RELATIONSHIP OF ADIPONECTIN LEVEL WITH GLYCEMIC STATUS AND LIPID PROFILE IN TYPE 2 DIABETIC MEN

SADAF DURRANI,[1,2] JASMIN SHAH,[*1] MUDASSAR AHMAD KHAN[2] AND M. RASUL JAN[1]
[1]*Institute of Chemical Sciences, University of Peshawar and* [2]*Khyber Medical College, Peshawar, KP – Pakistan*

ABSTRACT

Objective: To determine serum adiponectin level, glycemic status and lipid profile in type 2 diabetic men belonging to Khyber Pakhtunkwa (KPK), and to find any possible relationship between them.

Study Design / Methods: Thirty six healthy adult males and thirty six type 2 diabetic males were randomly selected in a cross – sectional study. After an overnight fasting their blood samples were taken and analyzed for serum adiponectin, glycosylated hemoglobin (HbA_1c), fasting blood glucose (FBG) and lipid profile including total cholesterol (TC), triglycerides (TG), low – density lipoprotein cholesterol (LDL – C), high – density lipoprotein cholesterol (HDL – C) and very low lipoprotein cholesterol (VLDL – C).

Results: Type 2 diabetic males when compared to healthy males showed significantly low levels of serum adiponectin (3.2 ± 1.3 vs. 11.06 ± 2.5, P = 0.01) and HDL – C (32.4 ± 9.6 vs. 42.4 ± 8.6, p = < 0.01) and significantly high level of FBG (190.4 ± 83.9 vs. 86.8 ± 16.7, p = < 0.01), HbA_1c (8.8 ± 1.8 vs. 5.2 ± 0.3, p = < 0.01) and LDL – C (137.7 ± 33.4 vs. 115.9 ± 29.4). Serum adiponectin level showed a significant negative correlation with FBG (r – 0.596; p = < 0.01), HbA_1c (r – 0.695; p = < 0.01), TC (r – 0.758; p = < 0.01), TG (r – 0.747; p = < 0.01) and LDL – C (r – 0.754; p = < 0.01) in type 2 diabetic men. Adiponectin also showed a significant positive association with HDL – C in controls (r – 0.948; p = < 0.01) and cases with type 2 diabetes (r – 0.860; p = < 0.01).

Conclusion: Serum adiponectin level is markedly decreased in type 2 diabetic cases. Moreover, it is associated positively with HDL – C and negatively with HbA_1c and TG levels. Hypoadiponectinaemia is associated with deranged glycaemic status and lipid profile in men having type 2 diabetes mellitus.

Key words: Adiponectin; glycosylated hemoglobin; lipid profile; type 2 diabetes mellitus.

INTRODUCTION

Adipose tissue acts like an active endocrine gland and secretes many hormones called adipokines.[1] Adiponectin is one of the most abundant adipokine and a protein hormone containing 244 amino acids. It is also called as ACRP 30, Adipo Q and gelatin binding protein – 28, (GDP – 28).[2-4] Its normal blood level is quite high ranging between 5 – 30 µg/mL and is more in females than in males. Adiponectin level tends to decrease in obesity.[5,6]

Structure – wise, adiponectin monomer has four important domains and has the ability to self – associate into larger structures. Thus, it can exist in at least three higher order complexes i.e. trimer (low molecular weight form, LMW), hexamers (medium molecular weight form, MMW) and higher order multimers (higher molecular weight form, HMW).[7] Adiponectin plays important functions in carbohydrate and lipid metabolism.[8] It increases insulin sensitivity and oxidation of fatty acids. So, it decreases blood glucose level, fatty acid level and triglyceride content of tissues.[1,9] Adiponectin has strong anti-inflammatory and anti-atherogenic properties and low adiponectin levels are associated with risk of development of diabetes mellitus (D.M), atherosclerosis and coronary heart disease (CHD).[10,11]

The term dyslipidemia refers to altered lipid profile. This includes raised serum cholesterol (T – C), raised serum triglyceride (TG), decreased serum high density lipoprotein cholesterol (HDL – C), raised low density lipoprotein cholesterol (LDL – C) and raised very low density lipoprotein cholesterol (VLDL – C). Dyslipidemia is found to be associated with both, insulin resistance and coronary heart disease.[11,12]

Glycemic control is best determined with the use of glycosylated hemoglobin, which is glucose attached non-enzymatically to hemoglobin throughout the 90 days life time of a red blood cell. It gives insight into the previous three months control of blood glucose level.[13,14] It is now believed that the aim of anti-diabetic treatment should be the reduction of glycosylated hemoglobin to less than 7%.[15]

The relationship of adiponectin level with glycosylated hemoglobin and lipid profile in patients of type 2 diabetes has been investigated in different regions and racial groups.[16-19] However; limited literature is available on serum adiponectin level and its

relationship with the above clinical and biochemical parameters in the population of KPK.

METHOD

It is a cross – sectional analytical study conducted on two groups, A and B, each containing randomly selected participants. Group A consisted of 36 healthy adult men while group B consisted of 36 men having type 2 diabetes. Physical examination and detailed medical history of each subject were recorded on a well – designed questionnaire. Blood pressure, height, weight and BMI (weight in kg/height in m^2) were measured for all participants. The study protocol was approved by the ethical committee of Khyber Medical College, Peshawar, and all the participants provided written informed consent.

Blood Collection

All blood samples were collected after an overnight, 12 hour, fast. Blood sample (5 mL) was withdrawn from the antecubital vein under aseptic technique and was centrifuged at 3000 rpm to obtain serum. Fasting blood glucose, glycosylated hemoglobin and lipid profile were measured on fresh samples while serum was stored at -70°C for analysis of adiponectin.

Biochemical Analysis

Fasting blood glucose concentration was measured by enzymatic colorimetric method (glucose pap. Cat. No. GLUP – 3700 Elitech – Sees, France). Glycosylated hemoglobin was measured colorimetrically using kit provided by Human Diagnostics, Germany. Serum lipid profile was measured including serum total cholesterol (Cat. No. CHOL – 0400 Elitech – Sees, France), serum triglyceride (Cat. No. TRIG – 0400 Elitech – Sees, France), high density lipoprotein cholesterol, HDL – C (Cat. No. 135 409990885 – Diasys Holzheim, Germany). Low density lipoprotein cholesterol (LDL – C) was calculated indirectly using Friedewald's formula.[19] Serum adiponectin level was measured by immunoassay method using Human adiponectin ELISA kit (Bionvendor Cat. No. RD 195023100, Germany).

Statistical Analysis

Data was analyzed using SPSS version 19. Results were expressed as Mean ± SD. Comparison of parameters between the two groups was done by two – tailed student t – test. The correlation of adiponectin with glycosylated hemoglobin, lipid profile and other parameters has been evaluated using Pearson correlation coefficient, *r*. *P* – value less than 0.05 was considered significant.

RESULTS

Clinical and biochemical characteristics of the study population, i.e. control and type 2 diabetic men are given in Table 1. Group A consisted of 36 normal males with a mean age of 47.2 years (SD 5.5 years) and group B consisted of 36 type 2 diabetic men with a mean age of 56.1 years (SD 9.7 years). The mean BMI was 27.02 kg/m^2 in control and 26.7 ± 3.7 kg/m^2 in the patients of type 2 diabetes, respectively. SBP and DBP are higher in the diabetic men than the control men, SDP gives a significance of p value of < 0.01. The comparison of variables between the two groups showed significantly high levels of FBG (< 0.01), HbA_1c (< 0.01), and LDL – C (0.005) in the diseased group than the normal control group. Serum adiponectin level is significantly lower in type 2 diabetic men with 3.2 ± 1.3 vs. 11.06 ± 2.4 in normal men, p value < 0.01. Serum HDL – C level is higher in the controls than the cases with a p value of < 0.01.

Table 1: *Clinical and biochemical parameters of the study population.*

Variable	*Group A Control*	*Group B Type 2 DM*	*P-value*
Age (years)	42.7 ± 5.5	56.1 ± 9.7	< 0.01**
BMI kg/m^2)	27.02 ± 2.02	26.7 ± 3.7	0.711
SBP (mmHg)	124.7 ± 7.6	134.9 ± 19.6	0.004**
DBP (mmHg)	81. ± 4.1	83.9 ± 9.2	0.144
FBG (mg/dL)	86.8 ± 16.7	190.4 ± 83.9	< 0.01**
HbA_1C (%)	5.2 ± 0.3	8.8 ± 1.8	< 0.01**
TC (mg/dL)	202 ± 29.6	213.7 ± 36.1	0.140
TG mg/dL)	212.6 ± 54.8	211.7 ± 68.4	0.951
HDL – C (mg/dL)	42.4 ± 8.6	32.4 ± 9.6	< 0.01**
LDL – C (mg/dL)	115.9 ± 29.4	137.7 ± 33.4	0.005**
VLDL – C (mg/dL)	43.7 ± 10.4	42.4 ± 13.4	0.664
Adiponectin (µg/mL)	11.06 ± 2.5	3.2 ± 1.3	< 0.01**

Significance at p < 0.05*, p < 0.01** level

Body mass index (BMI); Systolic blood pressure (SBP); Diastolic blood pressure (DBP); Fasting blood glucose (FBG); HbA_1c; Total cholesterol (TC); Triglycerides (TG); High density lipoprotein – cholesterol

(HDL – C); Low density lipoprotein – cholesterol (LDL – C); Very low density lipoprotein – cholesterol VLDL – C); Data is expressed as Mean ± SD, P < 0.05 is taken significant.

Table 2 showed Pearson correlation coefficient *r* of adiponectin with clinical and biochemical parameters in type 2 diabetic men and controls. Adiponectin level has a strong negative association with FBG and HbA_1c in type 2 diabetics with r -0.596; p = < 0.01 and r -0.695; p = < 0.01 respectively. The control group also shows a negative association of HbA_1c with adiponectin, however it is non-significant. HDLC – C is positively associated with adiponectin in control (r 0.948; p = < 0.01 and type 2 diabetic men (r 0.860; p = < 0.01). In cases with type 2 diabetes TC (r -0.758; p = < 0.01), TG (r -0.747; p < 0.01) and LDL – C (r -0.754; p < 0.01) are negatively associated with adiponectin. Normal healthy men also show negative association with TG (r -0.537; p = 0.001) and LDL – C (r -0.498; p = 0.002). DBP is negatively associated with adiponectin in type 2 diabetic men (r -0.441; p = 0.009) while BMI is negatively associated with adiponectin (r -0.457; p = 0.005) in normal control group.

Table 2: *Pearson correlation co-efficient of adiponectin with HbA_1c, lipid profile and other characteristics in male participants of the study groups (A, B).*

Correlation	*Group A (Control)*		*Group B (Type 2 DM)*	
	r	*p*	*r*	*p*
Age	0.262	0.122	0.170	0.336
BMI	-0.457	0.005**	0.036	0.838
SBP	0.488	0.003**	-0.148	0.403
DBP	0.305	0.071	-0.441	0.009**
FBG	0.097	0.573	-0.596	< 0.01**
HbA_1C	-0.251	0.140	-0.695	< 0.01**
TC	-0.154	0.369	-0.758	< 0.01**
TG	-0.537	0.001**	-0.747	< 0.01**
HDL – C	0.948	< 0.01**	0.860	< 0.01**
LDL – C	-0.498	0.002**	-0.754	< 0.01**
VLDL – C	-0.535	< 0.001**	-0.738	< 0.01**

*Significance at < 0.05 level **Significance at 0.01 level

DISCUSSION

In this study we observed negative correlation of adiponectin with BMI in healthy men. The same result is obtained in other studies conducted on people of Italy,[20] Taiwan,[21] Japan,[22,23] Indian Caucasian population[24] and healthy non-diabetic adolescents.[25] Thus it confirms the well – known fact that serum adiponectin level is decreased in obesity which is a risk factor for development of diabetes mellitus, dyslipidemia, hypertension and atherosclerosis.[1]

A relationship of adiponectin with glycosylated hemoglobin and lipid profile in type 2 diabetes men in studied population was observed. A significant negative association of adiponectin with HbA_1c, FBG, TC, TG and LDL – C was observed in type 2 diabetes while a significant positive association of HDL – C with adiponectin was seen in type 2 diabetes as well as controls. These results are confirmed by many other studies.[26-30] Adiponectin causes insulin sensitizing effect due to its role in the activation of peroxisome proliferator – activated receptors γ (PPARγ) in the liver.[31] In type 2 diabetes mellitus the serum adiponectin level markedly decreased leading to abnormal glucose and lipid metabolism. Hypoadiponectinemia causes insulin resistance and hyperglycemia in type 2 diabetes mellitus. The mechanism is not very clear till date however; diabetes susceptibility locus which is seen on chromosome 3q27 has been found to contain adiponectin gene, APMI. Multiple polymorphisms of the adiponectin gene have also been observed in type 2 diabetes mellitus.[32] Hypoadiponectinemia in type 2 diabetes also leads to raised TG and low HDL – C levels due to a decrease in the activation of peroxisome proliferator – activeted receptor α (PPAR α) in the liver and increased synthesis of VLDL – C.[33] Adiponectin level in type 2 diabetes mellitus can be regarded as a biomarker of better glycemic control and better lipid levels.

Adiponectin level in health and disease greatly depends on gender, age, ethnicity and life styles. Limited literature is available on serum adiponectin level and its relationship with the above clinical and biochemical parameters in the population of KPK. The limitations of this study are its small sample size which might have led to non-significant results, and the inclusion of the participants of specific age group (40 and above). The results may be different for individuals of different age groups with different life styles and activity levels. However, the randomized design of the study is its strength.

It is *concluded* that this study confirms the negative association of adiponectin with HbA_1c and TG and the positive association of adiponectin with HDL – C in type 2 diabetic male patients of Khyber Pakhtunkhwa.

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