ORIGINAL ARTICLE

RELATIONSHIP OF ADIPONECTIN LEVEL WITH LIPID PROFILE IN TYPE-2 DIABETIC MEN WITH CORONARY HEART DISEASE

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Background: Cerebro-vascular disease is a commonest long term complication of type-2 diabetes mellitus. The study was done to determine concentration of serum adiponectin and lipid profile in type-2 diabetic men with coronary heart disease (CHD) in the region of Khyber Pakhtunkhwa (KPK), and to find possible relationship between them. **Methods**: This was a cross-sectional study comprising of randomly selected thirty six healthy adult males and thirty six type-2 diabetic males with coronary heart disease. Their fasting blood samples were analysed for serum adiponectin, fasting blood glucose, glycosylated haemoglobin and lipid profile which included total cholesterol (T-C), triglycerides (TG), high-density lipoprotein cholesterol (HDL-C) and low-density lipoprotein cholesterol (LDL-C). The relationship of adiponectin with other variables in type-2 diabetic men with coronary heart disease was determined with Pearson correlations coefficient (r). **Results**: Type-2 diabetic males with coronary heart disease when compared to healthy males showed significantly low levels of serum adiponectin (p=<0.001) and HDL-C (p=<0.001) and significantly high level of FBG (p=<0.001), HbA1c (p=<0.001), TC (p=<0.05), TG (p=<0.05) and LDL-C (p=<0.05). Serum adiponectin level showed a significant negative correlation with FBG (r = -0.332; p= 0.04), HbA1c (r = -0.818; p=<0.01) and TG (r = -0.640; p=<0.01) in type-2 diabetic men with coronary heart disease. Adiponectin showed a significant positive association with HDL-C in controls (r = 0.948; p=<0.01) and patients of type-2 diabetes with CHD (r = 0.650; p=<0.01). **Conclusion**: Serum adiponectin concentration is markedly decreased in patients of type-2 diabetes with coronary heart disease. Hypoadiponectinemia is related with deranged lipid profile, i.e., high TG and low HDL-C levels in type-2 diabetic men with CHD. Moreover, adiponectin is associated positively with HDL-C and negatively with HbA1c and TG levels in the studied population.

Keywords: Adiponectin, Lipid profile, Type-2 diabetes mellitus, Coronary heart disease

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INTRODUCTION

World population of type-2 diabetes mellitus will increase up to 366 million by the year 2030, affecting more people in Asia and Africa.[1] Cerebro-vascular disease is a commonest long term complication of type-2 diabetes mellitus.[2] In the United States, type-2 diabetes mellitus has become the sixth leading cause of death, with most of them occurring due to associated cardiovascular disease.[3] The prevalence of coronary heart disease is considered to double by the year 2020; more people would be affected in the developing countries.[4]

Adiponectin, a protein hormone containing 244 amino acids and is secreted by adipose tissue.[5] It circulates in high concentrations in plasma, exists in various complex oligomeric forms and plays a key part in the carbohydrate and lipid metabolism.[6] Increased adiponectin level leads to increased insulin sensitivity, elevated level of HDL cholesterol and decreased level of serum triglycerides.[7] Adiponectin exerts anti-inflammatory and anti-atherogenic actions in the vascular system, rendering it a cardioprotective role.[8] Studies have related low serum level of adiponectin with obesity, type-2 diabetes mellitus and coronary heart disease.[9–11]

Investigation of the cardioprotective role of adiponectin in humans has revealed conflicting results so far.[12–14] Lawlor *et al* have also reported a gender based difference regarding this issue.[15] The exact relationship of adiponectin with atherosclerosis in humans remains unclear, making more research necessary.[16]

The objective of this study was to determine the correlation between adiponectin with lipid profile in type-2 diabetic men with coronary heart disease.

MATERIAL AND METHODS

This study was conducted at tertiary care hospitals, Khyber Teaching Hospital (KTH), Hayatabad Medical Complex (HMC), Lady Reading Hospital (LRH) and Rehman Medical Institute (RMI), Peshawar. The study was carried out for six months.

This cross-sectional analytical study consisted of two groups, A and B. Group A consisted of 36 normal control male individuals which were free of diabetes mellitus, coronary heart disease, diseases of kidney and thyroid. Group B consisted of 36 type-2 diabetic men with coronary heart disease, i.e., those who had myocardial infarction within last 10 days. A well-designed questionnaire recorded detailed history of all participants and their blood pressure, height, weight and BMI (weight in kg/height in m^2) were measured. Informed consent was taken from each participant and the study was approved by the Ethical Committee of Khyber Medical College, Peshawar.

A venous blood sample (5 mL) was collected from each participant after overnight fasting. Serum was obtained by centrifuging 3 mL blood sample at 3000 rpm for 5 minutes. Analysis of fasting blood glucose and lipid profile was done on fresh samples while glycosylated haemoglobin was measured on blood collected in EDTA tubes. Serum was stored at -70 ºC for analysis of adiponectin.

Fasting blood glucose, serum total cholesterol and serum triglycerides were measured colorimetrically using kits provided by Elitech-Sees, France. HDL cholesterol was measured by colorimetric method using kit provided by Diasys Holzheim, Germany. Friedewald's formula[15] was used to calculate low density lipoprotein cholesterol (LDL-C). Glycosylated haemoglobin was measured using kit provided by Human Diagnostics, Germany. Serum adiponectin level was analyzed on ELISA method (enzyme linked Immuno-sorbent assay) using Human adiponectin ELISA kit (Biovendor Cat. No. RD 195023100, Germany).

Analysis of the data was performed using SPSS version 19. All results were expressed as mean±SD. Independent samples *t*-test was used to compare variables between the studied groups; *p*-value ≤ 0.05 was considered statistically significant. Association of adiponectin with lipid profile and other variables was found using Pearson's correlation coefficient (r).

RESULTS

Mean and standard deviation of demographic, clinical and biochemical characteristics of the studied population are summarized in table-1. Group A consisted of 36 normal males with a mean age of 47.2 years±5.5 years and group B consisted of 36 type-2 diabetic men with CHD having a mean age of 61.8 years±9.9 years. The mean BMI was 27.02±2.02 kg/m² in control and 26.2±3.3 kg/m² in type-2 diabetic men with CHD. Significantly low level of adiponectin was seen in type-2 diabetic men with CHD, i.e., 3.02±1.1 vs. 11.06±2.5 in normal men, *p*-value <0.001. HDL-C level was significantly high in the normal controls as compared to the diseased group with a *p*-value of <0.001.

Type-2 diabetic men with CHD showed significantly high levels of FBG (*p*=<0.001), HbA1c (*p*=<0.001), TC (*p*=< 0.05), TG (*p*=<0.05) and LDL-C (*p*=<0.05) than the normal control group.

Body mass index (BMI); Systolic blood pressure (SBP); Diastolic blood pressure (DBP); Fasting blood glucose (FBG); Total cholesterol (TC); Triglycerides (TG); High density lipoprotein-cholesterol (HDL-C); Low density lipoprotein-cholesterol (LDL-C

Table-2 shows correlation of adiponectin with different parameters in cases and controls. Adiponectin showed negative association with FBG and HbA1c in type-2 diabetic men having CHD, with r = -0.332; *p*=0.04, and r = -0.818; *p*=0.01 respectively. Adiponectin was positively associated with HDL-C in control (r = 0.948; *p*=<0.01) and type-2 diabetic men with CHD (r = 0.650; *p*=<0.01). Serum triglyceride level showed negative association with adiponectin level in controls (r = -0.537; *p*=0.001) and type-2 diabetic men with CHD (r = -0.640; *p*=<0.01).

Table-1: Demographic, clinical and biochemical parameters of the studied population

Variables	Group A	Group B	*p*-value
Age	47.2±5.5	61.8±9.9	<0.001
BMI	27.02±2.02	26.2±3.3	NS
SBP	124.7±7.6	121.9±29.4	NS
DBP	81.±4.1	78.4±17.5	NS
FBG	86.8±16.7	191.08±104.5	<0.001
HbA1C	5.2±0.3	8.7±1.4	<0.001
TC	202±29.6	220.8±43.2	<0.05
TG	212.6±54.8	246.5±58.8	<0.05
HDL-C	42.4±8.6	31.7±8.9	<0.001
LDL-C	115.9±29.4	136.4±43.2	< 0.05
Adiponectin	11.06±2.5	3.02±1.1	<0.001

Table-2: Correlation of adiponectin with different parameters in the studied groups (A, B)

Variables	Group A		Group B	
	R	*p*	r	*p*
FBG	0.097	0.573	-0.332	0.048*
HbA1C	-0.251	0.140	-0.818	<0.01**
TC	-0.154	0.369	0.036	0.836
TG	-0.537	0.001**	-0.640	<0.01**
HDL-C	0.948	<0.01**	0.650	<0.01**
LDL-C	-0.498	0.002**	0.067	0.697

DISCUSSION

The study showed that serum adiponectin level was significantly decreased in type-2 diabetic men with coronary heart disease as compared to the healthy control individuals. Low serum adiponectin level has been observed in patients of coronary heart disease in other studies.[17–20] Hotta *et al*[7] observed low serum level of adiponectin in diabetic patients with CHD than diabetic patients without CHD. Schulze *et al*[21] investigated adiponectin's role in

type-2 diabetic patients with CHD. They followed elderly type-2 diabetic men (aged 46–81 years) for five years at the end of which they found 89 cases of CHD, 19 cases of myocardial infarction and 70 cases of coronary artery bypass surgery. They associated a reduced risk of CHD incidence with increasing adiponectin level. Pischon *et al*[22] observed that high adiponectin level led to reduced risk of myocardial infarction in men. Dunajska *et al*[23] observed significantly low level of adiponectin in men with CHD than healthy control subjects. Lindsay *et al*[24] studied adiponectin level in type-2 diabetic patients with CHD and confirmed no association between the two.

In this study hypoadiponectinemia was accompanied by dyslipidemia, i.e., low level of HDL cholesterol and high level of serum triglycerides, total cholesterol and serum LDL cholesterol levels. Same results were obtained in other studies.[25–27] Saely *et al*[25] made comparison of lipid profile among four groups including control, type-2 diabetic subjects, type-2 diabetic subjects with CHD and patients of CHD without type-2 diabetes mellitus. They reported highest level of TG and lowest level of HDL-C (both with *p*-value <0.001) in type-2 diabetic subjects with CHD.

Adiponectin exerts its anti-atherosclerotic action through several mechanisms. These include: increased insulin sensitivity, increased endothelial nitric oxide (NO) release, decreased endothelial monocyte adhesion, decreased transformation of macrophages to foam cells, decreased vascular smooth muscle cells proliferation, migration and calcification.[28] Atherosclerosis is propagated in the presence of raised serum TG level and decreased HDL cholesterol level.[29] Hypoadiponectinemia causes increased TG by decreased activation of peroxisome proliferator activated-receptor α (PPAR α) in liver and increased production of VLDL cholesterol (very low density lipoprotein). It also causes decreased HDL cholesterol by reducing the activity of the enzyme lipoprotein lipase.[30] HDL cholesterol is protective against atherosclerosis as it takes up excess cholesterol and excretes it through bile.[31]

Our study showed positive association of adiponectin with HDL-C and negative association with TG, HbA1c and FBG in type-2 diabetic men with coronary heart disease. The same findings are reported in studies performed in various regions of the world, in type-2 diabetic patients with and without CHD.[32–35] The results supports the hypothesis that low level of adiponectin is associated with prevalence of cardiovascular disease.

CONCLUSION

This study confirmed low adiponectin and HDL-C levels and high TG level in type-2 diabetic men with CHD. Adiponectin showed negative association with TG, HbA1c and positive association with HDL-C in the studied population. The positive relation of adiponectin and HDL-c in type-2 diabetic men with CHD confirmed the cardiovascular protective effect of adiponectin. It could be predicted that in future there may be treatment due to its anti-atherosclerotic affects.

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