Original Article

Association of Serum Adiponectin Levels with the Progression of Coronary Artery Disease

Muhammad Kashif Nisar[1], Erum Afaq[2] and Riaz Ahmed Shahid[3]

ABSTRACT

Objective: To identify whether serum adiponectin level was associated with varying degrees of CAD severity, both among hemodynamically non significant CAD group, which was considered as a control group in this study and in patients with stable CAD.

Study Design: Descriptive study

Place and Duration of Study: This study was conducted at the Ziauddin University Hospital, Karachi from 1st January 2008 to 31st December 2010.

Materials and Methods: Eighty participants who were advised angiography on the basis of ECG findings and blood parameters were selected for this study. They were assessed for CAD. Anthropometric parameters were checked by standard protocol. Serum adiponectin level was estimated by ELISA kit method.

Results: Serum adiponectin levels were found to be significantly high with increased BMI and waist hip ratio at p value of <0.001 while strong negative correlation was observed in CAD patients as the disease progresses.

Conclusion: Serumadiponectin levels can be used as anindicator of the severity of coronary artery disease.

Key Words: Association, Adiponectin, Progression, Coronary artery disease

Citation of articles: Nisar MK, Afaq E, Shahid RA. Association of Serum Adiponectin Levels with the Progression of Coronary Artery Disease. Med Forum 2017;28(8):92-95.

INTRODUCTION

Coronary artery disease (CAD) is one of the major contributors of mortality and morbidity not only in the developed world but also in the developing countries.[1] People of Indo-Asian origin have one of the highest susceptibility to coronary artery disease in the world.[2,3] During the last two decades researchers emphasized that adipose tissue produces and secretes some proteins of specific biological activities. These proteins are well known as a term adipokines.[4] Adiponectin is known to be the most abundantly secreted adipocytokine by the fat cells[5] It is known to exert anti-inflammatory[6,7], insulin sensitizing[8] antiatherogenic[6,9,10] and cardioprotective effects[11] in animals. Adiponectin is unique among other adipocytokines in that it is found in plasma in large quantities, but its concentration is decreased in diabetics[12], obese[5] and CAD[13] and a high serum adiponectin level is believed to be associated with cardioprotection.

1. Department of Biochemistry, Jinnah Medical & Dental College, Karachi.
2. Department of Physiology, Liaquat National Hospital & Medical College Karachi.
3. Department of Physiology, Dow University of Health Sciences, Karachi.

Correspondence: Dr. Muhammad Kashif Nisar, Associate Professor Biochemistry, Jinnah Medical & Dental College, Karachi.
Contact No: 0321-2318813
Email: drkashif2003@yahoo.com

Received: May 01, 2017; Accepted: June 10, 2017

Previously, conflicting results were observed when adiponectin was studied as a marker of cardiovascular disease. Low serum levels were found to be associated with increased risk of CVD in dyslipidemics and diabetic patients and in healthy subjects as well.[14] Contrary to this, other studies shows association of high serum adiponectin level with increased risk of CVD among blacks and elder age groups. [15]

MATERIALS AND METHODS

This descriptive study was conducted in Ziauddin University Hospital Karachi over a period of 2 years from 1st January 2008 to 31st December 2010. A total of 80 patients were included. All the participants were explained about the study and they gave written informed consent. All the participants were referred by a cardiologist for angiography for their preliminary diagnosis of CAD. A detailed history was taken and subjects were included in the study on the basis of inclusion criteria. Patients of both sexes having CAD with age range between 40-55 years were included in the study. Patients with recurrent surgery, endocrinological disorders,revascularization procedure, and patients taking lipid lowering drugs were excluded from this study. Physical examination of all the participants was done and anthropometric measurements such as height, weight, BMI, hip circumference, waist circumference and WHR was calculated by standard methods.[16,17]

Blood was collected at time of angiography. Serum sample aliquots were subsequently stored at −70°C to be used in future. Biological assay was performed in a

laboratory of Ziauddin University Hospital. The plasma concentration of adiponectin was determined by a commercially available sandwich ELISA (human Adiponectin ELISA; from Gesendet: Donnerstag (DRG instruments GmbH, Marburg, Germany). Angiography was performed on TOSHIBA infinix 2000A. Coronary guide wires were selected while keeping in mind the anatomy and morphology of coronary lesion. Coronary artery stenosis ≥50% of luminal narrowing was considered significant. Coronary artery occlusion of <50% was considered as hemodynamically non-significant lesion as taken as a control group for comparison in this study.

Data was entered in Microsoft Excel and analyzed using SPSS-17. Continuous variables like age, height, weight, BMI, waist circumference, hip circumference, waist hip ratio, and serum adiponectin levels were presented by mean and standard error of mean (SEM). ANOVA was performed to compare mean level among four study groups according to extent of CAD. Regression analysis was done to estimate relationship of serum levels of adiponectin with the extent of CAD. Statistical significance was considered if $p \leq 0.05$

RESULTS

Four subgroups were made out of total 80 participants that is non-significant disease group (Subjects whose coronary arteries are <50 % occluded and this group was considered as controls), single vessel disease group, two vessel disease group and three vessel disease group. Out of 80 study subjects, 30 (37.5%) had one vessel, 12 (15%) had two vessels, 24 (30%) had three vessels CAD and 14 (17.5%) had non-significant disease (Fig. 1). Overall mean age of subjects was 48.8±6.1. Analysis of variance (ANOVA) was performed to compare the all included anthropometric parameter in four subgroups groups of patients. Significant effect of larger waist circumference and waist hip ratio ($p<0.001$) was observed (Table 1).

Table No.1: Biometric measurements according to extent of coronary artery disease

Variable	Non Significant (n=14)	One vessel CAD (n=30)	Two vessels CAD (n=12)	Three vessels CAD (n=24)
	Mean±SEM	Mean±SEM	Mean±SEM	Mean±SEM
Age (years)	47.43±1.57	49.13±1.21	49.25±1.51	49.00±1.30
Height (m)	1.61±0.02	1.62±0.01	1.71±0.02	1.65±0.01
Weight (kg)	70.14±3.75	71.77±1.39	77.58±2.51	74.71±1.55
BMI (kg/ m^2)	26.84±1.34	27.15±0.71	26.30±0.54	28.03±0.49
Waist circumference(cm)	85.64±1.53	90.13±1.09	92.67±2.35	94.88±1.29•
Hip circumference(cm)	89.50±1.79	91.83±1.33	90.67±1.71	89.29±0.95
Waist hip ratio	0.94±0.01	0.98±0.01	1.06±0.01	1.07±0.01@

Values are expressed as mean and standard error of mean (SEM)

ANOVA applied

• P value <0.001 statistically significant for larger waist circumference among four study groups.

@ P value <0.001 statistically significant for waist hip ratio among four study groups

It was observed that serum adiponectin levels were highest (5.36±1.17) in subjects who had non significant occlusion (<50%) of coronary arteries and this group is taken as a control group of our study while as the disease progresses in terms of number of coronary arteries involved,levels of adiponectin decreases to 5.13±0.62 in single vessel disease, 2.96±0.30 in two vessel disease and 2.65±0.21 in patients with three vessels coronary artery disease. And this decline in serum adiponectin level is statistically significant at p value of <0.001 in two vessel and three vessel coronary artery disease group when compared with non significant and single vessel disease (Table-2). Figure 2 shows the negative correlation of serum adiponectin level with r value of -0.44 with the extent of coronary artery disease that is with the more number of vessels affected serum adiponectin levels decreases.

Table No.2: Serum adiponectin levels in multivessel coronary artery diseases

Study groups	Serum adiponectin levels (µg/ml)
Non significant disease (n=14)	5.36±1.17
Single vessel disease (n=30)	5.13±0.62
Two Vessels Disease (n=12)	2.96±0.30*S
Three Vessels Disease (n=24)	2.65±0.21*S

*P value <0.001 -Significant compared with hemodynamicallynon-significant (HNS) group.

$ P value < 0.001 Significant compared with one vessel disease group

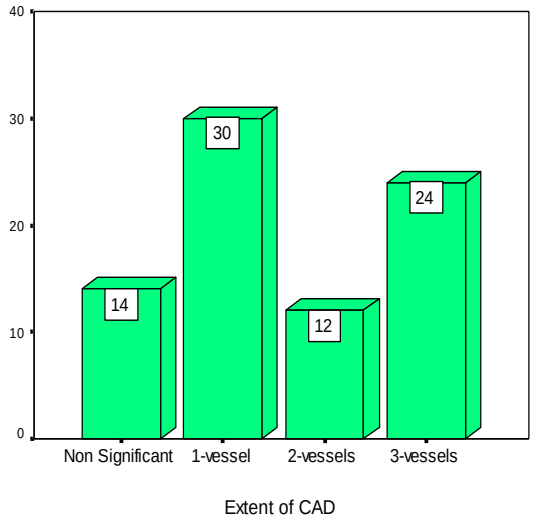

Figure No. 1: Pattern of extent of CAD

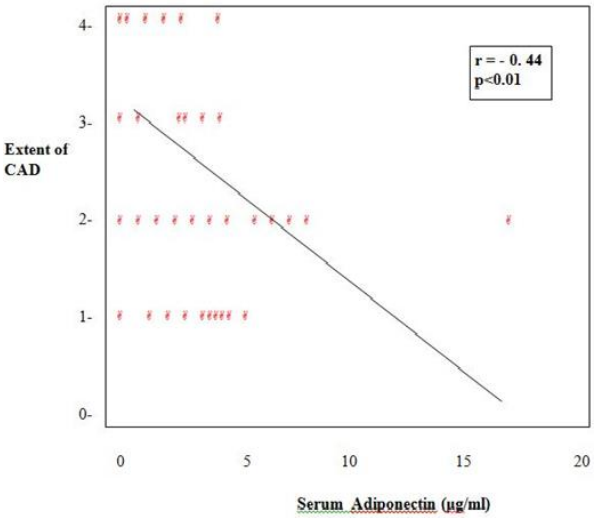

Figure No. 2: Correlation graph for serum adiponectin

DISCUSSION

Adiponectin is the highest circulating adipokine under normal conditions and its concentration decreases in the presence of obesity and its related disorders.[18] Endothelial dysfunction seems to be a pivotal event in the atherosclerotic plaque formation. It can be detected by angiography before appearance of gross morphological changes in the vessel wall. Endothelial dysfunction is a result of an imbalance between endothelial nitric oxide synthase (eNOS) activity and inactivation of nitric oxide (NO) through oxidative stress in the early stages of disease. Adiponectin activates endothelial nitric oxide synthase (eNOS) and eventually production of nitric oxide (NO) in endothelial cells. Adiponectin not only decreases free radicals production but also improves endothelial function in aortas of ApoE KO mice.[19] CAD patients showed significantly lower adiponectin concentrations when compared with those without CAD, concentration of adiponectin was lowest in those presenting with unstable CAD.[20] In another study, Kollias et al. 2011 measured decreased plasma adiponectin levels in CAD patients when compared to non CAD subjects (10.9 ± 3.1 vs. 13.8 ± 5.8 µg/ml respectively, $p < 0.033$). AdipoR1 and AdipoR2 protein levels were decreased in monocytes from CAD when compared to subjects without CAD (59.5 ± 24.9 vs. 80 ± 46 and 70.7 ± 39 vs. 95.6 ± 47.8, $p < 0.05$) [21]

Our findings are consistent with these studies. According to our study serum adiponectin decreased significantly with the progression of disease that is 2VD and 3VD compared with SVD and non significant group (Table-2). The values of adiponectin are significantly high in hemodynamicallynon significant (HNS) group and SVD group at the significance level of 0.05. An inverse correlation ($r = - 0.44$) with serum adiponectin with p value of < 0.001 was observed in multivessel coronary artery disease (Figure-2)..

CONCLUSION

High serum adiponection levels can be considered as a marker of cardioprotection as the levels decreases with the involvement of number of coronary arteries and their extent of occlusion.

Author's Contribution:
Concept & Design of Study: Muhammad Kashif Nisar
Drafting: Muhammad Kashif Nisar
Data Analysis: Erum Afaq, Riaz Ahmed Shahid
Revisiting Critically: Erum Afaq, Riaz Ahmed Shahid
Final Approval of version: Muhammad Kashif Nisar

Conflict of Interest: The study has no conflict of interest to declare by any author.

REFERENCES

1. Gaziano TA, Anand AS. Growing epidemic of coronary heart disease in low- and middle income countries. Curr Probl Cardiol 2010 ; 35(2): 72–115.
2. Gupta M, Singh N, Verma S. South Asians and cardiovascular risk: what clinicians should know? Circulation 2006; 113: 924–9.
3. Joshi P, Islam S, Pais P, et al. Risk factors for early myocardial infarction in South Asians compared with individuals in other countries. JAMA 2007;297:286–94.
4. Knudson JD, Dick GM, Tune JD. Adipokines and coronary vasomotor dysfunction. Exp Biol Med 2007; 232: 727–36.
5. Arita Y, Kihara S, Ouchi N, et al. Paradoxical decrease of an adipose-specific protein, adiponectin, in obesity. Biochem Biophys Res Commun 1999; 257:79–83.

6. Shibata R, Sato K, Pimentel DR, Takemura Y, Kihara S, Ohashi K, et al. Adiponectin protects against myocardial ischemia-reperfusion injury through AMPK- and COX-2-dependent mechanisms. Nat Med 2005;11:1096–1103.
7. Ouchi N, Kihara S, Arita Y, Maeda K, Kuriyama H, Okamoto Y, et al. Novel modulator for endothelial adhesion molecules: adipocyte-derived plasma protein adiponectin. Circulation 1999; 100:2473–2476.
8. Yamauchi T, Kamon J, Waki H, et al. The fat-derived hormone adiponectin reverses insulin resistance associated with both lipoatrophy and obesity. Nat Med 2001;7:941–6.
9. Ouchi N, Kihara S, Arita Y, Okamoto Y, Maeda K, Kuriyama H, Hotta K, Nishida M, Takahashi M, Muraguchi M, Ohmoto Y, Nakamura T, Yamashita S, Funahashi T, Matsuzawa Y. Adiponectin, an adipocyte-derived plasma protein, inhibits endothelial NF-kappaB signaling through a cAMP-dependent pathway. Circulation 2000;102:1296–1301.
10. Okamoto Y, Kihara S, Ouchi N, Nishida M, Arita Y, Kumada M, et al. Adiponectin reduces atherosclerosis in apolipoprotein E-deficient mice. Circulation 2002;106:2767–70.
11. Fujita K, Maeda N, Sonoda M, Ohashi K, Hibuse T, Nishizawa H, et al. Adiponectin protects against angiotensin II-induced cardiac fibro¬sis through activation of PPAR-alpha. Arterioscler Thromb Vasc Biol 2008;28:863–70.
12. Hotta K, Funahashi T, Arita Y, et al. Plasma concentrations of a novel, adipose-specific protein, adiponectin, in type 2 diabetic patients. Arterioscler Thromb Vasc Biol 2000;20:1595–9.
13. Kumada M, Kihara S, Sumitsuji S, Kawamoto T, Matsumoto S, Ouchi N, et al. Coronary artery disease. Association of hypoadiponectinemia with coronary artery disease in men. Arterioscler Thromb Vasc Biol 2003;23:85–9.
14. Bouhali T, Brisson D, St-Pierre J, Tremblay G, Perron P, Laprise C, et al. Low plasma adiponectin exacerbates the risk of premature coronary artery disease in familial hypercholesterolemia. Atherosclerosis 2008;196:262–9.
15. Kizer JR, Barzilay JI, Kuller LH, Gottdiener JS. Adiponectin and risk of coronary heart disease in older men and women. J Clin Endocrinol Metab 2008;93:3357–64.
16. Banks WND. Global Data Base on Obesity and Body Mass index (BMI) in Adults.(Accessed at htpp://www. who. Int/nut/db_bmi.htm). August; 2002
17. Organization WH. Waist circumference and waist-hip ratio: Report of a WHO expert consultation, Geneva, 8-11 December 2008: World Health Organization; 2011.
18. Karastergiou K, Ali VM, Jahangiri M and Kaski JC, et al. Review: Adiponectin for prediction of cardiovascular risk? Bri J Diabet Vasc Disease 2009; 9: 150.
19. Zhang H,CuiJ,Zhang C et al. Emerging Roles of Adipokines as a mediator of Atherosclerosis. World J Cardiol 2010; 2(11): 370–76.
20. Pilz S, Mangge H, Wellnitz B, Seelhors U, Winkelmann BR, Tiran B, et al. Adiponectin and mortality in patients undergoing coronary angiography. J Clin Endocrinol Metab 2006; 91:4277-86.
21. Kollias A, Tsiotra PC, Ikonomidis I, Maratou E, Mitrou P, Kyriazi E, et al. Adiponectin levels and expression of adiponectin receptors in isolated monocytes from overweight patients with coronary artery disease. Cardiovascular Diabetol 2011; 10:14.