Original Article

Visfatin and its relationship with the Severity of Coronary Artery Disease in Pakistani Population

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ABSTRACT

Objective: To determine plasma visfatin levels in patients with and without coronary artery disease and to correlate it with the coronary vessels blockage by using angiography.

Study Design: Comparative Cross Sectional Study.

Place and Duration of Study: This Study was conducted at the Department of Biochemistry, Ziauddin University and Jinnah Medical and Dental College, Karachi from June 2009 to November 2010.

Materials and Methods: The study includes 80 subjects (mean age48.8±6.15; 40-55 years age range) who underwent coronary angiography for suspected coronary artery disease. Plasma visfatin levels were determined by using ELISA.

Results: Out of these 80 study subjects, 30 (37.5%) had single vessel CAD, 12 (15%) had two vessels CAD, 24 (30%) had three vessels CAD and 14 (17.5%) had non significant disease. Serum Visfatin levels were higher in three vessel disease (5.82 ± 0.58) when compared with non significant (4.55 ± 1.10) single vessel disease (4.86±0.93) and two vessels disease (5.53± 0.79) respectively but these values were statistically nonsignificant in all four study groups.

Conclusion: Serum Visfatin levels were high in all three study groups when compared with non significant disease group and positive correlation of serum visfatin with the extent of the coronary artery disease was observed.

Key words: Visfatin; coronary artery disease; angiography; single vessel disease; non significant disease.

INTRODUCTION

Coronary artery disease shares a major burden of mortality worldwide. It remains the leading cause of death not only in industrialized nations but countries like Pakistan and India are also listed in the countries where prevalence of CAD is on the rise and surprisingly younger age group is the target in this region. Studies suggest an almost 2.5-fold rise in the prevalence of CAD in two decades—from 3.6% in the 1970s to 9.5% in the 1990s in people aged ⩾35 years in urban India [1]

According to World Health Organization (WHO) estimates, 60% of total world CAD deaths will be in India. India now is on the midway of CAD epidemic and Indians who live in urban areas have higher CAD rate [2] Although CAD rates become half in western populations in the past 30 years, rates doubled in India and no signs of decline in it is evident yet[3]

One out of five middle-aged adults in urban areas of Pakistan may have underlying CAD. Women are more at risk than men. Possibly this high prevalence of CAD in the Indo-Pakistan population is due to a greater vulnerability to the metabolic syndrome. Smoking is the major factor for greater prevalence of CAD in men [4] other reported contributors of CAD in Pakistani population are obesity, high blood cholesterol levels and atherosclerotic disease of vessels [5]

Adipose tissues synthesize and secrete some proteins which are known as adipokines and these include Visfatin, leptin, adiponectin, resistin and many others. Role of adipokines is well established in inflammation [6] Atherosclerotic lesions have been also reported to express these adipokines[7,8]

Visfatin is a newly identified adipokine having high expression in visceral adipocyte. Macrophages of adipose tissue are principle source. It has a molecular weight of 52 kDa and its gene encodes 491 aminoacids. Structurally it is similar to pre-B cell colony-enhancing factor (PBEF) It is widely distributed in bone marrow, liver, spleen, pancreas, heart, kidneys, thymus gland and other tissues. Visfatin is reported to be associated with endothelial dysfunction, atherosclerosis, plaque rupture and the metabolism of glucose and lipid [9, 10, 11, and 12]. However positive correlation has been found between the expression of visfatin and coronary atherosclerosis [13]

MATERIALS AND METHODS

Subjects: A total of 80 subjects aged in between 40-55 years were included in the study who were advised for angiography by the consultant cardiologist for their preliminary diagnosis of CAD. Before angiography detailed history was taken and patients with other cardiovascular diseases, and endocrinological disorders were excluded from the study.

All participants underwent detailed physical examination including measurement of height and weight with standard methods. The study was approved by ethical committee of Ziauddin University. All the participants were explained about the study and they gave written informed consent.

Sampling and assay: Blood samples were obtained by venipuncture at the time of angiography and then centrifuged at 3000rpm for 5 minutes within 20 minutes of its collection and stored at - 70ºC for its future use. Serum visfatin levels were determined by commercially available ELISA kit (Pheonix Pharmaceuticals, Belmont,CA,USA)

Angiography: Angiography was performed on TOSHIBA infinix 2000A. Coronary guide wires were selected while keeping in mind the anatomy and morphology of coronary lesion.

Statistical Analysis: Statistical analysis was performed by using SPSS (Statistical program for social sciences) version 17. Continuous response variables like age, height, weight, BMI, waist circumference, hip circumference, waist hip ratio, and serum visfatin levels were presented by standard error of mean (**s.e.m**) and 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 visfatin with the extent of CAD. Statistical significance was considered if $p \leq 0.05$.

RESULTS

80 Study participants were subdivided into four study groups 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.

Table No. 1: Physical characteristics of patients with multivessel Coronary artery disease(CAD) Values are expressed as mean and standard error of mean (s.e.m)

	Non Significant (n=14)	One vessel CAD (n=30)	Two vessels CAD (n=12)	Three vessels CAD (n=24)
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

Table No.2: Serum Visfatin levels in multivesssel Coronary Artery Disease. Values are expressed as mean and standard error of mean (s.e.m).No: of cases are given in parenthesis.

Study Groups	Serum Visfatin Levels (ng/ml)
Non Significant Disease (n=14)	4.55 ± 1.10
Single Vessel Disease (n=30)	4.86 ± 0.93
Two Vessels Disease (n=12)	5.53 ± 0.79
Three Vessels Disease (n=24)	5.82 ± 0.58

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. (Figure 1)
Overall mean age of subjects was 48.8±6.1. Significant effect of larger waist
Circumference and waist hip ratio ($p<0.001$) was observed. (Table 1)

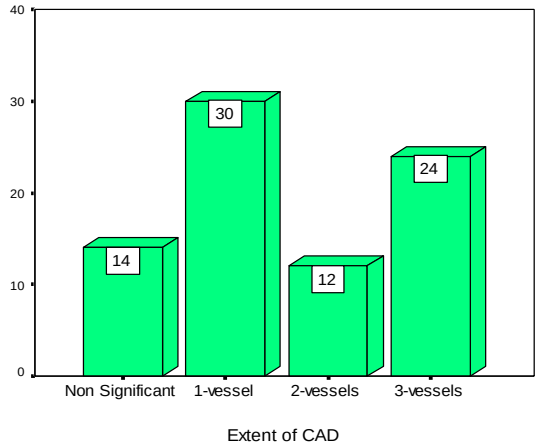

Figure 1: **Pattern of extent of CAD.**

Table -2 shows plasma levels of visfatin in multivessels coronary artery disease. Mean serum visfatin levels were statistically non-significant in all four study groups. Visfatin levels were higher in three vessel disease when compared with non significant group, single vessel disease and two vessels disease.

Moreover, statistically non significant (p value <0.176) positive correlation exists between serum visfatin and extent of CAD (r = 0.153) (Figure-2).

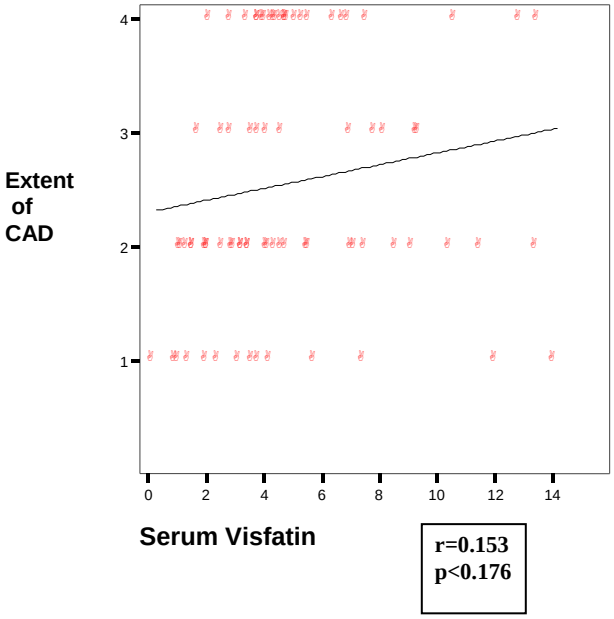

Figure-2: Correlation graph of serum visfatin with the extent of CAD.

DISCUSSION

Adipose tissues are no longer considered as fat store depot but they are recognized as a functional endocrine organ which releases numerous bioactive peptides knows as adipokines. These factors are not only active in adipose tissues but can circulate in blood reaches to distant sites and elicit their biological effects in the regulation of food and energy metabolism, insulin sensitivity, inflammation and vascular homeostasis[14,15] Visafatin is a newly found novel adipokine which is expressed in visceral fat. Obesity and type 2 diabetes mellitus are reported to be associated with high plasma visfatin levels. Visfatin is highly expressed in macrophages within human unstable atherosclerotic lesions, and has been proposed to potentially play roles in atherosclerotic plaque destabilization[16].

Fu et al. 2009 reported significantly higher plasma visfatin levels in CAD patients in Chinese population when compared with the controls and suggested plasma visfatin as a helpful marker of early CAD [17] In another study byYu Qin et al, 2010 demonstrated significantly higher levels of visfatin in obese CAD patients as compared with the controls [18] Kadogluo et al, 2011 also reported significantly high visfatin and hsCRP levels in CAD patients in Greece population [19]

To the best of our knowledge no such study has been carried out in Pakistan which can relate plasma visfatin levels with atherosclerosis and coronary lesions. In our study we demonstrated plasma visfatin levels with the extent of CAD in group of Pakisatni population.

Our findings are not consistent with the data that has been already published. Furthermore our results shows gradual rise of serum visfatin levels in all the four study groups when compared with the number of coronary arteries involved but this gradual rise is statistically non-significant in all four study groups. These findings are consistent with the data presented by Choi et al,2008[20], in which he compared serum lipocalin-2 and visfatin levels in patients of CHD and he concluded that circulating lipocalin-2 levels were significantly higher in patients with CHD compared with the control subjects (82.6±38.7 ng/ml versus 43.8±27.8 ng/ml; P<0.001). However, visfatin levels were not significantly different between patients with CHD and control subjects.

CONCLUSION

Visfatin levels increases in three vessel disease compared with two and single vessel disease but is nonsignificant. However positive correlation exists between visfatin and extent of CAD but is also nonsignificant.

Study on large scale may provide some significant results.

Limitation of the Study: Sample size was small due to budget constraints.

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