CORRELATION OF ADIPONECTIN WITH SERUM INSULIN IN DIABETICS WITH AND WITHOUT CORONARY HEART DISEASE

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ABSTRACT

Background: Coronary heart disease is a common complication of diabetes mellitus. Hyperinsulinemia associated with diabetes contributes to risk of coronary heart disease. Adiponectin is known to have anti-inflammatory and insulin sensitizing actions and may have a cardioprotective role.

Objective: To evaluate association of serum adiponectin with insulin in diabetic patients with and without coronary heart disease in province of Khyber Pakhtunkhwa.

Methods: This was a descriptive/ analytical study and consisted of three groups. Group A contained 100 diabetic patients, group B contained 100 diabetic patients with coronary heart disease and group C contained 100 normal controls. The study subjects were randomly selected from Hayatabad Medical Complex, Khyber Teaching Hospital and Lady Reading Hospital, the three tertiary care hospitals of Khyber Pakhtunkhwa. Levels of adiponectin, insulin, fasting blood glucose, glycated hemoglobin were estimated. Variables were compared using independent student's t test and correlation between adiponectin with variables was established with Pearson's correlation coefficient.

Results: Adiponectin was significantly decreased and insulin was increased (P= 0.0001) in diabetics with and without coronary heart disease. Adiponectin and insulin did not differ significantly between diabetics with and without coronary heart disease. FBG (190.5±92.7, 185.5±80.05 vs. 88.1±21.3) and HbA1c (8.8±1.1, 8.6±0.5 vs. 7.03±3.4, P< 0.05) were significantly higher in diabetics with and without coronary heart.
Adiponectin showed significant negative correlation with FBG (r -0.582), HbA1c (r -0.794) and insulin (r -0.844).
Conclusion: We found reduced adiponectin levels correlating negatively with insulin in diabetic cases with and without coronary heart disease.

Keywords: Adiponectin, Diabetes Mellitus, Coronary Heart Disease

INTRODUCTION

Global prevalence of coronary heart disease (CHD) has increased tremendously since the last two decades[1]. This increase has been linked to many factors one of which is diabetes mellitus (DM).

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Studies have reported several mechanisms through which DM contributes to CHD including insulin resistance and hyperinsulinemia as a crucial mechanism [2].

CHD has emerged as the leading cause of death in diabetic patients accounting for approximately upto 80% mortality rate in diabetic population. Classical risk factors of CHD include age, gender (male), lack of physical activity, obesity, positive family history, and abnormal lipid profile like raised cholesterol and triglycerides, hypertension, defective insulin secretion and diabetes mellitus[3]. Focus has been shifted to measurable biomarkers like adiponectin which may play beneficial role in decreasing cardiovascular risk in diabetic population[4].
Insulin is a protein hormone functioning as a key regulator of cellular metabolism of body

tissues. A decrease in cellular response to insulin stimulation is called insulin resistance. It leads to hyperinsulinemia and is accompanied by defects in glucose uptake and its oxidation, decreased glycogenesis and increased lipid oxidation[5]. This contributes to CHD by causing abnormalities such as hyperglycemia, dyslipidemia, inflammation, endothelial dysfunction and atheroma plaque formation[6].

Adiponectin is a protein hormone produced by the white adipose tissue. It is known to improve glucose oxidation and insulin resistance through multiple beneficial actions including increase in insulin-sensitivity, anti-inflammatory and vasculoprotective effects[4]. Many studies have reported the protective effects of adiponectin against diabetes mellitus and coronary heart disease[7-10]. Though the anti-diabetic role of adiponectin has been established, its cardioprotective effect is not yet fully clear, and the mechanisms linking the two require more studies[11].

Thus, in the present study we aimed to assess the association of serum adiponectin and insulin levels in diabetic patients with and without coronary heart disease.

MATERIALS AND METHODS

Study participants: This study had a cross-sectional/ analytical design carried out from January 2021- June 2021. It was carried out on three groups. Group A had hundred diabetic subjects, Group B had hundred diabetic subjects with coronary artery disease (included patients with first attack of myocardial infarction within last ten days) and Group C had hundred healthy cases that included subjects without any major health problems for example; hypertension, diabetes mellitus, coronary artery disease, liver, thyroid or kidney diseases. All the participants were selected randomly from the out-patients departments of the tertiary care hospitals of Peshawar i.e, Lady Reading Hospital (LRH), Khyber Teaching Hospital (KTH) and Hayatabad Medical Complex (HMC). All participants signed a well informed written consent and approval of the study was obtained by the Ethical Committee of Khyber Medical College, Peshawar. Complete history and physical examination, details including blood pressure, BMI (body mass index: weight

in Kg/height in m^2) etc were recorded on a questionnaire.

Blood sampling:

5 mL fasting blood sample was collected from the study subjects. Blood for HbA1c estimation was taken in EDTA tubes while serum was collected by centrifuging the remaining blood sample at 4000 rpm for ten minutes. FBG was estimated using fresh samples while for serum insulin and adiponectin the sera were frozen.

Blood Analysis:

Serum adiponectin was measured with enzyme linked immunosorbent assay technique (ELIZA), using Human Adiponectin ELISA kit (Biovendor Cat. No. RD 195023100, Germany). Fasting blood glucose concentration was measured colorimetrically by using kit obtained from Elitech System, France. Glycosylated hemoglobin was measured colorimetrically by using kit obtained from Human Diagnostics, Germany. An electro chemiluminescence method based on sandwich enzyme immunoassay, was used to estimate insulin levels.

Statistical analysis:

Data was analyzed using SPSS version 20 and all results were expressed as means ± SD (standard deviation). Independent student's t test was performed to compare variables between the three groups. Association between adiponectin and other variables was found using Pearson's correlation coefficient. P value of less than 0.05 was considered significant.

RESULTS

Table 1 shows the comparison of variables between the groups through independent student's t test. It can be seen that adiponectin levels are significantly lower in the cases groups' i.e, both diabetic with and without coronary heart disease, than the normal control group (4.2±0.04, 4.3±1.4 vs. 9.6±3.2 µg/mL, P< 0.05). Serum insulin levels are significantly higher in the cases groups' i.e, both diabetic with and without coronary heart disease, than the normal control group (18.91±17.27, 18.69±18.07 vs. 7.03±3.4 µu/mL, P< 0.05). The results also showed significantly higher FBG and HbA1c in both cases groups (P= 0.0001).

Table 1 Comparison of variables among the three study groups

Variables	Group A n=100	Group B n=100	Group C n=100
Age (years)	58.8±6.3	61.3±7.7§	56.9±2.3*¶
BMI (kg/m^2)	28.7±8.1	29.1±3.9	27.1±2.2¶
FBG (mg/dL)	185.5±80.05	190.5±92.7	88.1±21.3*¶
HbA1C (%)	8.6±0.5	8.8±1.1	5.4±0.1*¶
Insulin(μU/mL)	18.91±17.27	18.69±18.07	7.03±3.4*¶
Adiponectin(μg/mL)	4.2±0.04	4.3±1.4	9.6±3.2*¶

Note: *P value <0.05 when group A was compared to group C

¶ P value <0.05 when group B was compared to group C

§ P value <0.05 when group A was compared to group B

Table 2 shows the association of serum adiponectin with other variables in the study groups. The association was established using Pearson's correlation coefficient r. We observed a significant negative association of adiponectin with FBG (r -0.582, p <0.01), HbA1c (r -0.794, p <0.01) and serum insulin (-0.844, p <0.01).

Table 2 Correlation of adiponectin with other variables in the study groups

Parameters	R value	P value
Age	-0.160	0.451
FBG	-0.582	<0.01**
HbA1c	-0.794	<0.01**
Insulin	-0.844	<0.01**

*Significance at 0.05 level, S ** Significance at 0.01 level

DISCUSSION

Adiponectin has multifunctional aspects and is thought to act as an insulin sensitizer, anti-diabetic, anti-inflammatory and anti-atherogenic chemocytokine[12]. Reduced serum adiponectin levels have been observed in disorders such as type 2 diabetes, metabolic syndrome and cardiovascular disease. These observations have rendered adiponectin as a useful target for metabolic disorders.

In the current study we observed low levels of adiponectin and high levels of insulin in diabetic cases with and without coronary heart disease. The same results were reported by other[13-15]. Brand et al analysed relationship between insulin resistance with adiponectin and leptin in young children in their study and reported a positive relationship between insulin resistance and Leptin/ adiponectin ratio[16]. However, a study performed by Muratsu et al reported no significant association of adiponectin with insulin in patients with stroke and/ or coronary artery disease[17].

We observed significantly raised levels of BMI, FBS and HbA1c in our study. Raised BMI has been associated with metabolic disorders, diabetes mellitus and coronary heart disease. Timon et al and Aderbrigbe et al have stated that this association as due to abnormal lipid profile[18, 19].

Huang et al observed raised HbA1c and FBG in their recent study performed in 2021. They have also reported a positive association of hyperglycemia with diabetes and CHD[20].

Studies have observed improvement of diet-induced insulin resistance and hypertriglyceridemia by increasing adiponectin levels in mice [21-23]. Furthermore, increased production of inflammatory markers like TNF-alpha and IL-6 has been reported in obese and type 2 diabetic cases. The pro-inflammatory cytokines interfere with insulin signaling and cellular function [24]. Adiponectin

may exert its insulin sensitizing effect through activation of AMPK-activated pathway

CONCLUSION

This study shows significantly lower serum adiponectin and higher serum insulin levels in diabetic patients with and without coronary heart disease. Adiponectin levels do not differ significantly between diabetics and diabetics with coronary heart disease cases. Serum adiponectin also show a significant negative association with insulin levels, glycated hemoglobin and FBG. These findings suggest the negative relationship between adiponectin and insulin levels in diabetes and coronary heart disease.

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