GFR* glomerular filtration rate, *BMI* body-mass index, *CRP* C-reactive protein, *WBC* white blood cell count, *Hb* hemoglobin, *Plt* platelet count, *HDL-C* high-density lipoprotein cholesterol, *LDL-C* low-density lipoprotein cholesterol

baseline characteristics and laboratory parameters with regard tosmoking habit, height, sex, CRP, GFR, white blood cell, platelet, hemoglobin, white blood cell, cholesterol levels, and glucose levels ($P > 0.05$). HT group slightly older, and mean BMI of HT group was greater compared with the controls (Table 1). On the other hand, Omentin-1 levels were significantly lower both in stage 1 and 2 HT subgroup as compared with the normotensive controls (72.19 ± 54.33 ng/ml for stage 1 HT subgroup; 62.45 ± 47.01 ng/ml for stage 2 HT subgroup; and, 147.84 ± 58.55 ng/ml for healthy normotensive controls; overall $P <$ 0.001) (Table 1) Also, no significant difference was observed between smokers and non-smokers in terms of omentin-1 levels. ($P > 0.05$)

When the relationship of serum Omentin-1 level with baseline characteristics and laboratory parameters were analyzed, no significant correlation was detected (Table 2). Morover, mean Omentin-1 level was revealed to have decreased further in stage 2 HT patients compared with those with stage 1 HT (62.45 ± 47.01 ng/ml vs 72.19 ± 54.33 ng/ml, respectively; $P = 0.031$). However, weight, age and sex did not have any effect on the change in circulating Omentin-1 level.

In the group comparative analysis using anova test, it was observed that omentin-1 levels showed significant variability among the 3 groups ($P = 0.001$) (Table 3). When it was divided into two groups as those with and without hypertension, significant differences were observed between the Omentin-1 values between the groups. ($P < 0.001$) (Table 4)

Table 2 Relationship between serum omentin-1 level and baseline characteristics.

	n	Pearson correlation	P value
Age	121	−0.11	0.22
BMI	121	0.00	0.98
GFR	121	0.09	0.35
Hb	121	−0.03	0.73
WBC	121	−0.09	0.34
Glucose	121	−0.05	0.57
HDL-C	121	0.00	0.99
LDL-C	121	0.04	0.70
Triglyceride level	121	−0.04	0.65
Total cholesterol level	121	0.00	0.97
CRP	121	−0.03	0.78
Waist circumference	121	0.09	0.35

WBC white blood cell count, *Hb* hemoglobin, *BMI* body-mass index, *CRP* C-reactive protein (mg/dL), *GFR* glomerular filtration rate, *LDL-C* low-density lipoprotein cholesterol, *HDL-C* high-density lipoprotein cholesterol

Discussion

Our study demonstrated for the first time that the serum omentin-1 level decreased in HT patients compared with healthy normotensive subjects, independently of weight, age, and sex.

Adipose tissue is not only a triglyceride depository, but also secretes a veriety of enzymes and cytokines, thereby playing a key role in various metabolic reactions. These mediators secreted from the white adipose tissue are defined

Table 3 Omentin-1 explanatory statistics and group comparisons.

Omentin	*n*	Mean	Std. deviation	Std. error	95% confidence interval for mean		Minimum	Maximum	*P* value
					Lower bound	Upper bound			
None	60	147.84	58.55	20.47	106.88	188.80	36.30	385.00	0.001
Stage 2	30	62.45	47.01	8.58	44.9	80.00	20.90	278.30	
Stage 1	31	72.19	54.33	9.76	52.26	92.11	19.50	237.10	

Table 4 HT and control groups omentin-1 levels.

	Hypertension	*n*	Mean	Std. deviation	Std. error mean	*P* value
Omentin	NO	60	147.84	58.54	20.46	<0.001
	YES	61	67.39	50.67	6.48	

as adipokines [13]. Adipokines affect the functions of macrophages, endothelial cells, and arterial smooth muscle cells, as well as play an important role in many physiological processes [14, 15]. Furthermore, Omentin-1 is a novel adipocytokine which is mainly expressed in visceral (omental and epicardial) fat tissue besides a number of various other sites such as plasma, colon, ovary, vascular cells, small intestine, and mesothelial cells. The role of omentin-1 in clinical and pathophysiological areas has been increasingly curious recently. Several studies showed that Omentin-1 played important roles in insulin sensitivity and the body metabolism and also has anti-atherosclerotic, anti-inflammatory, and cardiovascular protective effects [16]. In in vitro studies, it was revealed that omentin-1 induced vasodilation by increasing endothelial nitric oxide synthase and decreasing tumor necrosis factor-a (TNF-a) [17, 18]. This pro-inflamatory citokines are also associted with physiopathology of hypertension [16] and may explain why Omentin-1 levels are low in hypertensive group in our study. Based on this, we can make a comment like this: as the omentin-1 level decreases, endothelial nitric oxide synthase decreases and vascular vasodilation decreases and HT stage increases [19].

In a study by Aliasghari et al. Omentin-1 level was shown to have a negative correlation with SBP in patients with nonalcholic fatty liver [20].

Moreno-Navarrete et al. In their study with patients with impaired glucose tolerance, it has been shown to be correlated between serum omentin-1 level and endothelial dysfunction [21]. Considering that the degree of endothelial dysfunction increases with increasing HT stage, we can say that there is a negative correlation between endothelial dysfunction and Omentin-1 level according to our study.

There are other studies showing that omentin-1 levels are also significantly lower in patients with peripheral artery disease [22, 23]. Kadoglou et al. showed that the sensitivity and severity of the carotid plaques may be associated with low omentin-1 serum levels [22]. Similarly, Xu et al. demonstrated significantly lower levels of serum omentin-1 in patients with ischemic stroke patients with unstable carotid plaque compared with than those of stable carotid plaque [24]. In another study by Shibata et al. serum omentin-1 level was found to be significantly lower in patients with coronary atherosclerosis compared with healthy subjects [25]. Based on these findings, we can think that omentin-1 level may be a biomarker of vascular dysfunction and atherosclerosis. Apart from such studies, Omentin-1 levels were also shown to be significantly lower in patients with heart failure who experienced more cardiac events such as death and rehospitalization in a given period of time, as well as in those heart failure patients with more severe symptoms as indicated by higher *New York Heart Association* classification [26].

In hypertensive patients, chronically elevated SBP reduces the ability of dilatation and narrowing of the afferent arteriole. Over time, high SBP transmitted to the kidney leads to nephrosclerosis and glomerular hypertension [27].

TAs the hypertension stage increases, kidney function declines and GFR decreases [28]. In our study, the level of Omentin 1 decreases as the HT stage increases. Thus, a correlation between Omentin-1 level and renal kidney damage can be considered. In our study, when patients with HT were compared with the control group, low GFR was observed.

In all of the afore-mentioned studies conducted on such cardiovascular cases as carotid disease, coronary artery disease and heart failure, lower serum Omentum-1 levels were demonstrated in common. In this regard, our study results are compatible with the previous reports.

Study limitations

Our study should be assessed in the light a a number of limitations. The main limitation of the present study is its designation as a cross-sectional study. Secondly, we did not evaluate the prognostic value of circulate omentin-1 in our

HT patient population. Thirdly, we performed only on the repeated office BP measurements,we did not use 24-h ambulatory BP monitoring. Furthermore, we did not seek to correlate additional novel inflammatory biomarkers of endothelial dysfunction with decreasing Omentin-1 levels in our HT population.

Conclusion

The present study demonstrated that serum Omentin-1 levels decreased in patients with HT compared with normotensive controls. These lower concentrations may be attributed to a combined outcome of endothelial dysfunction, renal injury and inflammation in the setting of hypertension. Omentin-1 has been associated with other hypertenison associated diseases such as diabetes, and obesity. Thus it is not very surprizing to find a similar correlation between low circulating omentin-1 levels and hypertension. However, such a correlation has not been reported for hypertension earlier and is therefore new. Future larger-population prospective studies are needed both to support our study findings and to reveal probable prognostic effect of serum Omentin-1 levels in patients with essential HT.

Summary table

What is known about the topic

- Hypertension (HT) is a disease that can cause death due to multiple target organ damage and eventually related vascular system damage
- High blood pressure is known increased inflammatoryactivity and to cause endothelial dysfunction
- TOmentin-1 played important roles in insulin sensitivity and the body metabolism and also has anti-atherosclerotic, anti-inflammatory, and cardiovascular protective effects

What this study adds

- Serum omentin-1 level decreased in HT patients compared with healthy normotensive subjects, independently of weight, age, and sex.
- These lower concentrations may be attributed to a combined outcome of endothelial dysfunction, renal injury, and inflammation in the setting of hypertension.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

References

1. Blüher M, Mantzoros CS. From leptin to other adipokines in health and disease: facts and expectations at the beginning of the 21st century. Metabolism. 2015;64:131–45. Epub 2014 Oct 23. PMID: 25497344
2. Sahin-Efe A, Katsikeris F, Mantzoros CS. Advances in adipokines. Metabolism. 2012;61:1659–65.
3. Blüher M. Adipose tissue dysfunction in obesity. Exp Clin Endocrinol Diabetes. 2009;117:241–50.
4. Yang RZ, Lee MJ, Hu H, Pray J, Wu HB, Hansen BC, et al. Identification of omentin as a novel depot specific adipokine in human adipose tissue: possible role in modulating insulin action. Am J Physiol Endocrinol Metab. 2006;290:1253–61.
5. De Souza Batista CM, Yang RZ, Lee MJ, Glynn NM, Yu DZ, Pray J, et al. Omentin plasma levels and gene expression are decreased in obesity. Diabetes. 2007;56:1655–61.
6. Onur I, Oz F, Yildiz S, Kuplay H, Yucel C, Sigirci S, et al. A decreased serum omentin-1 levelmay be an independent risk factor for peripheral arterial disease. Int Angiol. 2014;33:455–460.
7. Yin J, Hou P, Wu Z, Nie Y. Decreased levels of serum omentin-1 in patients with inflammatory bowel disease. Med Sci Monit. 2015;21:118–122.
8. Kocijancic M, Vujicic B, Racki S, Cubranic Z, Zaputovic L, Dvornik S. Serum omentin-1 levels as a possible risk factor of mortality in patients with diabetes on haemodialysis. Diabetes Res Clin Pract. 2015;110:44–50.
9. Kannel WB. Blood pressure as a cardiovascular risk factor: prevention and treatment. J Am Med Assoc. 1996;275:1571–6.
10. Bautista LE, Vera LM, Arenas IA, Gamarra G. Independent association between inflammatory markers (C-reactive protein, interleukin-6, and TNF alpha) and essential hypertension. J Hum Hypertens. 2005;19:149–54.
11. Panza JA, Casino PR, Kilcoyne CM, Quyyumi AA. Role of endothelium-derived nitricoxide in the abnormal endothelium dependent vascular relaxation of patients with essential hypertension. Circulation. 1993;87:1468–74.
12. Mattoo TK. Definition and diagnosis of hypertension in children and adolescents. In: UpTo Date. Stapleton FB, Fulton DR, Kim MS, eds. Waltham, MA: UpTo Date; 2009. http://www.uptodateonline.com/online/content/topic.do? topicKey=pedineph/11964&view=print. Accessed 8 Aug 2009.
13. Lau DCW, Dhillon B, Yan HY, Szmitko PE, Verma S. Adipokines: molecular links between obesity and atheroslcerosis. Am J Physiol-Heart C 2005;288:2031–41.
14. Fantuzzi G, Mazzone T. Adipose tissue and atherosclerosis: exploring the connection. Arterioscler Thromb Vasc Biol. 2007;27:996–1003.
15. Steffens S, Mach F. Adiponectin and adaptive immunity: linking the bridge from obesity to atherogenesis. Circ Res. 2008;102:140–2.
16. Watanabe T, Watanabe KK, Takahashi Y, Kojima M, Watanabe R. Adipose tissue-derived omentin-1 function and regulation 2017 American Physiological Society. Compr Physiol. 2017;7:765–81.
17. Yamawaki H, Tsubaki N, Mukohda M, Okada M, Hara Y. Omentin, a novel adipokine,induces vasodilation in rat isolated blood vessels. Biochem Biophys Res Commun. 2010;393:668–72.
18. Yamawaki H, Kuramoto J, Kameshima S, Usui T, Okada M, Hara Y. Omentin, a novel adipocytokine inhibits TNF-induced vascular inflammation in human endothelial cells. Biochem Biophys Res Commun. 2011;408:339–43.

19. Mehaffey E, Majid DSA. Tumor necrosis factor-α, kidney function, and hypertension. Am J Physiol Ren Physiol. 2017;313 (Oct):1005–8.
20. TAliasghari F, Izadi A, Jabbari M, Imani B, Gargari BP, Asjodi F, et al. Are vaspin and omentin-1 related to insulin resistance. Blood Press Inflamm NAFLD Patients? J MedBiochem. 2018;37 (Dec):470–5.
21. Moreno-Navarrete JM, Ortega F, Castro A, Sabater M, RicartW, Fern´andez-Real JM. Circulating omentin as a novel biomarker of endothelial dysfunction. Obesity. 2011;19:1552–9.
22. Kadoglou NP, Lambadiari V, Gastounioti A, Gkekas C, GiannakopoulasTG, Koulia K, et al. The relationship of novel adipokines, RBP4 and omentin-1, with carotid atherosclerosis severity and vulnerability. Atherosclerosis. 2014;235:606–12.
23. Onur I, Oz F, Yildiz S, Kuplay H, Yucel C, Sigirci S, et al. A decreased serum omentin-1 levelmay be an independent risk factor for peripheral arterial disease. Int Angiol. 2014;33:455–60.
24. Xu T, Zuo P, Cao L, Gao Z, Ke K. Omentin-1 is associated with carotid plaque instability among ischemic stroke patients. J Atheroscler Thromb. 2018;25:505–11.
25. Shibata R, Ouchi N, Kikuchi R, Takahashi R, Takeshita K, Kataoka Y, et al. Circulating omentin is associated with coronary artery disease in men. Atherosclerosis. 2011;219: 811–4.
26. Narumi T, Watanabe T, Kadowaki S, Kinoshita D, Yokoyama M, Honda Y, et al. Impact of serum omentin-1 levels on cardiac prognosis inpatients with heart failure. Cardiovasc Diabetol. 2014;13:84.
27. Ku E, Lee BJ, Wei J, Weir MR. Hypertension in CKD: core curriculum 2019. Am J Kidney Dis. 2019;74:120–131.
28. Yu Z, Rebholz CM, Wong E, Chen Y, Matsushita K, Coresh, et al. Association between hypertension and kidney function decline: the Atherosclerosis Risk in Communities (ARIC) study. Am J Kidney Dis. 2019;74:310–319.