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Study of Serum Omentin-1 and IL-6 in Patients with Obesity, Hypertension and Hypertensive Nephropathy

Mabrouk Ibrahim Ismail [1], Mohammed Ghanem Gabr[2]*, Nafesa Mohammed Kamal [1], Amir Mohamed Elokely[1], Samia Hassan El-Shishtawy [2]

[1]Internal Medicine and Nephrology Department, Faculty of Medicine, Zagazig University, Zagazig, Egypt

[2] Nephrology Department, Theodor Bilharz Research Institute, Giza, Egypt

*Corresponding Author: Mohammed Ghanem Gabr, Email: Ghanemnephrologist@gmail.com, Phone: +201111014772

ABSTRACT

Background: The pathogenesis of hypertension (HTN) relates to immune system as well as inflammatory indicators such C-reactive protein, TNF-α, and interleukin-6 (IL-6). **Objective:** To ascertain the connection between serum omentin-1 and IL-6 in obese, hypertensive and in hypertensive nephropathy patients. **Patients and Methods:** This case-control research was done on 126 patients between 18 and 60 years of age, both sexes, hypertensive patients, hypertensive nephropathy patients, and overweight obese subjects. Serum omentin-1 and serum IL-6 were quantified in all patients. **Results:** A statistically significant inverse relation was noted between serum omentin-1 and age, systolic, diastolic blood pressure, urea, creatinine. A statistically significant positive relation has been observed between serum omentin-1 and estimated glomerular filtration rate (eGFR). The best cutoff points of serum omentin-1 and IL-6 for diagnosis stage III and IV hypertensive nephropathy respectively was ≤215, ≥6.7 with area under curve 0.721, 0.785, sensitivity 66.7%, 81%, specificity 71.4%, 61.9% and overall accuracy 69% (p=0.014) and 71.4% (p=0.002). Statistically significant variation was observed between groups under study concerning age, creatinine, urea and serum IL-6 (significantly greater in hypertensive nephropathy stage III and IV subgroup). **Conclusions:** Omentin-1 concentrations decreased significantly with increasing body weight, as well as with HTN; mainly hypertensive nephropathy and higher stages of HTN. Furthermore, IL-6 increased significantly in obese, hypertensive and hypertensive nephropathy patients.

Keywords: Omentin-1, IL-6, Obesity, Hypertension, Hypertensive Nephropathy.

INTRODUCTION

Circulatory disorder disease mortality is still high worldwide despite medical advancements, and a number of lifestyle risk factors might contribute to this chronic condition. Furthermore, as a person ages, health issues mount, and as a result, age is positively correlated with the chance of developing such a disease. Notably, among circulatory disorders, hypertension (HTN) can be considered a chronic condition in and of itself. Moreover, it may cause complications like cardiovascular disease, hospitalization, and a low quality of life connected to health [1].

Hypertension is a condition that can be fatal because it damages several target organs and eventually the circulatory system as a whole. It is well recognized that high blood pressure can lead to endothelial dysfunction and increased inflammatory activity [2].

Pro- and anti-inflammatory chemicals, oxidative damage and cytokine markers are among the molecules via which endothelial dysfunction is intimately correlated with elevated oxidative stress, inflammation, remodeling, and atherogenesis [2].

Contributing to an elevated risk of morbidity and mortality resulting from cardiovascular illnesses, diabetes, malignancies, and other chronic illnesses, obesity constitutes a significant public health concern [3]. Patient obesity-related adipose tissue has the capacity to secrete a range of pro-inflammatory chemicals, such as chemerin, leptin, and resistin, while impeding the release of adipokines that regulate inflammation (Like that adiponectin and omentin-1) [4].

Omentin-1, a glucoprotein belonging to the adiponectins family, is secreted by stromal–vascular cells of visceral fat, endothelial cells and visceral adipose tissue. It has an anti-inflammatory impact, and there is a negative relation between circulating omentin-1 concentration and body mass index (BMI), insulin resistance and waist circumference. Omentin-1 is a biomarker that has been identified in serum as an indicator of obesity, cancer, diabetes, metabolic syndrome, coronary artery disorder, inflammatory disorder, and atherosclerosis [5]. Inflammatory marker expression was observed to be elevated in both visceral adipocytes and plasma of patients with hypertension in comparison to that of healthy persons. Visceral adipose tissue is responsible for secreting adipokines including interleukin-6 (IL-6), adiponectin, apelin, omentin-1, and vaspin, which are among the principal adipokines. These strong effectors regulate vascular homeostasis, inflammation, and fibrosis[6].

The goal of this research was to ascertain the connection between serum omentin-1 and IL-6 in obese, hypertensive and in hypertensive nephropathy patients.

PATIENTS AND METHODS

Study population

This case-control research was executed on 126 patients aged from 18 to 60 years old, both sexes, from December 2020 to June 2023.

Exclusion criteria were diabetic patients, acute severe infection, hemodialysis, serious illness in the previous three months, autoimmune diseases and chronic inflammatory diseases, malignancy, systolic heart failure (EF < 45%) and ischemic heart disease, liver disease (HBV and HCV), acute cerebrovascular accident and patients with restrictive or obstructive lung diseases.

The patients were categorized into four main groups:

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Group I: (Control Group) (N=21): normal healthy volunteers with a BMI of less than 25.
Group II: (N= 21) obese patients with a BMI more than 30 with no chronic medical disease history.
Group III: (N=42) HTN Group with HTN, divided into two subgroups: [subgroup A: (n=21) with HTN stage I and subgroup B: (n=21) with HTN stage II].
Group IV (N=42) hypertensive nephropathy, divided into two subgroups: [Subgroup A (n=21) chronic kidney disease (CKD) patients (stage I and II CKD) and subgroup B: (n=21) CKD patients (stage III and IV CKD)]. Each patient underwent the following: History gathering and clinical assessment, pelvi-abdominal ultrasound, echocardiography, laboratory investigations [complete blood count (CBC), lipid profile, renal and liver function tests] and research investigations; serum omentin-1 and IL-6.

Laboratory parameters

Blood sample collection: Fasting blood samples were collected in tubes from the patients and control groups after proper disinfection. The tubes were centrifuged at 4000rpm (10 min) to obtain plasma and serum. The plasma and serum samples were kept at −80°C until analysis. A commercially accessible enzyme-linked immunosorbent assay (ELISA) test kits were utilized to quantify the serum levels of omentin-1 and IL6. Routine examinations included complete blood picture, kidney function tests (serum creatinine, urea, sodium and potassium), liver function tests (alanine aminotransferase (ALT), aspartate aminotransferase (AST), and serum albumin), total cholesterol, low density lipoprotein cholesterol (LDL-C), high density lipoprotein-cholesterol (HDL-C), and triglycerides (TGs) using standard methods.

Pelvi-Abdominal Ultrasound Procedure: it was done to all participants.

Echocardiography (ECHO):

It was performed on the study participants in order to quantify left ventricular end-diastolic diameter (LVEDD) and fractional shortening 2D echocardiography was performed to assess left ventricular end-diastolic volume (LVEDV) and left ventricular ejection fraction (LVEF).

Ethical considerations:

The study was done after being accepted by the Research Ethics Committee, Zagazig University. All patients provided written informed consents prior to their enrolment. The consent form explicitly outlined their agreement to participate in the study and for the publication of data, ensuring protection of their confidentiality and privacy. This work has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans.

Statistical analysis

Statistical analysis was executed by SPSS v27 (IBM©, Chicago, IL, USA). Histograms and Shapiro-Wilks test were utilized to determine the normality of data distribution. Means and standard deviations (SD) of quantitative parametric data were utilized for analysis via one-way ANOVA (F) test in conjunction with Post Hoc test (Tukey) or with t-test. The quantitative non-parametric data were reported in the form of median and interquartile range (IQR) and were compared by Kruskal-Wallis test and Mann Whitney test. Ascertain qualitative data, which were expressed as frequencies and percentages (%), the chi-square test or Fisher's exact test was applied. A Pearson moment correlation equation was employed to establish the connection between many variables. A ROC curve was employed to ascertain the optimal cutoff value for a certain quantitative parameter in the diagnosis of a particular health issue. In order to establish statistical significance, a two-tailed P value must be below 0.05.

RESULTS

There was statistically significant variation among the hypertensive nephropathy and the others studied group regarding age, which tended to be higher in hypertensive nephropathy.

A statistically significant variation in BMI was observed across the groups under study except when comparing hypertensive and hypertensive nephropathy groups. No statistically significant variation was seen among the groups under study with respect to gender, height, sodium, AST, ALT, triglycerides, cholesterol, HDL, LDL, albumin, or sodium. A statistically significant disparity was seen in the SBP and DBP levels among the groups under investigation except when comparing control lean and obese groups. A statistically significant distinction existed among the groups under investigation concerning potassium, creatinine, eGFR and urea. On doing Post Hoc comparison, there was statistically significant variation between hypertensive nephropathy group and each other group. A statistically significant disparity was seen across the groups under investigation with respect to LVEDD and LVEDV. Variation was non-significant between control lean and obese group yet, on comparing each of them with hypertensive and hypertensive nephropathy, the difference was significant. Also, the variation was significant between hypertensive and hypertensive nephropathy. The observed variations in ejection percent among the groups under investigation were not statistically significant. A statistically significant distinction can be observed in the levels of serum omentin-1 and IL-6 between the groups under investigation. The difference was significant between control lean group and both hypertensive and hypertensive nephropathy groups. There was also a significant variation between hypertensive group and hypertensive nephropathy groups. Regarding IL-6, there was a substantial distinction between the obese group and the other groups. Regarding omentin-1, the variation was non-significant between obese group and either lean, hypertensive, or hypertensive nephropathy groups **(Table 1)**.

Table 1: Comparison between the studied groups regarding demographic data, anthropometric, clinical data, laboratory data, radiological investigation, serum IL-6 and omentin

Items		Control lean group (n=21)	Obese group (n=21)	Hypertensive group (n=42)	Hypertensive nephropathy group (n=42)	p
Sex	**Male**	11(52.4%)	13(61.9%)	23 (54.85)	24 (57.1%)	0.929
	Female	10(47.6%)	8(38.1%)	19 (45.2%)	18 (42.9%)	
Age (year)		43 ± 4.25	44 ± 9.5	47.86 ± 8.35	53.71 ± 6.89	**<0.001***
		P_1 =0.97, P_2 0.229, P_3>0.999, **P_4<0.003*, P_5<0.001*, P_6 <0.001***				
Weight (kg)		69.05 ± 7.84	96.0 ± 13.02	78.02 ± 10.74	77.07 ± 10.61	**<0.001***
		P1 <0.001*, P2 <0.001*, P3 =0.997, P4= 0.013*, P5= 0.035*, P6 <0.001*				
Height (cm)		167.05 ± 6.64	169.33 ± 9.65	170.17 ± 7.14	169.9 ± 7.2	**0.610**
BMI (kg/m^2)		24.01 ± 0.48	34.4 ± 4.0	26.94 ± 3.01	**26.57 ± 3.19**	**<0.001***
		P1 <0.001*, P2 <0.001*, P3= 0.933**, P4= 0.009*, P5= 0.003*, P6 <0.001***				
SBP (mmHg)		112.86 ± 8.45	115.0 ± 7.25	158.26 ± 11.18	135.64 ± 10.54	**<0.001***
		P1 >0.999**, P2 <0.001*, P3 <0.001*, P4 <0.001*, P5 <0.001*, P6 <0.001***				
DBP mmHg)		70.24 ± 7.16	74.29 ± 6.76	97.05 ± 6.99	85.48 ± 6.07	**<0.001***
		P1=0.312, **P2 <0.001*,** P3=0.933**, P4<0.001*, P5 <0.001*, P6 <0.001***				
Laboratory data						
Sodium (mg/dl)		139.38 ± 2.5	139.05 ± 1.86	139.31 ± 2.78	140.33 ± 3.14	0.2
Potassium (mg/dl)		4.05 ± 0.32	4.04 ± 0.27	4.11 ± 0.37	4.45 ± 0.45	**<0.001***
		P1 >0.999, P2 >0.999, **P3 <0.001*,** P4 >0.999**, P5 <0.001*, P6 <0.001***				
Triglycerides (mg/dl)		147.71 ± 24.53	130.71 ± 32.43	146.26 ± 7.08	138.81 ± 25.55	**0.297**
Cholesterol (mg/dl)		175.62 ± 23.01	161.24 ± 37.15	176.93 ± 35.98	171.5 ± 33.07	**0.44**
HDL (mg/dl)		50.52 ± 10.61	50.95 ± 6.38	49.02 ± 6.36	47.93 ± 9.04	**0.465**
LDL (mg/dl)		103.43 ± 21.88	94.14 ± 16.77	107.1 ± 23.71	99.93 ± 18.74	**0.356**
ALT (mg/dl)		15.5 ±2.54	25.57 ± 8.57	19 (17 – 23)	19.5(16.75 – 25)	**0.091**
AST (mg/dl)		13.5 ± 3.64	19.57 ± 4.02	19.17 ± 4.21	19.95 ± 6.42	**0.427**
Creatinine (mg/dl)		0.85 ± 0.12	0.85 ± 0.12	0.82 ± 0.13	2.17 ± 0.89	**<0.001***
		P1 >0.816, P2 >0.995, **P3 <0.001*,** P4 >0.999**, P5 <0.001*,** P6 ><**0.001***				
Urea (mg/dl)		28.14 ± 2.83	27.05 ± 2.18	23.45 ± 3.64	69.69± 15.34	**<0.001***
		P1 >0.999, P2 >0.999**, P3 <0.001*,** P4 >0.999**, P5 <0.001*, P6 <0.001***				
Albumin (g/dl)		4.18 ± 0.27	4.23 ± 0.3	4.18 ± 0.33	4.21 ± 0.3	**0.901**
eGFR (mL/min/1.73 m^2)		104.26 ± 14.31	101.27 ± 11.28	101.31 ± 10.27	45.11 ± 11.99	**<0.001***
		P1 >0.623, P2 >0.153, **P3 <0.001*,** P4=0.153**, P5 <0.001*, P6 <0.001***				
Echocardiograph parameters						
EF (%)		64.05 ± 4.5	64.29 ± 3.96	65.14 ± 4.22	63.4 ± 4.19	0.31
LVEDD (mm)		45.38 ± 1.8	45.84 ± 2.26	50.65 ± 5.23	52.71 ± 5.64	**<0.001***
		P_1 >0.999, **P_2 <0.001*, P_3=0.176, P_4<0.001*, P_5 <0.001*, P_6 <0.001***				
LVEDV(ml)		94.4 ± 9.04	98.05 ± 10.02	131.55 ± 29.96	139.49 ± 32.51	**<0.001***
		P_1 >0.999, **P_2 <0.001*, P_3-0.509, P_4<0.001*, P_5 <0.001*, P_6 <0.001***				
IL-6 (ng/ml)		3.5 ± 1.17	6.7 ± 1.94	6.8 ± 1.63	7.55 ± 1.12	0.164
		P_1 <0.001*, P_2 <0.001*, P_3 0.131, **P_4<0.001*, P_5 <0.001*, P_6 <0.011***				
Omentin (ng/ml)		366.14 ± 77.5	221.1 ± 56.88	239.62 ± 23.97	222.31 ± 36.83	**<0.001***
		P_1 >0.999, P_2 0.833, **P_3<0.001*, P_4<0.001*, P_5 <0.001*,** P_6 >0.999				

Data are displayed as mean ± SD, or frequency (%), or median (IQR), *: Significant p, p1: significant difference between control lean group and obese group, p2: significant difference between hypertensive group and obese group, p3: significant difference between hypertensive group and hypertensive nephropathy group, p4: significant difference between control lean and hypertensive groups, p5: significant difference between control lean and hypertensive nephropathy groups, p6: significant difference between obese and hypertensive nephropathy groups, BMI: Body mass index, ALT: alanine aminotransferase, AST: aspartate aminotransferase, HDL: high density lipoprotein, LDL: low density lipoprotein, eGFR: estimated glomerular filtration rate, EF: ejection fraction, LVEDD: left ventricle end diastolic diameter, LVEDV: left ventricular end-diastolic volume, IL-6: Interleukin 6, DBP: Diastolic blood pressure, SBP: Systolic blood pressure.

The best cutoff points of serum omentin-1 and IL-6 for diagnosis of HTN respectively was ≤266.5, ≥5.65 with area under curve 0.671, 0.565, sensitivity 86.9%,73.8% specificity 61.9%,54.8% PPV 82%,76.5%, NPV 70.3%, 51.1% and overall accuracy 78.6% (p=0.007), 67.5% (p=0.237). The best cutoff points of serum omentin-1 and IL-6 for diagnosis

of hypertensive nephropathy respectively were ≤237.5 and ≥6.45 with AUC 0.685 and 0.603, sensitivity 64.3% and 64.3%, specificity 63.1% and 52.4%, PPV 77.9% and 40.3%, NPV 46.6% and 74.6%, and overall accuracy 63.5% (p<0.001) and 56.3% (p=0.06). The best cutoff points of IL-6 and serum omentin-1 for diagnosis of obesity respectively were ≥5.55 and ≤288 with AUC 0.981 and 0.92, sensitivity 95.2% and 95.2%, specificity 90.5% and 81%, PPV 90.9% and 83.3%, NPV 95% and 94.4%, and overall accuracy 92.9% (p<0.001) and 88.1% (p<0.001) **(Figure 1)**.

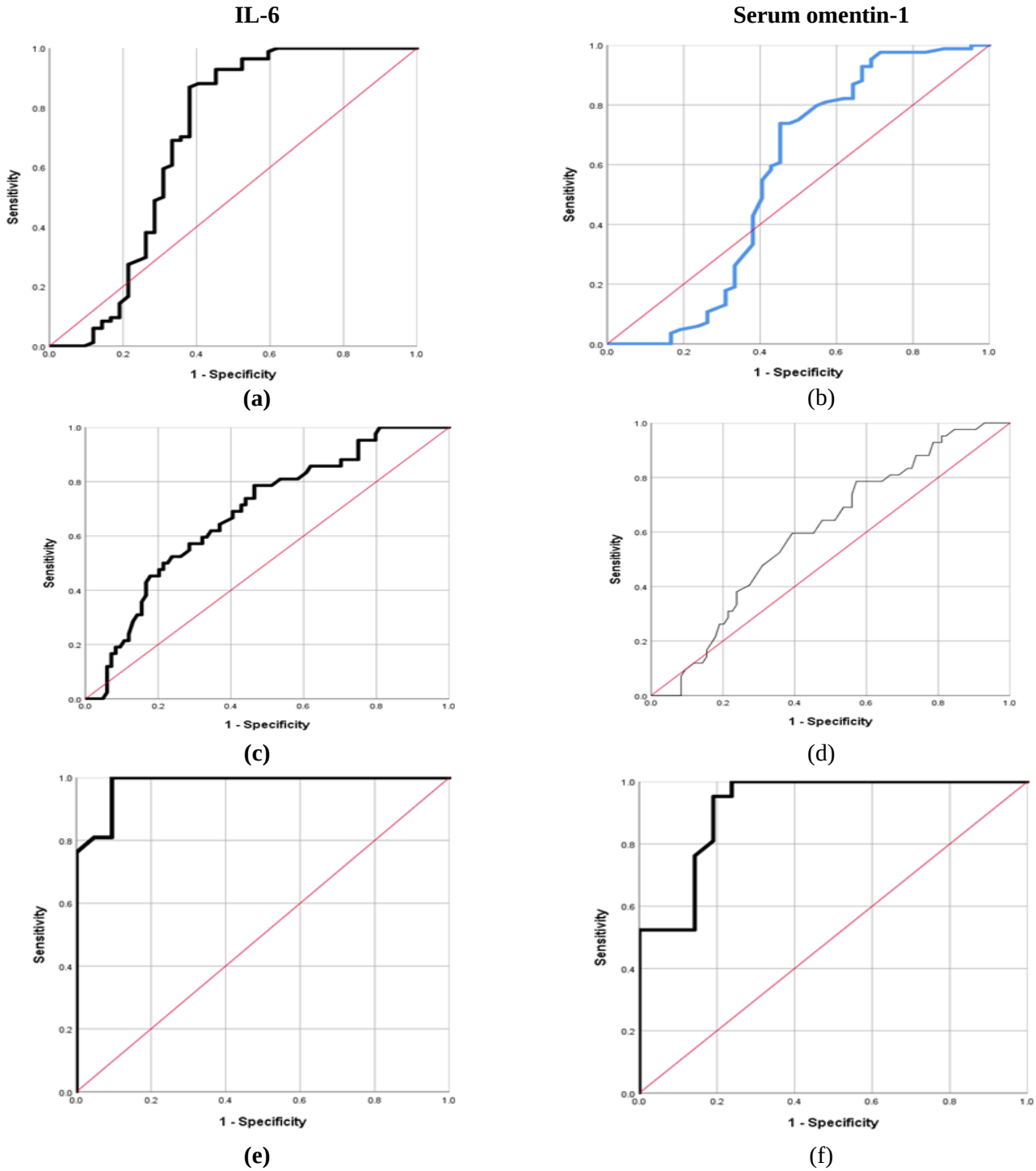


Figure 1: ROC curve showing performance of serum omentin-1 and IL-6 in diagnosis of (a, b) hypertension, (c, d) hypertensive nephropathy and (e, f) obesity.

There was a statistically significant negative connection between serum omentin-1 and age, weight, BMI, and ALT. There was statistically significant positive connection between serum omentin-1 and eGFR. There was non-significant relationship between serum omentin-1 and other variables. A statistically significant positive relation existed between serum IL-6 and age, weight, body mass index, and ALT. The relationship between serum IL-6 and other indicators was not statistically significant (**Table 2)**.

Table 2: Correlation between serum omentin-1 and IL-6 and studied parameters among healthy control group.

Items	Serum omentin-1		IL-6	
	r	p	r	p
Age (year)	**-0.356**	**0.021***	**0.406**	**<0.001***
Weight (kg)	**-0.699**	**<0.001***	**0.841**	**<0.001***
Height (cm)	0.09	0.57	-0.081	0.61
BMI (kg/m^2)	**-0.78**	**<0.001***	**0.913**	**0.006***
SBP (mmHg)	-0.141	0.374	0.002	0.99
DBP (mmHg)	-0.233	0.137	0.108	0.495
Creatinine (mg/dl)	-0.206	0.19	0.061	0.701
Urea (mg/dl)	0.023	0.885	-0.116	0.464
Sodium (mg/dl)	-0.129	0.416	-0.062	0.969
Potassium (mg/dl)	-0.099	0.532	0.072	0.65
Triglycerides (mg/dl)	0.053	0.738	-0.008	0.959
Cholesterol (mg/dl)	-0.033	0.833	0.025	0.876
HDL (mg/dl)	0.167	0.291	-0.069	0.664
LDL (mg/dl)	-0.111	0.484	0.086	0.59
ALT (mg/dl)	**-0.652**	**<0.001***	**0.573**	**0.004***
AST (mg/dl)	-0.341	0.111	0.355	0.096
Albumin (g/dl)	-0.032	0.842	0.175	0.268
eGFR (mL/min/1.73 m^2)	**0.329**	**0.024***	-0.219	0.164
EF (%)	-0.089	0.573	0.113	0.487
LVEDD (mm)	0.143	0.366	0.016	0.918
LVEDV (ml)	0.139	0.379	0.025	0.876

r: Pearson correlation coefficient, *: Significant p, BMI: Body mass index, SBP: systolic blood pressure, DBP: diastolic blood pressure, ALT: alanine aminotransferase, AST: aspartate aminotransferase, HDL: high density lipoprotein, LDL: low density lipoprotein, eGFR: estimated glomerular filtration rate, EF: ejection fraction, LVEDD: left ventricle ends diastolic diameter.

A statistically significant distinction can be observed in the systolic and diastolic blood pressure of the groups under investigation (all were HTN stage II group). No statistically significant variation was seen among the groups under study with respect to gender, height, weight, BMI or age, laboratory data, pelvi-abdominal US, EF, LVEDD or LVEDV, serum omentin-1 and serum IL-6 **(Table 3)**.

Table 3: Comparison between the studied groups (hypertensive patients without nephropathy) regarding demographic data, anthropometric, clinical data and laboratory data, radiological investigation, serum IL-6 and omentin

Items		HTN stage I subgroup (n=21)	HTN stage II subgroup (n=21)	p
Sex	Male	11 (52.4%)	12 (57.1%)	0.757
	Female	10 (47.6%)	9 (42.9%)	
Age (year)		47.33 ± 9.34	48.38 ± 7.41	0.689
Weight (kg)		75.43 ± 8.72	80.62 ± 12.1	**0.119**
Height (cm)		170.43 ± 7.43	169.9 ± 7.01	**0.815**
BMI (kg/m^2)		25.93 ± 2.6	27.96 ± 4.9	**0.105**
SBP (mmHg)		148.48 ± 5.57	168.05 ± 4.88	**<0.001***
DBP (mmHg)		91.24 ± 3.65	102.86 ± 3.99	**<0.001***
laboratory data				
Creatinine (mg/dl)		0.77 ± 0.15	0.85 ± 0.11	0.056
Urea (mg/dl)		22.52 ± 3.08	24.38 ± 3.99	0.099
Sodium (mg/dl)		138.9 ± 2.59	139.71 ± 2.97	0.352
Potassium (mg/dl)		3.98 ± 0.28	4.1 ± 0.41	0.478
Triglycerides (mg/dl)		141.38 ± 39.29	151.14 ± 5.32	0.900
Cholesterol (mg/dl)		174.95 ± 35.26	178.9 ± 37.45	0.727
HDL (mg/dl)		48.05 ± 5.78	50.0 ± 6.89	0.326
LDL (mg/dl)		106.29 ± 4.25	107.9 ± 3.99	0.970
ALT (mg/dl)		20.24 ± 4.28	21.67 ± 3.29	0.990
AST (mg/dl)		19.05 ± 4.01	19.29 ± 4.5	0.857
Albumin (g/dl)		4.14 ± 0.34	4.21 ± 0.32	0.487
eGFR (mL/min/1.73 m^2)		97.54 ± 10.27	95.09 ± 10.78	0.455
Radiological investigation				
PAUS	Bright liver	3 (14.3%)	8 (38.1%)	0.159
	Normal	18 (85.7%)	13 (61.9%)	
EF (%)		64.57 ± 3.3	65.71 ± 5	0.387
LVEDD (mm)		52.34 ± 5.21	50.59 ± 5.28	0.397
LVEDV (ml)		133.66 ± 29.69	125.43 ± 30.38	0.38
Omentin-1(ng/ml)		243.57 ± 23.28	235.67 ± 24.55	0.291
IL-6 (ng/ml)		5.86 ± 1.67	6.52 ± 1.55	0.66

Data are displayed as mean ± SD or frequency (%), *: Significant p, BMI: Body mass index, ALT: alanine aminotransferase, AST: aspartate aminotransferase, HDL: high density lipoprotein, LDL: low density lipoprotein, eGFR: estimated glomerular filtration rate, EF: ejection fraction, LVEDD: left ventricle end diastolic diameter, LVEDV: left ventricular end-diastolic volume, IL-6: Interleukin 6, HTN: hypertension, DBP: diastolic blood pressure, SBP: systolic blood pressure.

There was a statistically significant negative connection between serum omentin-1 and weight, BMI, triglycerides, cholesterol, LDL cholesterol, LVEDD and LVEDV. A positive connection that was statistically significant has been identified between serum omentin-1 and HDL cholesterol. The connection between serum omentin-1 and other measures is not statistically significant. The variables weight, triglycerides, total cholesterol, LVEDD, and LVEDV had a positive connection that was statistically significant. A statistically significant inverse relationship can be observed between serum IL-6 and eGFR. There was non-significant connection between serum omentin-1 and other variables **(Table 4)**.

Table 4: Correlation between serum omentin-1, IL-6 and studied parameters among patients with HTN

Items	Serum omentin-1		IL-6	
	r	p	r	p
Age (year)	-0.139	0.379	0.193	0.22
Weight (kg)	**-0.545**	**<0.001***	**0.532**	**<0.001***
Height (cm)	0.117	0.467	-0.347	0.024*
BMI (kg/m^2)	**-0.592**	**<0.001***	**0.708**	**0.006***
SBP (mmHg)	-0.152	0.336	0.209	0.184
DBP (mmHg)	-0.057	0.719	0176	0.264
Creatinine (mg/dl)	-0.091	0.565	0.121	0.445
Urea (mg/dl)	0.031	0.848	-0.167	0.289
Sodium (mg/dl)	-0.219	0.163	0.196	0.213
Potassium (mg/dl)	0.117	0.462	-0.106	0.502
Triglycerides (mg/dl)	**-0.451**	**0.003***	**0.472**	**<0.001***
Cholesterol (mg/dl)	**-0.472**	**0.002***	**0.336**	**0.03***
HDL (mg/dl)	**0.362**	**0.019***	-0.276	0.077
LDL (mg/dl)	**-0.432**	**0.004***	0.299	0.055
ALT (mg/dl)	-0.004	0.98	0.283	0.07
AST (mg/dl)	0.011	0.947	-0.004	0.98
Albumin (g/dl)	-0.203	0.196	0.214	0.173
eGFR (mL/min/1.73 m^2)	0.181	0.25	**-0.312**	**0.045***
EF (%)	-0.174	0.271	0.064	0.688
LVEDD (mm)	**-0.543**	**<0.001***	**0.501**	**<0.001***
LVEDV (ml)	**-0.54**	**<0.001***	**0.485**	**<0.001***

R: Pearson correlation coefficient, *: Significant P, BMI: Body mass index, SBP: systolic blood pressure, DBP: diastolic blood pressure, ALT: alanine aminotransferase, AST: aspartate aminotransferase, HDL: high density lipoprotein, LDL: low density lipoprotein, eGFR: estimated glomerular filtration rate, EF: ejection fraction, LVEDD: left ventricle end-diastolic diameter, LVEDV: left ventricular end-diastolic volume, HTN: hypertension.

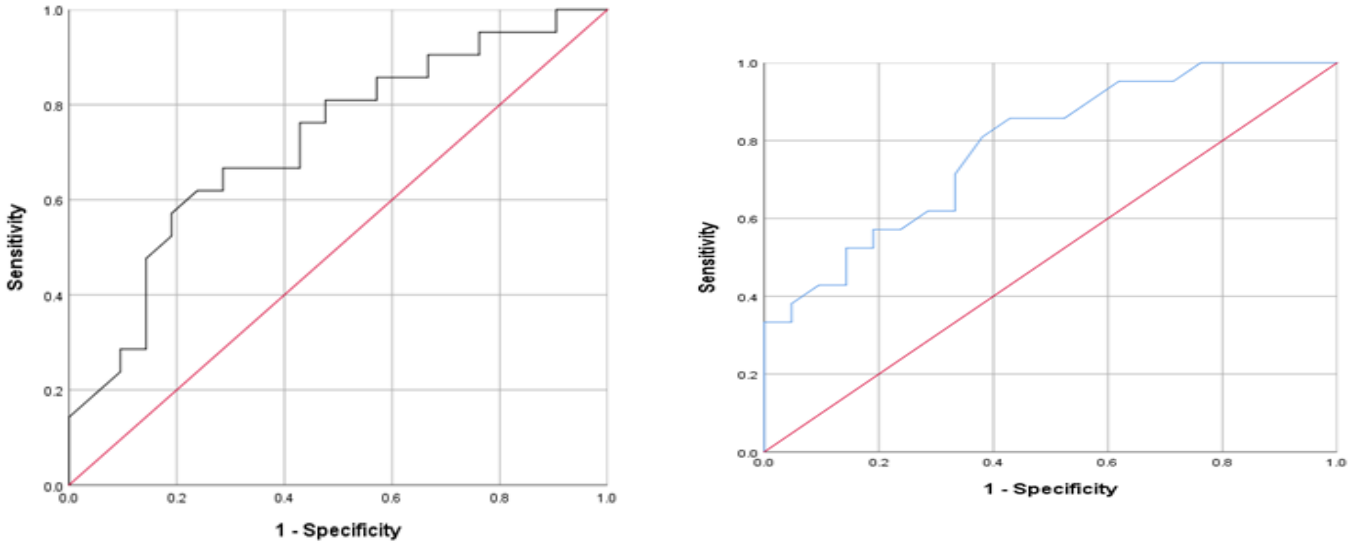
A statistically significant distinction existed among the groups under investigation with respect to age, creatinine, urea and serum IL-6 (significantly greater in hypertensive nephropathy stage III and IV subgroup), sodium, albumin, eGFR and serum omentin-1 (significantly lower in grade III and IV hypertensive nephropathy). There was no statistically significant distinction observed among the subgroups under investigation with respect to systolic and diastolic blood pressure, gender, height, weight, or body mass index, other laboratory data and pelvi-abdominal US, EF, LVEDD or LVEDV **(Table 5)**.

Table 5: Comparison between the studied groups (in hypertensive nephropathy group) regarding anthropometric, clinical data and laboratory data, radiological investigation, serum IL-6, and omentin

Items		Hypertensive nephropathy stage I, II (n=21)	Hypertensive nephropathy stage III, IV (n=21)	p
Sex	Male	15 (71.4%)	9 (42.9%)	0.061
	Female	6 (28.6%)	12 (57.1%)	
Age (year)		45.52 ± 6.39	49.9 ± 6.82	**0.038***
Weight (kg)		78.14 ± 10.79	76.0 ± 10.57	0.519
Height (cm)		172.38 ± 6.86	169.9 ± 7.2	0.022
BMI (kg/m^2)		26.25 ± 3.25	26.9 ± 3.17	0.515
SBP (mmHg)		137.19 ± 10.81	134.1 ± 10.3	0.348
DBP (mmHg)		86.24 ± 6.02	84.71 ± 6.18	0.423
Laboratory Data				
Creatinine (mg/dl)		1.42 ± 0.13	2.9 ± 0.67	**<0.001***
Urea (mg/dl)		41.48 ± 7.41	97.9 ± 3.65	**<0.001***
Sodium (mg/dl)		139.33 ± 2.69	137.33 ± 3.31	**0.038***
Potassium (mg/dl)		4.39 ± 0.43	4.51 ± 0.47	0.362
Triglycerides (mg/dl)		128.57 ± 5.77	149.05 ± 5.73	0.236
Cholesterol (mg/dl)		177.29 ± 41.19	165.71 ± 5.12	0.473
HDL (mg/dl)		48.57 ± 9.57	47.29 ± 8.66	0.65
LDL (mg/dl)		106.19 ± 9.93	93.67 ± 7.4	0.659
ALT (mg/dl)		23.19 ± 4.96	19.48 ± 3.34	0.398
AST (mg/dl)		21.43 ± 3.3	18.48 ± 3.16	0.337
Albumin (g/dl)		4.37 ± 0.25	4.05 ± 0.25	**<0.001***
eGFR (mL/min/1.73 m^2)		64.26 ± 6.1	25.96 ± 4.78	**<0.001***
Radiological investigation				
Sex	Male	15 (71.4%)	9 (42.9%)	0.061
	Female	6 (28.6%)	12 (57.1%)	
EF (%)		63.9 ± 4.35	62.9 ± 4.06	0.446
LVEDD (mm)		51.91 ± 5.63	51.52 ± 5.78	0.83
LVEDV (ml)		130.98 ± 31.75	129.97 ± 34.11	0.948
Omentin-1 (ng/ml)		237.48 ± 36.81	209.14 ± 31.7	**0.011***
IL-6 (ng/ml)		5.86 ± 1.87	8.04 ± 1.8	**<0.001***

Data are displayed as mean ± SD or frequency (%). *: Significant p, BMI: Body mass index, ALT: Alanine aminotransferase, AST: aspartate aminotransferase, HDL: high density lipoprotein, LDL: low density lipoprotein, eGFR: estimated glomerular filtration rate, EF: ejection fraction, LVEDD: left ventricle end-diastolic diameter, LVEDV: left ventricular end-diastolic volume, IL-6: Interleukin 6, DBP: Diastolic blood pressure, SBP: Systolic blood pressure.

The best cutoff points of serum omentin-1 and IL-6 for diagnosis of stage III and IV hypertensive nephropathy respectively were ≤215 and ≥6.7 with AUC 0.721 and 0.785, sensitivity 66.7% and 81%, specificity 71.4% and 61.9%, PPV 68.2% and 68%, NPV 70% and 76.5% and overall accuracy 69% (p=0.014) and 71.4% (p=0.002) **(Figure 2)**.



(A) **(B)**

Figure 2: ROC curve showing performance of (A) serum omentin-1 and (B) IL-6 in diagnosis of stage III and IV hypertensive nephropathy among hypertensive nephropathy.

A negative connection that was statistically significant has been seen between serum omentin-1 and age, systolic, diastolic blood pressure, urea, creatinine, serum IL-6 and eGFR. There was non-significant relation between IL-6 and other parameters. A statistically significant positive relation has been observed between serum omentin-1 and eGFR, serum IL-6 and age, systolic, diastolic blood pressure, urea, creatinine. The connection between serum omentin-1 and other measures was not statistically substantial **(Table 6)**.

Table 6: Correlation between serum omentin-1, IL-6 and studied parameters among patients with hypertensive nephropathy.

Items	Serum omentin-1		IL-6	
	r	p	r	p
Age (year)	**-0.451**	**0.003***	**0.38**	**0.013***
Weight (kg)	-0.213	0.176	0.186	0.239
Height (cm)	0.266	0.088	-0.205	0.193
BMI (kg/m^2)	-0.537	**<0.001***	0.417	0.006*
SBP (mmHg)	**-0.351**	**0.023***	**0.363**	**0.018***
DBP (mmHg)	**-0.342**	**0.027***	**0.345**	**0.025***
Creatinine (mg/dl)	**-0.547**	**<0.001***	**0.673**	**<0.001***
Urea (mg/dl)	**-0.546**	**<0.001***	**0.65**	**<0.001***
Sodium (mg/dl)	-0.025	0.874	-0.025	0.874
Potassium (mg/dl)	-0.168	0.289	0.187	0.235
Triglycerides (mg/dl)	-0.175	0.267	0.174	0.272
Cholesterol (mg/dl)	0.006	0.969	-0.019	0.903
HDL (mg/dl)	0.049	0.758	-0.177	0.262
LDL (mg/dl)	0.013	0.933	-0.042	0.792
ALT (mg/dl)	0.058	0.716	-0.149	0.347
AST (mg/dl)	-0.026	0.869	-0.02	0.899
Albumin(g/dl)	0.266	0.088	-0.263	0.091
eGFR (mL/min/1.73 m^2)	**0.486**	**0.001***	**-0.6**	**<0.001***
EF (%)	0.122	0.44	-0.047	0.767
LVEDD (mm)	-0.089	0.575	0.17	0.281
LVEDV (ml)	-0.106	0.509	0.188	0.238

r: Pearson correlation coefficient *: Significant, BMI: body mass index, SBP: systolic blood pressure, DBP: diastolic blood pressure, ALT: alanine aminotransferase, AST: aspartate aminotransferase, HDL: high density lipoprotein, LDL: low density lipoprotein, eGFR: estimated glomerular filtration rate, EF: ejection fraction, LVEDD: left ventricle end-diastolic diameter, LVEDV: left ventricular end diastolic volume.

DISCUSSION

Obesity is a significant characteristic of metabolic syndrome, and the association between the two has been ascribed to chronic inflammatory process [7]. Obesity causes dysregulation of many adipokines and may play a role in appetite and satiety disturbances, as well as changes in adipose tissue distribution, endothelial function, insulin secretion, regeneration, reproduction, inflammation, energy consumption, angiogenesis, BP, and insulin sensitivity[8].

Age was statistically significantly inversely correlated with serum omentin, according to our research (**p=0.021)**, weight, BMI (p=**<0.001)**, and ALT (p**<0.001**). A positive connection was statistically significantly existed between serum omentin-1 and eGFR (p=0.024). **Lis *et al.*[9]** discovered a negative connection between omentin-1 and the following variables in obese patients: waist circumference, hip circumference, percentage of adipose tissue, fasting insulin, Homeostatic Model Assessment for insulin resistance (HOMA-IR), and SBP. Although a positive correlation between high-density lipoprotein and obese patients as well as the general population has been established, we refrained from including this information in our research.**Moreno-Navarrete *et al.*[10]** identified a negative relation between baseline circulating omentin-1 concentrations and BMI (r = -0.58, p < 0.001), body weight (r = -0.35, p = 0.045), fat mass (r = -0.67, p < 0.001).

Regarding IL- 6 in obesity; in the current study we found statistically significant higher IL-6 in obese group 9.5 ± 2.94 than thin group 3.5 ± 1.17; and at cutoff point of IL-6 of ≥5.55, the sensitivity was high 95.2%, specificity (90.5%), PPV (90.9%), NPV (95%) and overall accuracy 92.9% (p<0.001) for diagnosis of obesity. The connection was statistically significantly positive between serum IL-6 and age (p**<0.001)**, weight (p**<0.001)**, BMI (p**<0.001)**, and ALT (p**<0.001)**. This is in consistence with **El-Mikkawy *et al.*[11]** that discovered very significant variations in weight, BMI, serum triglycerides, and serum LDL-C between research groups with varying degrees of obesity. Significantly elevated circulating concentrations of IL6 were seen in patients who were overweight or obese. **Baikpour *et al.*[12]** discovered insulin resistance to correlate with plasma levels of IL-8 and IL-6 in males with abdominal obesity; a strong positive connection was also observed between serum IL-6 levels and BMI in healthy participants with obesity [12]. When the number of adipocytes is held constant, IL-6 expression is greater in obese adipose tissue from fat persons than in non-obese individuals' adipose tissue[13]. Hypothalamic upregulation of IL-6 receptor expression suggests that IL-6 may play a function in regulating energy intake and appetite[14].

The findings of the current study highlight the need for further research into the regulation of inflammatory markers and omentin-1 level in obesity, the creation of novel medical approaches to mitigate obesity's metabolic risks, the potential utility of IL-6 levels as well as omentin-1 as a predictor of obesity and complications linked to obesity, and advancement of preventative therapies for these conditions. Additionally, omentin-1 may contribute to a function in regulating blood pressure. Experimental and clinical investigations provide evidence that this adipokine influences atherosclerosis and vascular reactivity. Omentin-1 enhances revascularization and boosts endothelial nitric oxide generation following ischemic events. Furthermore, omentin has the ability to impede the release of TNFα and additional pro-inflammatory cytokines from vascular endothelial cells[15,16].

Regarding the association between omentin-1 and hypertensive patients, we found statistically significant higher omentin- l level in control group (366.14 ± 77.5) compared with hypertensive group as well as hypertensive nephropathy group (P<0.001). Moreover, hypertensive nephropathy group showed lower omentin-1 levels (223.31 ± 36.83) than hypertensive group without nephropathy (239.62 ± 23.97) but without statistically significant difference. In the same line we found lower level of omentin-1 in nephropathy stage I, II group than nephropathy stage III, IV group without substantial difference. These findings indicate the connection between omentin-1 level and HTN grade and severity. This is in agreement with **Çelik *et al.*[17]** who exhibited that individuals with HT had lower serum omentin-1 levels than normotensive controls. The decreased concentrations observed in individuals with hypertension may be ascribed to a confluence of factors including endothelial impairment, kidney damage, and inflammation. In research by **Aliasghari *et al.*[18]**, connection between omentin-1 level and SBP in nonalcoholic fatty liver patients was shown to be negative.

In this research, a statistically significant inverse association existed between serum omentin-1 and age, systolic, diastolic blood pressure, urea, and creatinine. A statistically significant positive connection has been observed between eGFR and serum omentin-1. This is in consistence with **Çelik *et al.*[17]** research, where the concentration of omentin-1 diminished with the progression of the HT stage. Thus, it is possible to investigate a connection between omentin-1 concentration and renal kidney damage.

A continuously increased SBP impairs the dilation and causes constriction of the preglomerular afferent arteriole in hypertension individuals. High SBP that is transferred to the kidneys eventually results in nephrosclerosis and glomerular HTN [19]. GFR drops and renal function deteriorates as the HTN stage advances [20]. **Aliasghari *et al.*[18]** exhibited that omentin-1 levels were modestly in relation to SBP but had no connection with DBP. In this study, the best cutoff point of serum omentin-1 for diagnosis of HTN was ≤266.5 with sensitivity of 86.9%, specificity 61.9%, PPV 82%, NPV 70.3% and overall accuracy 78.6%. Furthermore, the best cutoff point of serum omentin-1 for diagnosis of HTN stage I and stage II was ≤215 with sensitivity of 66.7%,

specificity 71.4%, PPV 68.2%, NPV 70% and overall accuracy 69% (p=0.014).

In our study, we finally assessed the association between HTN and IL 6; found statistically significant positive connection between serum IL-6 and age, systolic, diastolic blood pressure, urea, creatinine. A statistically significant inverse relationship could be observed between serum IL-6 and eGFR. **Elsayed *et al.*[21]** study aimed to show a plausible connection between IL-6 levels, insulin resistance, and essential hypertension. IL-6 concentrations in HTN group were significantly greater than in control group (mean ± SD = 5.99 ± 0.84 pg/ml and 1.35±0.38 pg/ml, respectively). IL-6 promotes the synthesis of artery wall collagen, impedes its breakdown, and induces fibrinogen formation[22]. IL-6 exhibits potential as a biomarker; elevated serum concentrations of IL-6 and TNF-α have been suggested by several studies as autonomous risk factors for the onset of hypertension in individuals who are in good health. A link was seen in hypertensive patients between plasma levels of IL-6 and TNF-α and coronary endothelial impairment[23]. Significant positive relationships were seen between circulating IL-6 levels and BMI (P<0.001), which is comparable to **El-Mikkawy *et al.*** results[11]. This can be elucidated by the fact that IL-6 controls disclosure of additional cytokines that enhance the inflammatory response and governs the synthesis of chemotactic mediators, acute phase protein and cell adhesion molecules[24].

In our study, at cutoff point of serum IL-6 of ≥5.65 for diagnosis of HTN, the sensitivity was (73.8%), specificity (54.8%), PPV (76.5%), NPV (51.1%) and overall accuracy (67.5%) and at cutoff point of IL-6 of ≥6.45 for diagnosis of hypertensive nephropathy, the sensitivity was 64.3%, specificity 52.4%, PPV 40.3%, NPV 74.6% and overall accuracy 56.3%.

Limitations of this study included that this study was in a single location; we were unable to generalize our findings. The medicine prescribed to the patients with hypertension and hypertensive nephropathy may have had an impact on their metabolic balances as well as the concentrations of omentin-1 or IL-6.

CONCLUSIONS

Omentin-1 concentrations decreased significantly with rising body weight, as well as with HTN; mainly hypertensive nephropathy and higher stages of HTN. Furthermore, IL-6 increased significantly in obese patients, but insignificant increase was found with hypertensive patient or hypertensive nephropathy. Further studies are needed to assess this relation more.

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REFERENCES

1. **Ji C, Zheng L, Zhang R *et al.* (2018)**: Handgrip strength is positively related to blood pressure and hypertension risk: results from the National Health and nutrition examination survey. Lipids Health Dis., 17:86-92.
2. **Çelik M, Nar R, Nar G *et al.* (2020)**: Serum omentin-1 levels in hypertensive patients. J Hum Hypertens., 22:26-31.
3. **Choe S, Huh J, Hwang I *et al.* (2016)**: Adipose tissue remodeling: Its role in energy metabolism and metabolic disorders. Front Endocrinol., 7:30-9.
4. **Xu X, Xu J (2020)**: Effects of different obesity-related adipokines on the occurrence of obstructive sleep apnea. Endocr J., 67:485-500.
5. **Kocijancic M, Vujicic B, Racki S *et al.* (2015)**: Serum omentin-1 levels as a possible risk factor of mortality in patients with diabetes on haemodialysis. Diabetes Res Clin Pract., 110:44-50.
6. **Watanabe T, Watanabe-Kominato K, Takahashi Y *et al.* (2017)**: Adipose tissue-derived omentin-1 function and regulation. Compr Physiol., 7:765-81.
7. **Rohm T, Meier D, Olefsky J *et al.* (2022)**: Inflammation in obesity, diabetes, and related disorders. Immunity, 55:31-55.
8. **Saeidi A, Jabbour G, Ahmadian M *et al.* (2019)**: Independent and combined effects of antioxidant supplementation and circuit resistance training on selected adipokines in postmenopausal women. Front Physiol., 10:484.
9. **Lis I, Pelczyńska M, Miller-Kasprzak E *et al.* (2020)**: Association of serum omentin concentration with anthropometric, physiological, and biochemical parameters in obese individuals. Nutrition, 153:110-8.
10. **Moreno-Navarrete J, Catalán V, Ortega F *et al.*(2010)**: Circulating omentin concentration increases after weight loss. Nutrition & metabolism, 7:1-6.
11. **El-Mikkawy D, El-Sadek M, El-Badawy M *et al.* (2020)**: Circulating level of interleukin-6 in relation to body mass indices and lipid profile in Egyptian adults with overweight and obesity. Egypt J Hosp Med., 47:7.
12. **Baikpour M, Baikpour M, Hosseini M *et al.* (2017)**: Variations in levels of interleukins and adiponectin in normal and obese adults; a case-control study. J Med Physiol., 2:56-62.
13. **Fried S, Bunkin D, Greenberg A (1998)**: Omental and subcutaneous adipose tissues of obese subjects release interleukin-6: depot difference and regulation by glucocorticoid. J Clin Endocrinol Metab., 83:847-50.
14. **Stenlöf K, Wernstedt I, Fjällman T *et al.* (2003)**: Interleukin-6 levels in the central nervous system are negatively correlated with fat mass in overweight/obese subjects. J Clin Endocrinol Metab., 88:4379-83.
15. **Çimen A, Cerit E, Iyidir O *et al.*(2017)**: Serum omentin-1 levels and endothelial dysfunction in obesity. Acta Endocrinologica, 13:138-44.
16. **Ohashi K, Shibata R, Murohara T *et al.*(2014)**: Role of anti-inflammatory adipokines in obesity-related diseases. TEM., 25:348-55.
17. **Çelik M, Nar R, Nar G *et al.* (2021)**: Serum omentin-1 levels in hypertensive patients. J Hum Hypertens., 35:290-5.
18. **Aliasghari F, Izadi A, Jabbari M *et al.*(2018)**: Are vaspin and omentin-1 related to insulin resistance, blood pressure and inflammation in NAFLD patients? J Med Biochem., 37:470-5.
19. **Ku E, Lee B, Wei J *et al.* (2019)**: Hypertension in CKD: core curriculum 2019. AJKD., 74:120-31.
20. **Yu Z, Rebholz M, Wong E *et al.* (2019)**: Association between hypertension and kidney function decline: the Atherosclerosis Risk in Communities (ARIC) study. AJKD., 74:310-9.
21. **Elsayed A, lbrahim W, Grawesh S *et al.* (2022)**: Study of the relation between il-6, insulin resistance, and blood pressure in essential hypertensive patients. Egypt J Hosp Med., 88:2549-53.
22. **Bautista L, Vera L, Arenas I *et al.*(2005)**: Independent association between inflammatory markers (C-reactive protein, interleukin-6, and TNF-alpha) and essential hypertension. J Hum Hypertens., 19:149-54.
23. **Naya M, Tsukamoto T, Morita K *et al.* (2007)**: Plasma interleukin-6 and tumor necrosis factor-alpha can predict coronary endothelial dysfunction in hypertensive patients. Hypertens Res., 30:541-8.
24. **Fisman E, Tenenbaum A (2010)**: The ubiquitous interleukin-6: a time for reappraisal. Cardiovasc Diabetol., 9:62.