Research Article

Association between plasma adiponectin and risk of myocardial infarction in Asian Indian patient with diabetes

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Abstract

Context: Recent epidemiological studies have established association of adiponectin with insulin resistance and cardiovascular risk factors. However, newer reports state an ethnic difference in this association.

Objectives: The present study was done to assess the association between plasma adiponectin levels and coronary event in Asian Indian patients with diabetes. The relation between plasma adiponectin and various cardiovascular risk factors in an acute coronary event was also studied.

Methodology: The prospective study was conducted at a tertiary care center in Bangalore, India. Three groups of 30 patients-Patients with diabetes with Myocardial Infarction (MI), Patients with diabetes without MI and controls (age and sex matched non-patients with diabetes)- were included in the study. The association between plasma adiponectin level and MI in patients with diabetes was studied in comparison to patients with diabetes without MI.

Statistical analysis used: Analysis of Variance, Spearman Correlation

Results: Patients with diabetes with MI had significantly lower plasma adiponectin when compared to patients with diabetes without MI which in turn was lower than in normal subjects (P<.001). Plasma adiponectin was significantly correlated with abdominal obesity (r=-.31), fasting glucose level (r=-.61), glycated haemoglobin (r=-.63) and triglycerides (r=-.54) (all P <.001). There was no significant correlation between plasma adiponectin levels and High Density Lipoprotein-Cholesterol in the present study.

Conclusions: The present study and the recent evidence suggest that cross-talk between inflammatory signalling pathways and insulin signalling pathways may result in insulin resistance and endothelial dysfunction that synergize to predispose to cardiovascular disorders.

Key Messages: Adiponectin is a potential target in future research for reducing morbidity and mortality associated with atherosclerotic disease.

Keywords: Adiponectin, Diabetes, Myocardial infarction, HDL cholesterol.

Introduction

Adiponectin, first reported in 1995 by Scherer et al, is a novel and important member of the adipokine family.[1] It is a collagen-like protein that is exclusively synthesised in white adipose tissue and is the gene product of adipose most abundant gene transcript 1 (apM1).

Adiponectin has been postulated to play an important role in the modulation of glucose and lipid metabolism in insulin-sensitive tissues in both humans and animals. Various studies have reported a protective effect of plasma adiponectin against type 2 Diabetes Mellitus (T2DM)[2-6]. Adiponectin is also inversely associated with traditional cardiovascular risk factors, such as total and low-density lipoprotein cholesterol (LDL-C) and triglyceride levels, and is positively related to high-density lipoprotein cholesterol (HDL-C).[7] Recent studies suggest that it may have anti-atherogenic and anti-inflammatory properties.[8-10] A few researchers who studied the combined effects of these findings reported inverse correlation between plasma adiponectin and risk of coronary heart disease.[11-15]

Recent epidemiological studies have shown that association of adiponectin with insulin resistance and cardiovascular risk factors vary with ethnicity. Mente et al studied the ethnic variations in adiponectin concentrations and insulin resistance and found that South Asians and aboriginal people display a greater increase in insulin resistance with decreasing levels of adiponectin compared to Chinese and Europeans.[16] However, a similar study involving Asian Indian teenagers showed that adiponectin did not correlate directly with measures of insulin sensitivity, overweight, and other cardio-metabolic variables.[17] Similar studies in adults are not available.

The present study was done to assess the association between plasma adiponectin levels and coronary event in patients with diabetes. Also the relation between plasma adiponectin level and various cardiovascular risk factors were studied in patients with diabetes with and without acute coronary event.

Subjects and Methods:

The prospective study was conducted at a tertiary care centre in Bangalore, India from January 2008 to December 2009. The study was approved by the institution ethics committee. Three groups of patients, age and sex matched, were included in the study. The first group included 30consecutive T2DM patients admitted with a diagnosis of myocardial infarction (MI) at the study centre. While the second consisted of patients with T2DM without MI, the third group were patients without diabetes without any history of acute coronary event. MI was diagnosed as per World Health Organization's criteria.[18] Patients aged less than 18 years were not included in the study. Patients with diabetes with chronic kidney disease or receiving Thiazolidinediones were also excluded from the study as it would alter plasma adiponectin levels.

Fasting Blood Glucose (FBG), Post-Prandial Blood Glucose (PPBG), Glycated Hemoglobin (HbA₁C), Fasting Lipid Profile, Baseline Electrocardiogram and Plasma Adiponectin were done for all the study subjects. In addition, Coronary Angiogram was done for patients with diabetes with MI to confirm Coronary Artery Disease (CAD) and treadmill tests were done for patients with diabetes without MI to exclude underlying CAD.

FBG and PPBG, serum total cholesterol and serum triglycerides were estimated using enzymatic kit method (Vital Diagnostics, Mumbai, India); and serum HDL-C (Bayer Diagnostics, Baroda, India) using a semi-auto-analyser.

Plasma Adiponectin levels was estimated using Human Total Adiponectin/Acrp30 Quantikine ELISA Kit (R&D Systems Inc., India). This assay employs the quantitative sandwich enzyme immunoassay technique. A monoclonal antibody specific for the Adiponectin globular domain has been pre-coated onto a microplate. Standards and samples are pipetted into the wells and any Adiponectin present is bound by the immobilised antibody. After washing away any unbound substances, an enzyme-linked monoclonal antibody specific for the Adiponectin globular domain is added to the wells. Following a wash to remove any unbound antibody-enzyme reagent, a substrate solution is added to the wells and colour develops in proportion to the amount of Adiponectin bound in the initial step. The colour development is stopped and the intensity of the colour is measured.

Statistical Analysis

Statistical analyses were performed using Statistical Package for Social Sciences (SPSS) for Windows 16.0 (SPSS Inc., Chicago, USA). The results for each parameter (numbers and percentages) for discrete data and average (mean ±standard deviation) for continuous data are presented in tables and figures using Microsoft office 2007 software package.

Two-way Analysis of Variance (ANOVA) was performed for plasma adiponectin in patients with diabetes with MI, patients with diabetes without MI and controls as the grouping factor. Two tailed 'P' values less than 0.05 were considered significant. Spearman correlation was performed to analyse the association between plasma adiponectin, BMI, FBG, PPBG, HbA₁C, serum triglycerides, HDL-C and LDL-C.

Results

The following results are expressed as mean± standard deviation. The mean age of the study subjects in the three groups-patients with diabetes with MI, patients with diabetes without MI and Controls- was 58.00±8.77 years, 57.17±9.34 years and 54.20±7.28 years respectively. The descriptive statistics of the various parameters under study is given in table 1.

Patients with diabetes with MI had significantly lower plasma adiponectin levels (6.11±1.82) when compared to patients with diabetes without MI (9.47±1.55) which in turn was lower than normal subjects (17.82±1.30) (P<.001) . Plasma adiponectin was significantly correlated with BMI (r=-.31), FBG (r=-.61), HbA₁C (r=-.63) and triglycerides (r=-.54) (all P<.001). We did not find any significant correlation between plasma adiponectin levels and HDL-C (Table 2).

Discussion

In the present study, we found decreased plasma adiponectin concentrations in the patients with diabetes which was further lower in patients with an acute coronary event indicating that it may be a predictor of macroangiopathy. Hotta et al found similar results in their study and proposed that accumulation of adiponectin in atherosclerotic vascular walls may accelerate its half-life in plasma, resulting in the reduction of the plasma concentration of adiponectin in subjects with CAD .[19] Ouchi et al studied the molecular basis of link between adiponectin and vascular disease and found that adiponectin modulates endothelial inflammatory response and that the measurement of plasma adiponectin levels may be helpful in assessment of CAD risk. [20]

Table 1: Descriptive statistics of various parameters under study

Variable	Controls Mean (±Std. Dev)	Patients with diabetes without MI Mean (±Std. Dev)	Patients with diabetes with MI Mean (±Std. Dev)
Plasma Adiponectin	6.11(±1.82)	9.47(±1.55)	17.82(±1.30)
Fasting Blood Glucose	123.50(±17.85)	133.23(±16.14)	88.80(±6.27)
Post-Prandial Blood Glucose	190.53(±19.27)	209.33(±28.72)	125.30(±6.200
Glycated Haemoglobin	7.81(±0.92)	8.04(±1.24)	4.06(±0.62)
Total Cholesterol	205.77(±19.92)	214.43(±21.54)	138.07(±10.38)
Serum Triglycerides	148.80(±11.32)	160.53(±14.61)	127.23(±6.11)
Serum HDL	45.13(±8.57)	37.43(±9.73)	44.87(±7.78)
Serum LDL	129.30(±22.55)	137.27(±18.83)	120.03(±8.27)
Body Mass Index	27.82(±2.39)	27.08(±2.20)	25.40(±2.63)

Patients with diabetes with MI had significantly lower plasma adiponectin when compared to patients with diabetes without MI which in turn was lower than in normal subjects

Table 2: Spearman correlation between adiponectin and body mass index, blood lipids, HbA$_{1C}$, fasting and post-prandial glucose levels

	Adiponectin	BMI	FBG	HBA1C	TG	HDL	LDL
Adiponectin	1.00	-0.31**	-0.61**	-0.63**	-0.54**	0.02	-0.16
BMI		1.00	0.37**	0.29**	0.25*	-0.14	0.10
FBG			1.00	0.62**	0.61**	-0.17	0.21*
HBA1C				1.00	0.83**	-0.45**	0.35**
TG					1.00	-0.53**	0.33**
HDL						1.00	-0.07
LDL							1.00

** Correlation is significant at the 0.01 level (2-tailed); * Correlation is significant at the 0.05 level (2-tailed); (BMI- Body Mass Index, FBG- Fasting Blood Glucose, HDL- High Density Lipoprotein, LDL-Low Density Lipoprotein, HBA1C- Glycated Haemoglobin, TG- Serum Triglycerides); Plasma adiponectin was significantly correlated with BMI, FBG, HbA$_{1C}$ and triglycerides (all P<.001). The correlation between plasma adiponectin levels and HDL-C was not statistically significant.

Large scale prospective experimental research is needed to clarify these theories.

The relation between plasma adiponectin and the various known metabolic risk factors were on par with the world literature, except for HDL-C. Koenig et al reported an additive effect of HDL-C and adiponectin on CAD risk prediction. [21] In their joint analyses, the highest risk for T2DM as well as acute coronary events was observed in men with low adiponectin in combination with low HDL-C levels. In the present study, the mean HDL-C levels were lower in patients with diabetes with MI compared to patients with diabetes without MI. However, we did not find any significant correlation between plasma adiponectin levels and HDL-C in the present study. Similar findings were obtained by Schulze et al indicating that although plasma adiponectin has been established to be correlated with insulin resistance, CAD and metabolic disease, the interrelation between these is far more complex.

The molecular mechanisms by which adiponectin exerts its multiple functions and whether its actions are receptor mediated still remain a mystery. Is the primary activity of adiponectin antiatherosclerotic, or is it principally a modulator of lipid metabolism and regulator of insulin sensitivity, or is it all of the above? The answers to these and other intriguing questions will undoubtedly provide additional insight into the metabolic roles of this new adipocyte hormone.

Conclusion

The present study and the recent evidence suggest that cross-talk between inflammatory signalling pathways and insulin signalling pathways may result in insulin resistance and endothelial dysfunction that synergise to predispose to cardiovascular disorders. Large scale prospective studies are needed to examine the ability of increase in adiponectin levels and insulin sensitivity to improve primary end points including incidence of diabetes and outcomes of cardiovascular events.

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