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Serum adiponectin concentration in patients with type 1 diabetes

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ABSTRACT

Adiponectin (AdipoQ) is known as one of the major mediators of adipose tissue metabolism with beneficial effects on carbohydrates and lipids. The effect of low concentrations of adiponectin on the development of obesity, insulin resistance, type 2 diabetes and cardiovascular disease is quite well understood. However, there is still little research available defining the role of adiponectin in the pathogenesis of type 1 diabetes (DM1) and its' complications. Therefore, it seems appropriate to undertake research aiming to evaluate serum levels of adiponectin in the blood of patients with DM1 and to evaluate the correlations between this adipocytokine concentration and selected clinical data as well as biochemical parameters evaluated in routine diagnosis and monitoring of diabetes. The study included 40 patients aged 41.9±12.7 years, diagnosed with type 1 diabetes and group of healthy controls (n=26) with mean age of 41.2±15.3 years. In serum samples of all patients single-time determination of adiponectin, glucose, total cholesterol, HDL cholesterol, LDL cholesterol, triglycerides, urea, creatinine, glycated hemoglobin levels and alanine aminotransferase and aspartate aminotransferase activity were performed. The mean AdipoQ concentration was significantly higher in the study group than in healthy subjects (16.2±11.7 μg/ml vs. 7.3±2.0 μg/ml; $p<0.001$). Significantly higher levels of AdipoQ in women than in men with DM1 (23.1±14.0 μg/ml vs. 11.0±5.8 μg/ml; $p<0.001$) were found. AdipoQ was directly correlated with disease duration ($r=0.539$, $p=0.003$) as well as inversely with patients' body mass ($r=-0.423$, $p=0.025$). Observed increased levels of AdipoQ in patients with DM1 with concomitant vascular complications as compared to patients without the complications, however not statistically significant, suggests that this protein may play important role in the pathogenesis of diabetic angiopathy.

Keywords: adiponectin, adipose tissue, diabetes, type 1 diabetes, vascular complications

INTRODUCTION

Diabetes mellitus type 1 (DM1) is a chronic, autoimmune disease that leads to the slow destruction of the β cells of the Langerhans islets and consequently to the loss of insulin secretion. Approximately 10% of all cases of diabetes is DM1. Etiopathogenesis of the disease is still not fully understood, involves the interaction between polygenic genetic predisposition and environmental factors that are involved in the process of breaking tolerance to self-antigens and trigger cellular and humoral autoimmunity to β cells selected structures [1,7].

At present it seems that adipose tissue plays an important role in the pathogenesis of many metabolic disorders. It is no longer seen only as an energy storage, but through the secretion of proteins called adipocytokines actively participate in the body metabolism, inflammation and immune response [2,10,15,19].

Among the adipocytokines particular interest is directed towards the adiponectin. It is one of the most abundant proteins in circulation, with concentrations between 3 to 30 μg/ml, and accounts for 0.01% of total plasma protein content [20,24]. It was discovered and described in 1995-1996 by four independent research groups, therefore, in literature it is known under four names: ACRP 30 (adipocyte complement related protein of 30 kDa), AdipoQ (C1q and collagen domain containing), APM1 (adipose tissue bridge abundant gene transcript) and GBP28 (gelatin-binding protein of 28kDA) [2,10,12].

Adiponectin in adipocytes and blood is present in the distinct multimeric forms of different molecular weights, as it has been shown that its monomers are capable of forming the oligomeric structures. High molecular weight (HMW) dominates among all and it's also most active form, and most closely associated with insulin sensitivity.

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The direct effects of adiponectin isoforms of lower molecular weight like low molecular weight (LMW), and middle molecular weight (MMW) are still undefined and mechanisms that regulate formation and distribution of these isoforms remain poorly defined so far [10,15]. Adiponectin in addition to the effects on the adipose tissue structure and metabolism plays well-documented role in enhancing insulin sensitivity of peripheral tissues. This protein apart of anti-diabetic function has also a profound anti-atherogenic, anti-inflammatory, protective to the endothelium, and anti-proliferative effects [9,10,17,19,20,24].

Adiponectin levels are significantly related to the type of diabetes [12,18,24]. The effect of low concentrations of adiponectin on the development of obesity, insulin resistance, type 2 diabetes (DM2) and cardiovascular disease is quite well understood [2,10,11,15,20]. However, there is still little research available defining the role of adiponectin in the pathogenesis of type 1 diabetes and its' complications. It seems that adiponectin, being a mediator of the peripheral tissues insulin resistance may simultaneously have direct or indirect effect on the residual insulin secretion in DM1. Available data indicate that adiponectin is elevated in patients with DM1, however, changes in the secretion of this protein are still poorly understood is in these disease [9,12,24]. Therefore, it seems appropriate to undertake research aiming to evaluate serum levels of adiponectin in the blood of patients with DM1 and to evaluate the correlations between this adipocytokine concentration and selected clinical data as well as biochemical parameters evaluated in routine diagnosis and monitoring of diabetes.

MATERIAL AND METHODS

Participants. The study included 40 patients aged 41.9±12.7 years, diagnosed with type 1 diabetes, recruited from the Department of Endocrinology of the Medical University of Lublin. The studied group consisted of 18 women (mean age 46.6±13.2 years) and 22 men (38.3±11.5 years). The mean duration of the disease from onset was 16.3±10.8 years. All patients underwent clinical examination. The prevalence and the degree of severity of chronic vascular complications of the disease were clinically evaluated. Macro- and microvascular complications were found in 22 (55%) cases; hypertension in 16 (73%), ischemic heart disease in 7 (32%), retinopathy in 7 (32%), nephropathy in 6 (27%), neuropathy in 7 (32%), diabetic foot in 2 (9%) cases. Average body mass index (BMI) of the patients was 23.8±4.4 kg/m^2.

The study also included a small group of healthy controls (n=26), who were recruited from healthy population who reported for the routine health checks to the Department of Laboratory Diagnostics SPSK No. 1 in Lublin. The control group consisted of 14 women and 12 men with mean age of 41.2±15.3 years and with normal BMI <25 kg/m^2.

Written informed consent was obtained from every patient qualified to enter the study. The study protocol was approved by the local Ethics Committee of Medical University in Lublin.

Blood sampling and measurements. All investigations were performed in the morning (between 8-10 am) following an overnight fast. Venous blood was drawn from an antecubital vein into 5 ml K_3EDTA tube for HbA1c and separate serum tube for adiponectin and biochemical parameters. Clotted blood after 30 minutes was centrifuged for 10 min at 2000 rpm. Obtained serum was aliquoted to clean eppendorfs and stored at -20°C pending analysis.

In samples of all patients single-time determination of glucose (GLU), total cholesterol (T-CH), HDL cholesterol (HDL-CH), triglycerides (TG), urea, creatinine, glycated hemoglobin (HbA1c) levels and alanine aminotransferase (ALT) and aspartate aminotransferase (AST) activity were performed with use of standard laboratory methods on the biochemical autoanalyser Cobas 6000 (Roche, Basel, Switzerland). LDL cholesterol (LDL-CH) was calculated with the Friedewald formula: T-CH-TG/5-HDL-CH.

Serum adiponectin (AdipoQ) was measured with the use of commercial reagent kit Human Adiponectin ELISA (BioVendor Company, Czech Republic). Inter-assay coefficient of variation (CV) was 8.2% at a concentration of 5.27 μg/ml, 7.3% at 17.78 μg/ml, while the intra-assay CV was 7.0% at 7.14 μg/ml and 6.4% at a concentration of 21.17 μg/ml. The sensitivity of the Human Adiponectin ELISA kit was 210 ng/ml in a 50 μl volume of 30-fold diluted sample.

All patients underwent measurements of height and weight for body mass index (BMI) calculations according to the formula BMI= body weight (kg)/body height (m^2) (kg/m^2). Measurements were performed with precision of 1cm for body height and 0.1 kg of body weight.

Statistical analysis. All statistical analyses were conducted with the StatSoft STATISTICA 10.0 statistical package. All variables in the study group and controls are presented as the elements of descriptive statistics (mean X, standard deviation, SD, median Me, percentile range of 25-75%). Distribution of the variables was tested using the Shapiro-Wilk's test. Normally distributed variables were compared with use of Student's t-test, and variables with skewed distribution were compared with the use of nonparametric Mann-Whitney U test. The correlations between variables were tested using Pearson or Spearman tests respectively of the type of distribution. Statistical significance for all analyses was set at $p \leq 0.05$.

RESULTS

Biochemical characteristics and adiponectin concentration in the study and the control group are presented in Table 1.

The mean adiponectin concentration was significantly higher in the study group than in healthy subjects (16.2±11.7 μg/ml vs. 7.3±2.0 μg/ml; p<0.001). Additionally as expected significantly higher concentrations of glucose, creatinine and urea were found in DM1 group (p<0.001 for both). The other biochemical parameters concentrations as T-CH, HDL-CH, LDL-CH, TG and ALT and AST did not show significant differences between groups. The mean value of HbA1c in the DM1 group was 8.2±1.3%.

Significantly higher levels of adiponectin in women than in men with DM1 (23.1±14.0 μg/ml vs. 11.0±5.8 μg/ml; p<0.001) were found. There was no additional gender related significant differences in concentrations of other biochemical parameters in DM1 group. Results of all biochemical parameters in relation to gender are shown in Table 2.

Biochemical characteristics and adiponectin concentrations in the DM1 group depending on the presence of micro- and macrovascular complications are shown in Table 3.

Table 1. Biochemical characteristics of selected biochemical parameters and adiponectin concentration in the study and the control group

Parameters	Study group n=40			Control group n=26		
	X±SD	Me	25–75%	X±SD	Me	25–75%
AdipoQ (μg/ml)	16.2±11.7‡	12.4	8.0-21.9	7.3±2.0	7.1	6.0-8.4
Glucose (mg/dl)	222±100.2‡	186	136-320	82.6±10.4	80.5	74.3-88
HbA1c (%)	8.2±1.3	8.1	7.5-9.0	–	–	–
T-CH (mg/dl)	195.3±50.5	186	153-228	188.3±35.4	184.5	158-212.2
HDL-CH (mg/dl)	61.2±16.3	66.4	46.4-75.5	57.1±12.7	56.5	50.4-62
LDL-CH (mg/dl)	110.8±41.4	108.2	81.8-133.1	109.8±31.6	110.9	85.4-130.8
TG (mg/dl)	116.6±59.1	100	69-169	106.7±63.7	89.5	60-133
Urea (mg/dl)	37.1±12.7‡	33.3	28.2-48.3	30.9±8.2	29.1	25-33.9
Creatinine (mg/dl)	1.0±0.4‡	1.0	0.8-1.2	0.8±0.2	0.7	0.6-0.9
ALT (U/l)	22.4±6.8	22	16-26.5	26.6±14.7	23.7	15.6-38
AST (U/l)	23.2±5.7	21.5	19.5-27	23±9.8	20.1	19-25

n – number of subjects
‡ p<0.001

Table 2. Biochemical characteristics and concentration of adiponectin in women and men with DM1

Parameters	Study group n=40					
	Women n=18			Men n=22		
	X±SD	Me	25-75%	X±SD	Me	25-75%
AdipoQ (μg/ml)	23.1±14‡	22	12.6-26	11±5.8	9.5	6.8-12.3
Glucose (mg/dl)	229.2±86.4	204	156-288	216.5±111.9	176	120-328
HbA1c (%)	8.2±1.7	8.1	6.8-9.6	8.3±1.1	8.0	7.5-8.8
T-CH (mg/dl)	211±56	213	179.5-229	183.6±44.2	179.5	150.5-221.5
HDL-CH (mg/dl)	66.5±17	73.5	56.9-77	57.2±15	55	46.6-70.9
LDL-CH (mg/dl)	120.1±47	114.3	85-138.9	103.8±36.7	94.6	74.9-122.9
TG (mg/dl)	121.9±61.7	100	80.5-167	112.6±58.8	89	69-169
Urea (mg/dl)	38.1±15.4	37.7	26.1-50	36.2±10.3	31.9	28.2-41.5
Creatinine (mg/dl)	1.0±0.3	0.85	0.75-1.25	1.1±0.4	1.1	0.9-1.2
ALT (U/l)	20±4.4	20.5	16-23	24.3±7.7	25.5	17.5-29
AST (U/l)	23.6±5.0	21.5	20.5-27.5	22.9±6.4	21.5	18.5-27

n- number of subjects
‡ p<0.001

Table 3. Biochemical characteristics and AdipoQ concentration in DM1 patients with and without micro- and macrovascular complications

Parameters	Study group n=40					
	Patients without complications n=18			Patients with complications n=22		
	X±SD	Me	25-75%	X±SD	Me	25-75%
AdipoQ (μg/ml)	13.4±7.0†	10.6	8.1-18.8	18.3±14.1	12.6	9.3-24.2
Glucose (mg/dl)	235.7±111.1	192	164-288	211.5±93	176	136-320
HbA1c (%)	8.6±1.4	8.7	7.7-9.3	8.0±1.3	7.6	7.0-8.3
T-CH (mg/dl)	189±62.5	173	151-228	199.4±42.7	205	177-228
HDL-CH (mg/dl)	56.1±18.6	46.8	40-76	64.5±14.1	69.8	54-75
LDL-CH (mg/dl)	110.6±52.7	92.4	80.6-136	111±34	113.8	83-130.2
TG (mg/dl)	111.7±72	80	69-152	119.7±51.2	100	73-179
Urea (mg/dl)	34.1±10.9	31.6	28.5-39.4	38.9±13.5	39.6	27.2-50.3
Creatinine (mg/dl)	1.0±0.2	0.9	0.8-1.1	1.1±0.4	1.1	0.7-1.4
ALT (U/l)	24.3±7.8	26	19-28	21.2±5.9	22	16-25
AST (U/l)	24.2±6.3	27	20-28	22.5±5.4	21	19-23

n – numer of subjects
† p>0.05

DM1 patients with complications had higher adiponectin levels as compared to patients without the complications, however the difference did not reach statistically significance. There were no further significant differences in levels and activity of other biochemical parameters examined in the study group in regard to the presence of chronic complications. The relationship between adiponectin and the basic demographic, anthropometric and selected biochemical parameters in the group of DM1 are presented in Table 4.

Table 4. Association of adiponectin levels with anthropometric and biochemical parameters in DM1 patients

	Parameters	Study group n=40	
		Correlation coeff. r	p value
ADIPONECTIN (µg/ml)=	Age (years)	0.308	0.111
	Time from onset (years)	0.539	**0.003**
	Body mass (kg)	-0.423	**0.025**
	BMI (kg/m^2)	-0.097	0.622
	Glucose(mg/dl)	0.199	0.292
	HbA1c (%)	0.127	0.520
	T-CH (mg/dl)	0.107	0.589
	HDL-CH (mg/dl)	0.314	0.104
	LDL-CH (mg/dl)	-0.012	0.950
	TG (mg/dl)	-0.002	0.992
	Urea (mg/dl)	0.338	0.085
	Creatinine (mg/dl)	0.040	0.841
	ALT (U/l)	-0.252	0.196
	AST (U/l)	0.127	0.519

n – number of subjects
$p<0.05$

Adiponectin was directly correlated with disease duration (r=0.539, p=0.003) as well as inversely with patients' body mass (r=-0.423, p=0.025), while there was no significant correlation between serum adiponectin levels and the patients' age and BMI, glucose, T-CH, HDL-CH, LDL-CH, TG, urea, creatinine, and HbA1c as well as ALT and AST activities.

DISCUSSION

Adiponectin is known as one of the major mediators of adipose tissue metabolism with beneficial effects on carbohydrates and lipids [9,10,12,15,20]. Multiple studies have shown that low levels of adiponectin in the blood serum are closely associated with insulin resistance [15], the presence of metabolic syndrome [2], increased risk of developing type 2 diabetes [11] and cardiovascular disease [20].

The present study yielded similar results to obtained by others authors (Celi F. et al. [3], Galler A. et al. [6], Hadjadj S. et al. [9], Immagawa A. et al. [12], Morales A. et al. [18], Saraheimo M. et al. [23], Schalkwijk C.G et al. [24]) showing elevated adiponectin concentrations in serum of DM1 patients. The mean concentration of serum adiponectin in DM1 in this study was significantly higher as compared to the control group (16.2±11.7 µg/ml vs 7.3±2.0 µg/ml; ($p<0.001$). Imagawa A. et al. [12] observed higher adiponectin levels among patients with short disease duration of approximately 3 years with levels of 13.6 µg/ml in males and 16.1 µg/ml in females as compared with matched for BMI healthy controls (6.9 µg/ml in males and 10.0 µg/ml in females; $p<0.01$). Study by Perseghin G. et al. [22] revealed higher adiponectin levels detected in insulin resistant patients with DM1 (25 µg/ml) than in controls (16 µg/ml, p=0.05) or patients with DM2 (7 µg/ml, p=0.01), and non-diabetic, insulin resistant offspring of parents with DM2 (11 µg/ml, p=0.03).

The cause of elevated concentrations of adiponectin in patients with DM1 is not entirely clear [12]. Increased levels may be caused by changes in the synthesis, secretion or degradation of this protein [10,15]. Glucose and insulin are one of probable regulators of adiponectin synthesis and secretion, but due to the fact that hyperglycemia is a common feature of DM1 and DM2 it is not a key determinant of the adiponectin levels in vivo [10,12,17,18,23]. Experimental studies have shown that insulin substantially inhibits the expression of the adiponectin gene [4]. Based on this data, it can be concluded that insulin deficiency contributes to the elevated adiponectin levels in DM1. It cannot be also excluded that treatment with exogenous insulin can influence adiponectin secretion [3,12,17,24]. Interesting results were published by Szalecki M. et al. [26] who found highest adiponectin levels in children treated with continuous subcutaneous insulin infusion, lower levels in the group treated with conventional insulin therapy whilst the lowest concentrations were observed the group treated with intensive insulin therapy.

Other authors explain that the differences in the adiponectin concentration between DM1 and DM2 (with lower levels in DM2) are due to visceral fat content which is higher in DM2 [17,18]. On the other hand, according to Galler A. et al. [6] adipocytes in different types of diabetes are controlled differently, with adiponectin level at baseline being the strongest predictor of adiponectin levels at the end of their study in patients with DM1. Despite of above cited data the mechanisms responsible for significant adiponectin elevation in DM1 patients are yet to be fully elucidated.

The results of our research have shown higher levels of adiponectin in women compared to men with DM1. Similar data were obtained by Schalkwijk C.G et al. [24] as well as low circulating adiponectin levels associated with male sex were previously reported [2,11]. Androgens reduce adiponectin levels what may be the explanation of reduced plasma protein levels observed among men, as well as some of the increased risk of insulin resistance and atherosclerosis in these individuals, compared with women population [19]. A gender-stratified Cox model used in study by Kollerits B. et al. [13] revealed that adiponectin in men is a significant predictor of progression of chronic kidney disease (CKD) after adjustment for age,

glomerular filtration rate, and proteinuria. Male patients with adiponectin levels above optimal cut-off (4 μg/ml) had a significantly faster progression of CKD than patients with levels below. Although others authors (Celi F. et al. [3], Galler A. et al. [6], Hadjadj S. et al. [9], Morales A. et al. [18]) in their studies did not observed gender related differences in adiponectin concentrations.

The results of this study confirmed direct relationship of serum adiponectin levels with DM1 duration (r=0.539, p=0.003), which was on average 16.3±10.8 years from the onset. This is consistent with previous studies conducted by Lindstrom T. et al. [16] and Frystyk J. et al. [5]. Lindstrom T. et al. [16] also found lower mean adiponectin concentration (8.1 μg/ml) in DM1 lasting for less than ten years as compared to patients with disease duration over 10 years (14.7 μg/ml). Other authors, however, did not report significant correlation between adiponectin and the mean disease duration [6,21,26]. Additionally we did not find association between adiponectin and age in our study group, which is consistent with the data available in the literature [6,26].

Data from literature have shown that serum adiponectin levels are decreased in patients with obesity and type 2 diabetes and are inversely associated with parameters of overall adiposity (eg. body mass index (BMI), fat mass, and percentage of body fat). The paradox of higher adiponectin concentrations in the serum of lean people than in obese remains unclear. This is in contrast to most of other adipocytokines, whose levels are increased in obesity, although adiponectin expression is activated during adipogenesis it is possible that there is a feedback loop inhibiting its production during the obesity development [2,11]. In this study adiponectin showed negative correlation with the body weight (r=-0.423, p=0.025) in the group of DM1 patients with normal BMI<25 kg/m^2. Unclear is lack of correlation with BMI in our group of patients, which is consistent with results published by Szadkowska A. [25]. This author examined over 300 DM1 patients and did not found any correlations of adiponectin with anthropometric parameters of body fat content. However, significant negative correlation of adiponectin with BMI in DM1 was reported by Galler A. et al. [6] and Schalkwijk C.G et al. [24]. According to Martos-Moreno G.A. et al. [17] BMI is not a significant factor influencing the levels of adiponectin in DM1, and increased its concentration should be regarded as the body's adaptation to a disturbances in metabolic processes.

Glycosylated hemoglobin (HbA1c) level is a biochemical parameter routinely assessed in patients with DM1 as an index of the degree of diabetes metabolic compensation. In this study we did not find statistically significant relationship between adiponectin and HbA1c levels, which remains consistent with the results of other authors [6,21]. However, Celi F. et al. [3] have demonstrated the impact of glycemic control on adiponectin levels as confirmed by positive correlation of adiponectin with glycosylated hemoglobin levels. According to these authors, insulin inhibits the synthesis of adiponectin and its' higher levels in people with DM1 can be caused by inefficient and inadequate insulin therapy.

Little is known about the degradation of circulating adiponectin. Kidneys are most likely to be involved in this process as the concentration of this protein was found significantly higher in patients with chronic kidney disease [23]. To evaluate kidney function we used commonly measured parameters as endogenous concentrations of urea and creatinine in serum and we analyzed the adiponectin concentration in relation these renal function parameters. Although urea and creatinine were significantly higher in DM1 as compared to healthy controls, yet no significant correlation parameters with serum adiponectin was detected. However, Schalkwijk C.G et al. [24] in their study observed increased adiponectin levels in DM1 patients with renal failure and further demonstrated a negative correlation between adiponectin levels and GFR (glomerular filtration rate). It is still not entirely clear why patients with impaired renal function have increased levels of adiponectin. The authors suggest that poor renal function, as vital organs for biodegradation and excretion of variety of proteins and hormones may be responsible for the accumulation of adiponectin. It is also possible that kidney failure can be a factor that stimulates adiponectin synthesis.

In the present study there was no significant correlation between serum adiponectin and parameters of lipid metabolism and activity of AST and ALT in DM1 patients, which is consistent with available literature [3,16]. However it should be noted, that in this study we focused on total adiponectin concentration and none of the isoforms were analysed. Among three multimeric forms in circulation HMW appears to be the major, biologically active form [20]. Lack of correlations between total adiponectin and lipid profile in DM1 was also described by Leth H. et al. [14]. They found stronger correlations of lipid parameters and metabolic compensation assessed by HbA1c with HMW adiponectin than with total adiponectin concentration. These authors concluded that HMW adiponectin significantly contributes to the increased concentration of total adiponectin in DM1.

Many studies indicate that adiponectin acts as an anti-inflammatory factor and inhibits atherosclerotic processes in the blood vessels walls [15, 20]. For this reason we analyzed the levels of adiponectin in DM1 patients based on the presence and the absence of vascular complications (micro- and macrovascular). Levels of adiponectin were higher in DM1 patients with complications as compared to patients without the complications, however the differ-

ence was not statistically significant. Our results also confirm recent reports published by Habeeb N.M. et al. [8], who found elevated levels of adiponectin in patients with DM1 with complications such as: nephropathy, retinopathy, neuropathy and cardiomyopathy. Similarly, Frystyk J. et al. [5] in their study observed higher serum levels of adiponectin in patients with type 1 diabetes and microvascular complications in comparison to patients without complications. These studies also confirm usefulness of adiponectn as a biomarker of vascular complications of DM1. Furthermore, Hadjadj S. et al. [9] hypothesized that elevated levels of adipokines observed in patients with micro- and macrovascular complications of DM1 may indicate the altered regulation of the adiponectin synthesis in this group of patients. Additionally interesting observations were published by Schalkwijk C.G. et al. [24], who found positive correlation between adiponectin and the soluble adhesion molecule VCAM-1 concentration, which is a common indicator of the risk of vascular endothelial dysfunction.

Contradictory results were obtained by Peczyńska J. et al. [21], who observed lower adiponectin concentrations in DM1 patients with the microvascular complications. Authors explained that as adiponectin inhibits vascular remodeling hence may be a risk factor for the development of microvascular complications in DM1.

Currently, in type 1 diabetic patients, the relationship between adiponectin and the presence of vascular complications is largely unknown. Discussion is still open, whether elevated adiponectin levels seen in patients with DM1, are phenomenon related to the development of microvascular complications of diabetes, or it is a counterbalance mechanism which rather protects against the development of vascular complications in this disease [5].

In conclusion the role of adiponectin in DM1 is significant and understanding of adiponectin clinical relevance may be useful for the treatment of DM 1 and prevention of development of its complications. In light of conflicting studies and discussed results the adiponectin implications in the development of DM1 complications are not yet fully convincing. Knowledge in this area is still insufficient and numerous important questions about adiponectin role in DM1 pathogenesis await further study.

CONCLUSION

1. Higher serum levels of AdipoQ are observed in DM1 patients as opposed to the healthy controls.
2. Higher concentrations of serum AdipoQ are seen in women than in men with DM1.
3. Concentration of AdipoQ is negatively correlated with body mass and positively with the duration of disease in study group.
4. Observed increased levels of AdipoQ in patients with DM1 with concomitant vascular complications suggests that this protein may play important role in the pathogenesis of diabetic angiopathy.

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