ORIGINAL ARTICLE

Association of Omentin-1 and Central Obesity with Coronary Heart Disease

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ABSTRACT

Background: Omentin-1 is a novel adipocytokine expressed from visceral adipose tissues and is closely associated with obesity, inflammation and coronary artery disease. Central or abdominal obesity has a dynamic role in the development of coronary heart disease by enviably effecting conventional risk factors. Waist circumference is a sensitive, reliable and specific anthropometrical indicator of central obesity. Thus, the present study aimed to evaluate the correlation between central obesity measured by waist circumference and plasma omentin-1 in patients with coronary heart disease.

Methods: The study was performed in cardiac unit of Civil Hospital Karachi and Karachi Institute of Heart Diseases (KIHD), Pakistan from January 2016-August 2016. A total of 250 patients (92 females, 158 males) with coronary artery disease were evaluated. Waist circumference was measured at the level of umbilicus. Determination of Omentin-1 was done by an enzyme-linked immunosorbent assay (ELISA). Data was evaluated by SPSS and one way ANOVA was performed to determine the baseline characteristics of study population. Pearson's correlation was used for association between waist circumference and plasma omentin-1.

Results: There was a negative association between waist circumference and plasma omentin-1 ($R = -0.68$, $p < 0.01$) in males and ($R = -0.50$, $p < 0.01$) in female patients of coronary heart disease. Waist circumference was found an independent determinant of circulating omentin-1 while performing multivariate logistic regression analysis, after adjusting cardio-metabolic risk factors like age, body mass index, lipid profile, blood sugar levels and smoking.

Conclusion: There was a negative correlation of plasma omentin-1 and central obesity in coronary heart disease.

Keywords: Central Obesity; Coronary Heart Disease; Omentin-1; Waist Circumference.

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INTRODUCTION

Coronary heart disease (CHD) is world number one killer[1]. According to latest data published by world health organization, CHD deaths in Pakistan reached 21.76% of total deaths, out of which 50% deaths occur before the age of 65 years[2]. Obesity is an emerging community health concern in both developed and developing countries. Now it is considered as a momentous risk factor for premature deaths due to its strong association with cardiac disease, diabetes mellitus, dyslipidemia and metabolic syndrome via secretion of anti and pro-inflammatory adipo-cytokines[3]. Central obesity (visceral fat deposits) is a sick hidden fat. It is supposed to have a dynamic role in the progress of CHD by way of enviably effecting conventional risk factors of CHD[4]. Waist circumference (WC) is a

sensitive, reliable and specific anthropometrical indicator of central obesity within population groups of different body builds as compared to body mass index (BMI) and waist hip ratio. BMI cannot differentiate between fats around the hips or the waist[5], whereas, waist hip ratio could not reveal abdominal obesity in case of disproportionate and large circumference of hips[6].

Visceral adipose tissue (VAT) is an important endocrine organ of the body, which secretes number of chemical mediators called adipocytokines. Omentin-1 is an adipokine express from visceral adipose tissue[7]. It is a circulating protein with molecular weight 38-kDa. Omentin-1 is considered to have not only anti-inflammatory but also anti-atherogenic and insulin-sensitizing effects, having momentous role in myocardial remodeling, endothelial cells dysfunction[8]. Patients with CHD are reported with reduced levels of plasma omentin-1. Omentin-1 exerts its cardio-protective and anti- inflammatory actions by the inactivation of NF- κB, tissue necrosis factor alpha-1 and cyclooxygenase-II pathway[9].

In general, population, visceral fat is considered as the most important determinants of serum omentin-1. Excessive VAT is associated with decrease omentin-1 secretion. Much research has been done across the world to evaluate the association of anthropometric markers and adipocytokine in cardiovascular diseases however; the correlation has seldom been addressed in Pakistani population. Therefore, the aim of our research was to evaluate the association of waist circumference and omentin-1 in patients with CHD in local population of Karachi, Pakistan.

METHODS

This study was conducted in Cardiac Unit of Civil Hospital Karachi and Karachi Institute of Heart Disease. The sample size of 250 was calculated by open-epi software. The study design was cross-sectional and approved by ethical advisory committee of Dr. Abdul Qadeer Khan Institute of Biotechnology and Genetic Engineering (KIBGE); reference no. KIBGE/ICI: 6/30/05/16. The study protocol and significance of the research was discussed with all participants. After obtaining informed written consent, every participant had an initial assessment, including, collection of medical history regarding diabetes, hypertension, infections, family history of heart disease and smoking.

The patients, who were diagnosed on coronary angiography with more than 50% obstruction in one of the major coronary arteries, were included in study. Patients with infectious diseases, neoplastic diseases and severe liver and kidney dysfunction were excluded from the study. Clinical examination including body weight and height was done to calculate BMI. Waist Circumference was assessed using un-stretchable measuring tape at umbilical level in standing posture. The measurements were performed twice and for the analysis, we used the average value. Both systolic and diastolic blood pressure was measured. Patients were categorized into three groups according to Asian cut off points for waist circumference; that are less than 94 cm in males and 80 cm in females. Group I (Normal); < 94 cm in males; < 80 cm in females, Group II (Moderate risk); 94–101 in males; 81-87 cm in females, Group III (Significant risk); ≥ 102 cm in males; ≥ 88 cm in females[10].

Blood samples were collected from every participant after overnight fasting. The quantitative measurement of omentin-1 was done by using an Enzyme Linked Immunosorbent Assay (ELISA) (Bio-Vendor); according to the company's instructions. Data was analyzed by SPSS version 16.0 (Chicago, USA). Comparison of parametric values between the sub groups was done by one-way ANOVA. The association between study variables and omentin-1 was evaluated by Pearson's correlation test. To determine the independent predictors of Coronary Artery Disease (CAD), multivariable logistic regression analysis was done and *p* value < 0.05 was considered as statistically significant.

RESULTS

Patients were similar with regard of age (Table 1), Systolic Blood Pressure (SBP), Diastolic Blood Pressure (DBP), Total Cholesterol (TC) and Triglycerides (TG). It illustrates the baseline features of the study population (92 females, 158 males). Female patients had low High-Density Lipoprotein (HDL-C) concentrations whereas, increased Low Density Lipoprotein (LDL-C) plasma levels were observed in males. Significant low omentin-1levels were found in patients placed in study group II (25.3±1.0, 26.32±2) and III (13±4.10, 19.1 ± 2.1) as compared to patients placed in group I (29.9 ± 12.7, 28.1 ± 1.7).

Table 1: Demographic, anthropometric and biochemical characteristics of patient categorized in three groups according to waist circumference.

	Male Patients with CHD				Female Patients with CHD			
Parameters	**Group I n=24**	**Group II n=33**	**Group III n=101**	***p* Value**	**Group I n=19**	**Group II n=24**	**Group III n=49**	***p* V alue**
Age(years)	54.56±6.54	55.3 ±6.38	55.7±6.4	0.12	51.98±5.6	52.32±3.32	51.90±3.54	0.11

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BMI(kg/m)²	31.76±4.71	30.05± 4.80	29.19± 5.98	0.22	27.6±8.07	34.5± 4.8	29.09± 4.98	0.03*
SBP(mmHg)	130±12.78	135 ± 13.60	128 ± 10.09	0.21	140±12.0	140±9.02	142±10.75	0.45
DBP(mmHg)	109±8.90	114 ± 0.09	94 ± 16.89	0.01*	88±2.03	93± 4.43	97± 5.08	0.05*
FBS(mg/dl)	98±10.03	104 ± 4.9	99 ± 13.8	0.11	113±4.54	112±12.13	115± 4.9	0.10
TC(mg/dl)	240±14.98	239 ± 25	230± 21.8	0.23	200±9.5	191±3.3	198±2.7	0.10
TG(mg/dl)	154±16.87	158 ± 9.40	161 ±12.32	0.43	159±6.3	160±10.09	163±14.03	0.97
HDL(mg/dl)	43±15.76	45.9 ± 6.2	42.3 ± 10	0.34	40.9±12.4	44.23±3.3	31.05±9.03	0.01*
LDL(mg/dl)	145±7.76	153 ±7.85	173 ± 6.78	0.02*	164±3.5	160±4.3	162±8.72	0.91
Omentin-1 (Pg/dl)	29.9 ± 12.7	25.3 ± 1.0	13±4.10	0.01*	28.1 ± 1.7	26.32±2.09	19.1 ± 2.1	0.01*

*Values are expressed in mean and standard deviation, waist circumference (WC); body mass index (BMI); systolic blood pressure (SBP); diastolic blood pressure (DBP); total cholesterol (TC); triglycerides (TG); low density lipoprotein (LDL); high density lipoprotein (HDL) and fasting blood sugar (FBS), *p value less than 0.05 considered significant.*

The prevalence of central and general obesity (Figure 1) in study population was obtained in both male and female 82.8% patients (n=207). It was proportional to increased waist circumference 34% (n=85) with BMI ≥ 30.

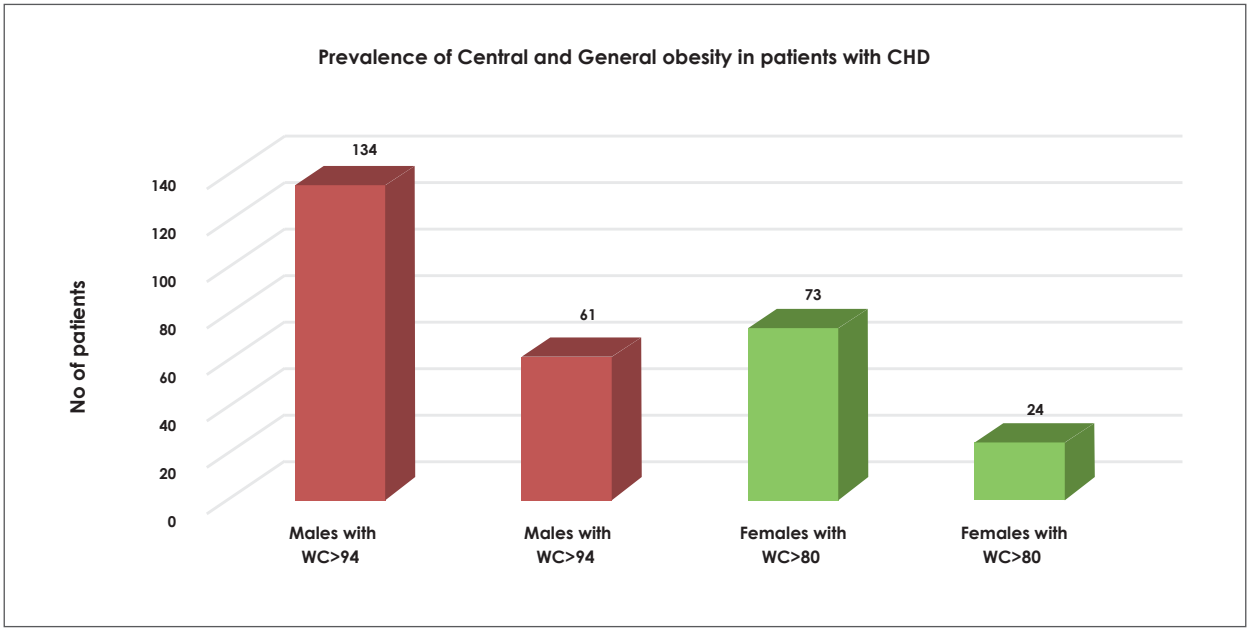

Figure 1: Comparison of waist circumference (WC) in male and female patients with Coronary heart disease (CHD).

Pearson's correlation test (Figure 2) analyzed the association between continuous variable. In male patients of CAD Omentin-1 correlated negatively with LDL-c (R = -0.28 p < 0.2), BMI (R = -0.37, p < 0.2), DBP (R = -0.39, p < 0.6); however; these correlations were not found to be statistically significant. The significant negative correlation was found between WC and omentin-1 (R = -0.68, p < 0.01) in male patients and (R = -0.50, p <0.01) in female patients of CHD.

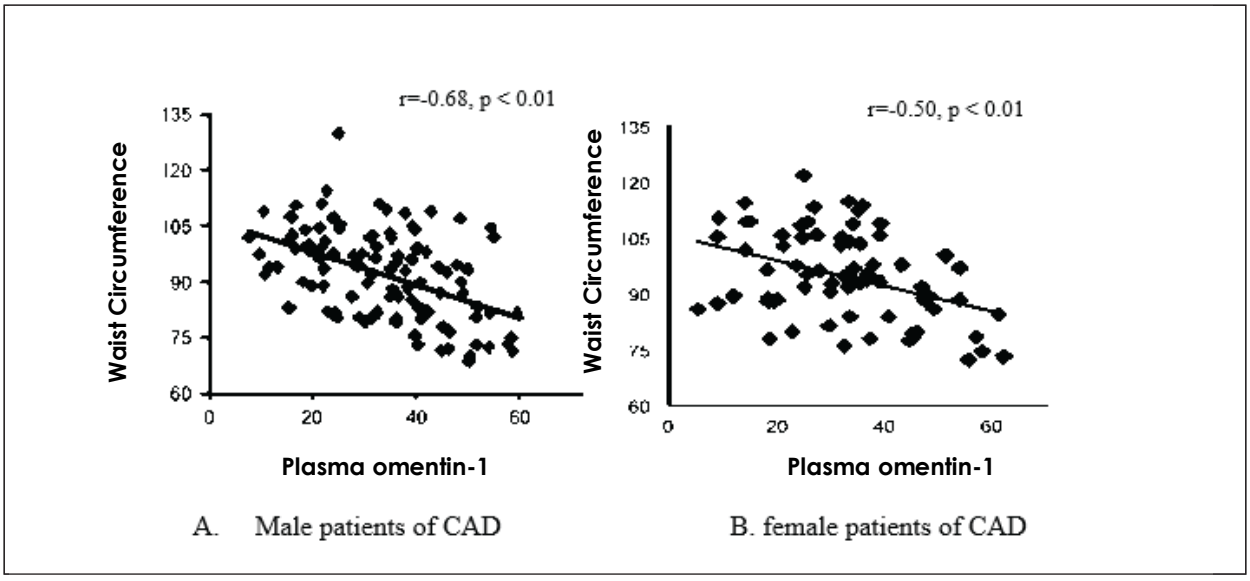

Figure 2: Scattered plot showing pearsons corelation (R) between plasma omentin-1(pg/dl) and waist circumference(cm), *p*< 0.05 considered significant.

In multi-variate logistic regression analysis, we adjusted omentin-1 as the dependent variable, while, cardio-metabolic risk factors (Table 2) including WC as the independent variables. Omentin-1 remains associated with waist circumference in all unadjusted and adjusted models.

Table 2: Multi-variable-logistic regression analysis between omentin-1 (dependent) and waist circumference (independent) variable.

Cardio-metabolic Risk Factor	Model Unadjusted		Model II Adjusted for Age, Sex and BMI		Model III Adjusted for all Parameters	
Parameters	**OR(CI-95%)**	***p*-value**	**OR(CI-95%)**	***p*-value**	**OR(CI-95%)**	***p*-value**
Age	0.08(0.02 -0.2)	0.16	0.1(0.07 -0.2)	0.110	0.10(0.03 -0.2)	0.16
BMI	0.07(0.03 -0.1)	0.12	0.1(0.06 -0.2)	0.21	0.05(0.007 -0.01)	0.22
WC	1.32 (0.002_0.009)	0.001*	2.14 (0.002_ 0.006)	0.001*	2.91 (0.003_0.005)	0.001*
SBP	2.2(1.2 -3.1)	0.91	2.5(1.6 -3.4)	0.61	2.7(0.07 - 0.12)	0.71
DBP	1.9(1.3 -2.5)	0.22	2.3(1.7 -2.9)	0.21	0.1(0.08 -1.9)	0.21
TC	0.07(0.02 -0.2)	0.45	0.01(0.07 -0.2)	0.72	0.01(0 .03-0.2)	0.95
TG	0.07(0.03 -0.1)	0.105	0.01(0.06 -0.2)	0.122	0.05(0.007 -0.01)	0.102
HDL-C	2.12 (0.03_0.09)	0.14	1.09 (0.03_ 0.06)	0.05	1.33 (0.03_0.05)	0.03*
LDL-C	0.08(0.02 -0.08)	0.19	0.1(0.05 -0.2)	0.12	0.06(0.005 -0.1)	0.13
FBS	0.1 (0.2 -0.03)	0.50	0.05 (0.13 -0.01)	0.30	0.07 (0.01 -0.2)	0.90

OR= odd ratios, CI= confidence interval, BMI=body mass index, WC= waist circumference, TC= total cholesterol, TG=total glycerides, LDL-c= low density lipoproteins, HDL-c= high density lipoproteins, FBS= fasting blood sugar, p value less than 0.5 significant.

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DISCUSSION

The current study highlighted the waist circumference, which reflects central obesity, might be considered as an important predictor of CAD by showing its negative correlation with circulating cardio-protective adipocytokine Omentin-1. Recent studies have revealed the increase mortality rate due to CAD with high waist circumference[11-13]. Deficiency of functional adipose tissue and reduced lean muscle mass may be the underlying causing factors.

Studies have revealed that prevalence of central obesity is more as compared to general obesity[14-16]. The present study verifies these findings. We have observed 82.2% (n= 207) of CAD patients had increased WC as compared to 32% (n=81) patients with BMI ≥ 30. The prevalence of increases WC was 84.8% in male patients as compared to female patients with 79%. Matoulek et al., found 95% diabetic females, whereas, 66% diabetic male participants with increases waist circumference[17] Studies conducted in India[18], China[19] and Iran[20] also declared the same conclusions.

Dysregulated secretions of adipocytokine have been observed with excess visceral adipose tissue. Due to reduced expression of omentin-1 gene, circulating omentin-1 and excess visceral adipose tissues are correlated negatively[21-22]. Our findings offer additional support to this perception as omentin-1, anti-inflammatory cytokine, shows decrease expression with increased waist WC. Omentin-1 is considered to have a beneficial role in averting atherosclerosis[23]. It restrains revascularization and endothelial cell functions. Some data indicated that low levels of omentin-1 were closely linked with the presence of CHD and its severity[24-25], which is supported by our study statistics.

To the best of our knowledge, it is reported for the first time in this study, different concentrations of omentin-1 in CAD patients who are categorized according to waist circumference. Our results demonstrated that serum omentin-1 concentrations are significantly higher in male and female patients with WC less than 94cm and 80cm respectively, comparing with those with WC more than 102cm and 88cm. These findings are in line with the results obtained by Elsaid et al., observed omentin-1 in diabetic patient and observed significantly low omentin-1 levels in patients with increased waist circumference (124.1±11.7, 116.5±2.6, $p<0.001$)[26]. The researchers also found decreases omentin-1 levels in insulin resistant patients with increases waist circumference (71.28 ± 27.75; 117.5 ± 15.0, $p<0.0\ 01$)[27].

The current study has also observed strong negative connection between waist circumference and omentin-1 in male patients as compared to females, who showed moderate correlation. Elsaid et al., demonstrated the strong negative association between WC and omentin-1 in Iranian women with diabetes ($R=-0.697$, $p<0.001$)[26]. Although, Alissa et al., and Çimen et al., [21-22] could not find any correlation between omentin-1 and the anthropometric parameters ($R= -0.055$, $p= 0.580$). Although, literature has also reported inverse relationship between serum omentin-1 and BMI[26-28] however, Auguet et al., were failed to find this association[29], probably because BMI is not an ideal predictor of obesity.

CONCLUSION

The prevalence of central obesity is more than general obesity in our local population. This study had also revealed the negative association of WC and cardio-protective adipocytokine omentin-1. As WC is more reliable and inexpensive measure of central obesity, we may propose to include it for CHD risk assessment.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

ETHICS APPROVAL

The study protocol was approved by ethical advisory committee of Dr. Abdul Qadeer Khan Institute of Biotechnology and Genetic Engineering (KIBGE); reference no. KIBGE/ICI: 6/30/05/16.

PATIENTS CONSENT

Written informed consents were taken from all patients.

AUTHORS' CONTRIBUTION

SN did study design, sample collection, data collection, writing the manuscript and analysis the data. AMZ performed the statistical analysis and data collection. MK did the data collection and statistics. SS also performed data analysis, wrote the discussion part and BZ helped in the bench work.

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