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Adiponectin and body composition in cystic fibrosis ☆

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Abstract

The aim of the study was to evaluate adiponectin (AD) serum concentrations in 43 stable CF patients and 27 healthy subjects and to correlate them with their nutritional status. Body Composition (Bioelectrical Impedance), visceral/subcutaneous adipose tissue (VAT-SAT) in CF patients (CT-scan at L4), insulin resistance (HOMA-IR) and AD serum concentrations (ELISA) were studied. CF patients and controls had comparable weight, height, %BF, %FFM, fasting glucose, insulin and insulin resistance. CF patients had significantly lower BMI-SDS. CF males had higher %FFM and total FFM and lower %BF and total BF than females ($p<0.001$). Serum AD was higher in CF patients than controls (11.53±5.37 vs. 9.07±4.41 μg/ml) and comparable between females and males. AD was lowest among young malnourished patients (8.06±1.85 μg/ml) and highest among young patients with normal nutrition (14.56±7.69 μg/ml). Patients with biliary cirrhosis had higher levels than patients with normal liver (10.52±5.49 vs. 14.04±4.52 μg/ml, $p<0.05$). AD correlated with %BF, %FFM, FFM (kg) ($p<0.05$).VAT was significantly increased in malnourished patients. AD was not affected by VAT. Conclusions: Adiponectin is higher in CF patients than healthy individuals. It is decreased in malnourished young patients and increased in patients with normal nutrition and in patients with liver disease. This may be attributed to the reduced BF and to the energy deficit inherent to the disease.

Keywords: Cystic fibrosis; Adiponectin; Malnutrition; Body composition; Energy deficiency; Liver disease

1. Introduction

Adipose tissue (AT) is a major site of energy storage, important for lipid and glucose homeostasis. [1,2] It also secretes several biologically active molecules called "adipokines". [3] Adiponectin is an adipokine, exclusively secreted by adipocytes. It has recently attracted much attention because of its anti-inflammatory, anti-diabetic and anti-atherogenic effects. Low serum adiponectin levels are related to obesity [4] [especially to the amount of visceral adipose tissue (VAT)], [5] insulin resistance, [6] type 2 diabetes mellitus [7] and cardiovascular disease [8] in adults as well as in children. [9] Furthermore, adiponectin levels are reduced among adult and paediatric patients with lipodystrophy [10] (especially HIV-related). [11] On the other hand, elevated serum adiponectin levels have been reported in conditions with energy deficit such as anorexia nervosa. [12] Adiponectin tissue mRNA expression increases with low calorie diets. [13]

Cystic Fibrosis (CF) is an inherited disease often associated with malnutrition as a result of malabsorption because of pancreatic insufficiency. Malnutrition leads to decreased body weight and height. Decreased body weight is a combination of decreased body fat and fat free mass. [14,15] Cystic fibrosis patients suffer from malnutrition and depletion of body fat. On the other hand, they have an energy deficit because of increased energy requirements. Recent publications had conflicting results on the role of adiponectin among stable adult CF patients. [16,17]

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The aim of the present study was to examine serum adiponectin levels in CF patients (children, adolescents, adults), to associate them with their nutritional status and body composition (fat mass, fat free mass, visceral adipose tissue) and to compare them with those of healthy controls matched for age and gender.

2. Materials and methods

2.1. Patients

Forty-three cystic fibrosis (CF) patients were included in the study. They were recruited from the cystic fibrosis outpatient clinic of a University Hospital. The diagnosis of CF was confirmed by increased concentration of sweat chloride on two occasions and genetic testing in all patients. Patients had to be free from infection for 4 weeks prior to their examination. Thirty-nine patients had pancreatic insufficiency, thirteen had CF associated liver disease (CF-LD) and twelve had CF related diabetes mellitus (CF-DM). Thirty-four patients were colonised with *Pseudomonas aeruginosa* and eight had *Staphylococcus aureus*.

Twenty-seven healthy subjects, matched for age and gender were also included in the study. Children and adolescents were recruited among patients hospitalized in the department for non-infectious causes. Adult controls were recruited among medical students and Pediatric residents. They had a BMI between 15th and 85th percentile for their age and gender. Control subjects also had to be free from infection during the 4 weeks preceding the study.

2.2. Study design—methods

Patients were admitted to the hospital after an overnight fast. They underwent physical examination. Body weight and height were recorded and body mass index (BMI) was calculated as the weight (in kg) divided by the square of height (in m^2). BMI—*z* score (BMI-SDS) was calculated for all subjects using the on-line software provided by Baylor College of Medicine. [18] The body composition of the participants was determined by Bioelectrical Impedance Analysis (B I A) (Body stat, Body Composition Analyzer, Isle of Man, UK), according to the instructions of the manufacturer and the National Institute of Health. [19] Body Fat percent (% BF), BF in kg, Fat Free Mass percent (FFM %) and FFM in kg, were measured for all subjects. The amounts of abdominal visceral and abdominal subcutaneous adipose tissue were estimated with a single-slice CT scan at the level of the umbilicus or at the level of the L3–L4 vertebrae (Spiral Single Slice scanner: PQ 5000, Picker. Software: Analyze, version 5.0, Mayo Clinic). [20] Blood samples were drawn from CF patients and healthy controls. The following tests were performed in all subjects: complete blood count, biochemistry (glucose, albumin, total cholesterol, triglycerides, HDL- and LDL-cholesterol), C-reactive protein, fasting insulin, HbA1c %. Serum insulin levels were measured applying a solid-phase, two-site chemiluminescent immunometric assay (Immulite 2000; DPC, USA) with a 2 μIU/mL sensitivity. Fasting whole blood samples were centrifuged immediately after collection and serum samples were stored at −24 °C, for the measurement of adiponectin. For this purpose a commercial quantitative sandwich enzyme immunoassay technique was used according to the manufacturer's guidelines (Quantikine Human Adiponectin, R & D Systems, USA). The minimum detectable level of the assay was 0.25 ng/ml.

For the estimation of insulin resistance (IR), indices derived from fasting glucose and fasting insulin values were used: Homeostasis Model Assessment for Insulin Resistance (HOMA: IR) = [(fasting glucose [mmol/L) × (fasting insulin [μU/mL)])/22.5 [21] and Fasting Glucose to Fasting Insulin Ratio (FGIR). [22]

The patients were divided according to their age into individuals younger than 17 years (children and adolescents) and patients older than 17 years (adults). They were also divided according to their nutritional status. Patients having a BMI below the 15th percentile for their age and gender

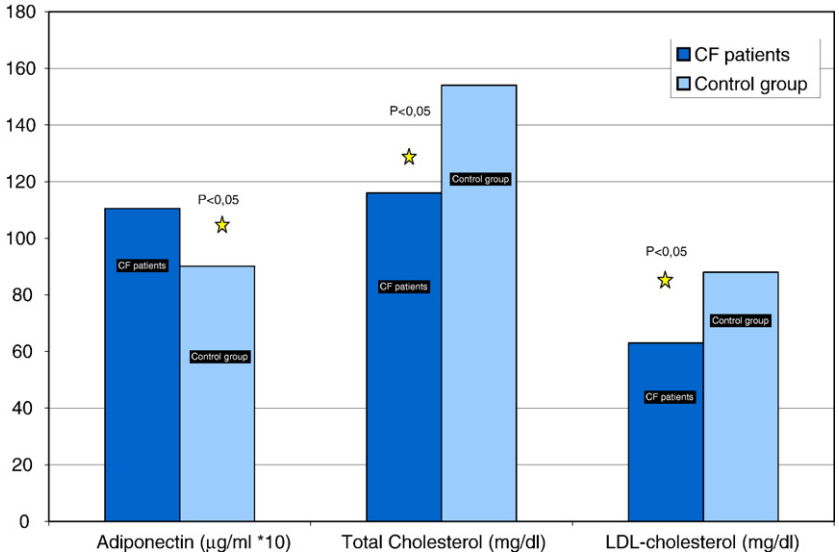

Fig. 1. Adiponectin, total and LDL-cholesterol in CF patients and controls.

were considered as malnourished. [23] Patients with BMI between the 15th and 95th percentiles were regarded as having normal nutritional status. Patients having a BMI above the 95th percentile were excluded from the study as "obese".

Seventeen malnourished CF patients (mean age±SD: 20.52±7.41 years) were compared with 26 normally nourished CF patients (mean age±SD: 19.71±9.36 years) and with 27 healthy subjects (BMI between the 15th and 85th percentiles) matched for age and gender.

2.3. Statistical analysis

Descriptive statistics were computed for all variables of interest. Kolmogorov-Smirnov test was used to test the normality of distribution. Data are shown as means±SD for normally distributed variables. For variables that were normally distributed, differences between subgroups were calculated using a Student's *t*-test for independent samples. For variables not normally distributed, Mann–Whitney *U* test for independent samples was used. Pearson correlation analysis was used to analyze bivariate relationships and to test for association between adiponectin concentrations and body composition and nutrition indices (BMI, BMI-SDS, % BF, BF in Kg, % FFM, FFM in Kg, VAT and % VAT), metabolic parameters (fasting insulin, glucose, and serum albumin and lipid levels) as well as insulin resistance indices (HOMA-IR, FGIR). Linear regression was used to test for the association between adiponectin levels and liver disease. Chi-square test was used for categorical variables. Statistical analysis was performed using the SPSS version 12.0 software (Statistical Package for Social Science Inc, Chicago, Ill. USA). Statistical significance was set at the $p<0.05$ level.

2.4. Ethical considerations

The study was approved by the Aristotle University of Thessaloniki Medical School Ethics Committee and fulfilled the criteria of the Helsinki Declaration. Written informed consent was obtained from the parents of the children and adolescents.

3. Results

Cystic fibrosis patients had significantly higher adiponectin levels (11.53±5.37 μg/ml) than control subjects (9.07±4.41 μg/ml) ($p<0.05$). They also had significantly lower BMI-SDS, total and LDL-cholesterol levels (Fig. 1). In comparison to CF patients with normal nutrition, malnourished CF patients had lower adiponectin, total and LDL-cholesterol (Table 1). In comparison to healthy controls, CF patients with normal nutrition had higher adiponectin (12.58±6.12 vs. 9.07±4.41 μg/ml, $p<0.05$), significantly higher %BF and BF in kg, significantly lower total and LDL-cholesterol levels. In comparison to CF patients with malnutrition, CF patients with normal nutrition had lower percentage of visceral adipose tissue and significantly higher FEV1% predicted (Table 1). There was no difference

Table 1
Anthropometric and metabolic characteristics and adiponectin levels in CF patients with and without malnutrition and control subjects

	BMI<15th		BMI 15th–95th	Controls	*p*
Number (N)	17		26	27	–
Age (yrs)	20.52±7.41		19.78±9.29	19.88±9.42	ns
Weight (kg)	47.51±10.77		51.83±14.77	56.58±18.81	ns
Height (cm)	163±12		156±16	164±20	ns
BMI (Kg/m^2)	17.51±1.92		20.62±2.36	20.04±3.11	0.001
BMI-SDS	−1.81±0.79		0.079±0.56	−0.05±0.60	0.000
% BF	14.17±5.02		24.21±5.89	18.84±5.89	0.000
BF (kg)	6.79±2.28		12.22±3.71	10.63±4.95	0.000
% FFM	85.28±5.02		75.58±5.89	81.15±5.89	0.000
FFM (kg)	40.72±10.52		39.68±12.87	45.94±16.29	ns
FEV1 (% pred)	55.50±17.86		76.60±26.41	–	<0.05
VAT/Total adipose tissue	52%		31%	–	0.003
Adiponectin (μg/ml)	9.91±3.55		12.58±6.12	9.07±4.41	<0.05
(All CF patients)		11.53±5.37		9.07±4.41	<0.05
Cholesterol (mg/dl)	98.92±26.07		126.78±27.04	154.18±29.05	0.000
Triglycerides (mg/dl)	63.69±19.79		83.65±51.97	66.54±31.04	ns
HDL-Cholesterol (mg/dl)	38.70±11.09		58.95±88.52	57.60±15.31	ns
LDL-Cholesterol (mg/dl)	54.40±14.26		67.52±21.24	88.20±23.15	0.000
Albumin (mg/dl)	4.01±0.54		4.22±0.43	–	ns
Fasting Glucose (mg/dl)	93±13		94±28	88±10	ns
Fasting Insulin (μIU/ml)	9±8		8±7	6±3	ns
FGIR	21.59±17.28		18.26±14.52	17.62±11.78	ns
HOMA-IR	2.13±2.10		2.38±3.80	1.49±0.86	ns

CF: Cystic Fibrosis, HDL-Cholesterol: High Density Lipoprotein-cholesterol, LDL-cholesterol: Low Density Lipoprotein-cholesterol. FGIR: Fasting Glucose to Insulin Ratio, HOMA-IR: Homeostasis Model assessment for Insulin Resistance, BMI: Body Mass Index, BMI-SDS: Body Mass Index-Standard Deviation Score, % BF: percent Body Fat, % FFM: percent fat free mass.
Data are expressed as: Mean±Standard Deviation.

Table 2
Demographic and anthropometric characteristics of CF and control subjects

	CF with malnutrition		CF without malnutrition		Control group	
	<17 years (A)	>17 years (B)	<17 years (C)	>17 years (D)	<17 years (E)	>17 years (F)
Number (N)	5	12	11	15	13	14
Age (yrs)	12.73±3.89	23.76±5.95	11.45±3.48	25.88±7.10	11.67±3.2	27.5±6.19
Sex (male/female)	3/2	7/5	4/6	8/8	7/6	6/8
Weight (kg)	37.5±11.5	51.66±7.55 $^{\#\ \$}$	39.51±13.2	60.8±7.6 $^{\#,\ *}$	42.7±15.9	69.47±10.04$^{*,\$}$
Height (cm)	152±17	168±7 $^{\#}$	143±15 $^{\$}$	166±8 $^{\$,*}$	151±20	177±8 $^{*,\ \#}$
BMI (Kg/m^2)	15.84±1.72 $^{\$}$	18.21±1.57 $^{\#,\ *}$	18.6±2.16 $^{\$}$	21.94±1.45 $^{\#}$	17.8±2.5	22.05±2.15*
BMI-SDS	−1.56±0.76 $^{*,\$}$	−1.09±0.81 $^{\#,\ \$}$	0.38±0.76 $^{\$}$	−0.11±0.40 $^{\#}$	−0.039±0.55*	−0.065±0.67 $^{\$}$
% BF	14.88±4.3 $^{\$}$	14.61±5.47 *	27.9±4.06 $^{\#,\ \$}$	21.48±5.25 *	17.7±4.1 $^{\#}$	19.82±7
BF (kg)	4.85±3.56	7.26±2.11 *	11.2±4.46	12.93±3.05 *	7.3±3.4	13.48±4.29
% FFM	85±4.3	85.38±5.47 *	72±4.65	78.5±5.25 *	82.3±4.10	80.17±7.09
FFM (kg)	31.9±9.67	44.4±8.7	28.3±9.31	47.9±7.96 *	34.2±13	55.99±10.94 *
VAT/Total Fat	49% *	53% $^{\#}$	34% *	29% $^{\#}$	–	–
FEV1 (% pred)	65.3±18	61±23	85.8±4	74±20	–	–

CF: cystic fibrosis, BMI: Body Mass Index, BMI-SDS: Body Mass Index-Standard Deviation Score, % BF: percent Body Fat, % FFM: percent Fat Free Mass, VAT: Visceral Adipose Tissue, FEV1%: Forced Expiratory Volume in 1 s, % predicted.
Data are expressed as: Mean±Standard Deviation.
Statistically significant differences $^{\$,\ \&}$: $p<0.05$ $^{\S,\ *}$: $p<0.001$ $^{\#,\ \ddagger}$: $p<0.000$.

between male and female CF patients except for body composition parameters [CF males had higher %FFM and total FFM and lower %BF and total BF than females ($p<0.001$)].

The demographic and anthropometric characteristics of CF patients as well as those of healthy controls are shown in Table 2. By definition, young and adult malnourished CF patients (groups A and B) had significantly lower BMI and BMI-SDS, when compared to normally nourished CF patients (groups C and D) and to healthy controls (groups E and F). They also had significantly lower % BF, absolute BF in kg, % FFM, but comparable absolute FFM in kg. Furthermore, adult CF patients (Groups B and D) were significantly shorter than healthy controls (Group F). Young CF patients with normal nutrition (Group C) had significantly higher absolute body fat in kg and percent body fat than healthy control subjects (Group E). Both young and adult malnourished CF patients had significantly higher percentage of visceral adipose tissue in comparison to CF patients without malnutrition. Finally, malnourished CF patients had lower (but not significantly) FEV1% than CF patients with normal nutrition.

Biochemical data (adiponectin, serum lipids, albumin), fasting glucose and insulin concentrations and IR indices derived from these values (FGIR, HOMA-IR) in CF patients according to their nutritional status and in healthy controls are demonstrated in Table 3. Malnourished CF patients had significantly lower serum lipid levels when compared to patients with normal nutrition and healthy controls. All groups had comparable glucose, insulin and insulin resistance levels. With regard to adiponectin (Table 3, Fig. 2), young malnourished CF patients had significantly lower levels (Group A: 8.06±1.85 μg/ml) when compared to young CF patients with normal nutrition (Group C: 14.56±7.69 μg/ml)] ($p<0.05$). Young malnourished CF patients had lower levels (but not significantly) than those of healthy controls (Group E: 9.84±4.45 μg/ml).

Table 3
Biochemical investigations of CF and control subjects

	CF with malnutrition		CF without malnutrition		Control group	
	<17 years (A)	>17 years (B)	<17 years (C)	>17 years (D)	<17 years (E)	>17 years (F)
Number (N)	5	12	11	15	13	14
Adiponectin (μg/ml)	8.06±1.85 $^{\$}$	10.68±3.86	14.56±7.69 $^{\$}$	11.13±4.40	9.84±4.45	8.35±4.42
Cholesterol (mg/dl)	88±37 $^{\&}$	102±23 $^{\$}$	129±35 $^{\$}$	124±20 $^{\$}$	154±29 $^{\&}$	208±42 $^{\#}$
Triglycerides	48±26	68±16	69±39 $^{\$}$	94±59 $^{\$}$	66±31	60±27
HDL-Cholesterol (mg/dl)	43±16*	37±10	42±12 $^{\$}$	38±6 $^{\$,\ \#}$	57±15 *	49±7 $^{\#}$
LDL-Cholesterol (mg/dl)	50±10 $^{\$}$	55±15	71±25	64±18, $^{\#}$	88±23$^{\$,\ *}$	101±34 $^{\#}$
Albumin (mg/dl)	4.12±0.69	4.09±0.51	4.38±0.37	4.11±0.04	6.05±0.68	6.38±0.46
Fasting Glucose (mg/dl)	90±9	94±15	88±12	97±36 $^{\#}$	84±9	92.7±9.5 $^{\#}$
Fasting Insulin (μIU/ml)	12.7±9.3	7.51±7.82	6.6±3.9	10.06±9.73	8.26±4.36	5.39±2.18
FGIR	11.58±8.10	26.16±18	18±10	18.4±17	13.15±8.44	21.76±13.18
HOMA-IR	2.77±1.87	1.84±2.2	1.5±1.1	3.01±4.89	1.77±1.09	1.22±0.49

CF: Cystic Fibrosis, HDL-Cholesterol: High Density Lipoprotein-cholesterol, LDL-cholesterol: Low Density Lipoprotein-cholesterol. FGIR: Fasting Glucose to Insulin Ratio, HOMA-IR: Homeostasis Model assessment for Insulin Resistance.
Data are shown as: mean±SD for normally distributed variables.
*, #, ‡, &, $: statistically significant differences ($p<0.05$).

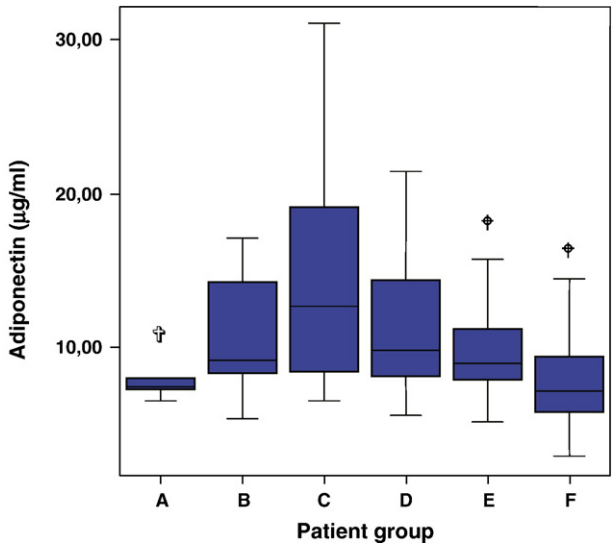

Fig. 2. Adiponectin levels in various subgroups according to age and nutritional status.

Young CF patients with normal nutrition had higher levels (but not significantly) than those of healthy individuals. Among adult CF patients, the presence of malnutrition did not affect adiponectin levels (10.68±3.86 vs. 11.13±4.40 µg/ml). They were higher but not significantly than those of healthy controls (8.35±4.42 µg/ml).

One significant parameter that seemed to influence adiponectin levels was the presence of liver disease. Patients with nodular biliary cirrhosis had significantly higher levels than patients with normal liver (10.52±5.49 µg/ml vs. 14.04±4.52 µg/ml, Mann–Whitney U test, $p<0.01$) (Fig. 3). More specifically, in the patient group with liver disease the presence of malnutrition did not significantly affect adiponectin levels (13.026±3.98 µg/ml vs. 14.9±6.14 µg/ml, respectively,

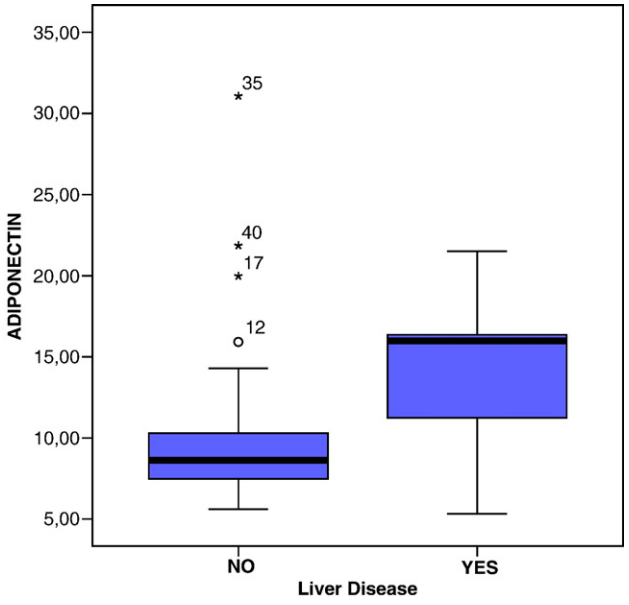

Fig. 3. Adiponectin levels according to the presence of liver disease.

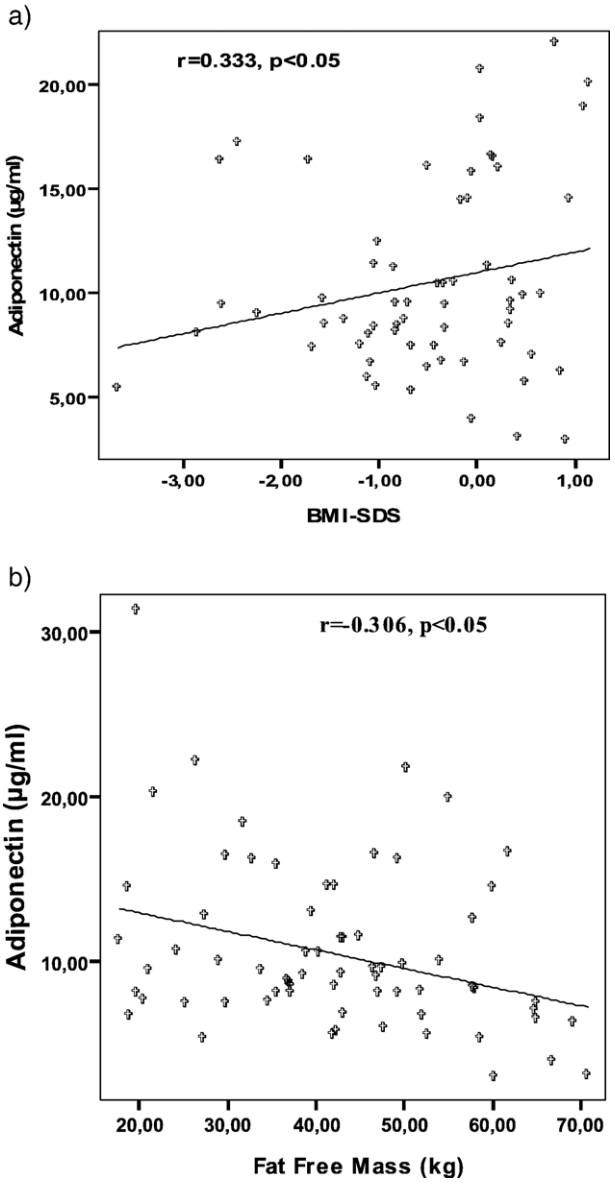

Fig. 4. Pearson correlation of adiponectin a) with BMI-SDS among CF patients b) with fat free mass (in Kg) in all subjects.

$p>0.05$). On the other hand, in the patient group without liver disease the presence of malnutrition significantly affected adiponectin levels (8.22±1.82 µg/ml vs. 11.7±6.01 µg/ml, respectively, $p<0.05$). Stepwise linear regression analysis with adiponectin as a dependent variable and liver disease, BMI-

Table 4
Pearson correlation between adiponectin levels and anthropometric characteristics in all subjects ($n=70$)

	R	P
Weight	−0.259	0.030
Height	−0.323	0.006
%BF	0.292	0.015
%FFM	−0.292	0.015
FFM (kg)	−0.306	0.010

% BF: percent Body Fat, % FFM: percent fat free mass, FFM: Fat Free Mass in kg.

percentile, % BF and age as independent variables showed that the only predictors in the model were liver disease and BMI-percentile.

Furthermore, adiponectin levels appeared to be associated with BMI-SDS (Pearson correlation coefficient, $r=0.333$, $0<0.05$) (Fig. 4a). There was no correlation of adiponectin with demographic and anthropometric parameters, with biochemical and insulin resistance indices regardless of gender and age. When patients and control subjects were examined as a group, adiponectin levels correlated significantly to weight, height, %BF, %FFM and FFM in kg (Table 4, Fig. 4b).

4. Discussion

This is the first time that adiponectin levels were related to the nutritional status in CF patients. Young malnourished CF patients had the lowest levels of adiponectin. This may be related to their reduced absolute amount and percentage of body fat. This finding is in accordance with studies which have shown low adiponectin levels in patients with congenital or acquired lipodystrophy. Reduced adiponectin levels were found in an experimental animal model of lipoatrophic subjects [24] and in patients with generalised lipodystrophy, in proportion to the extent of fat loss. On the contrary, adiponectin was similar in patients with partial lipodystrophy and normal healthy subjects. [10] Reduced adiponectin levels have been demonstrated in HIV-positive patients with Highly Active Antiretroviral Treatment (HAART)-induced lipodystrophy. [11] Low adiponectin in malnourished CF patients may be attributed to the reduced amount of total body fat and the increased percentage of VAT.

The second finding was that adiponectin levels were increased in young CF patients having normal nutrition as compared to malnourished young CF patients as well as healthy controls. Moriconi et al., demonstrated elevated adiponectin among adult CF patients. They showed increased central fat accumulation in adult CF patients as compared to healthy controls matched for BMI, age, and sex. The serum concentrations of adiponectin were higher in CF patients than in controls, even after adjustment for known confounders. This was attributed to the negative energy balance that often characterizes CF. [16] A recent study by Hammana et al., compared 90 CF patients with 15 healthy controls. Contrary to the first study, they did not find any alterations in adiponectin levels despite insulin resistance, glucose intolerance and subclinical chronic inflammation. Women had higher adiponectin concentrations. Adiponectin correlated significantly with total and HDL-cholesterol. They concluded that CF appears to be one of the rare conditions in which discordance between adiponectin and insulin resistance or inflammation is evident. [17]

As far as we know this is the first study of adiponectin levels in relation to the nutritional status of CF patients. Furthermore, it is the first study of adiponectin among CF children and adolescents. In the study by Hammana et al., adiponectin was viewed as a marker of insulin resistance and inflammation, therefore its relationship to fibrinogen and CRP was examined. Moriconi et al., examined adiponectin as a marker of energy deficiency. Qi et al., showed that adiponectin acted on the brain to reduce body weight. Both systematic administration and intra-ventricular injection of adiponectin resulted in increased thermogenesis, reduction of blood glucose and lipids. Body weight was reduced through an increase in energy expenditure. [25] Other animal studies however, suggested a negative effect on energy expenditure. [26] Studies in humans showed a negative correlation between resting metabolic rate and adiponectin in Caucasians. [27] Among Pima Indians, a negative correlation was found between adiponectin and energy expenditure, probably related to body fat distribution. [28] Adiponectin levels have been related to energy deficiency conditions. Adiponectin mRNA in subcutaneous fat (but not in plasma) rose quickly during significant, short-term energy intake restriction (Very Low Calorie Diet, VLCD, 600–800 Kcal/day). [13] Others failed to demonstrate that VLCD-induced weight reduction and metabolic changes were accompanied by elevation of adiponectin. [29] The same applied to patients who followed an intensive exercise program. [30,31] Anorexia nervosa (AN) patients are a group experiencing severe negative energy balance. They have increased adiponectin [12,33–37] while resistin and leptin are decreased. [32] They also have increased insulin sensitivity possibly related to increased adiponectin levels. [38] Only one study showed that patients with AN and bulimia had lower adiponectin than controls, which returned to normal after body weight restoration. [39] It is widely accepted that CF patients have an increased risk of malnutrition because of the chronic energy deficiency and the negative energy balance. [40] This may explain our findings. Yet, contrary to Moriconi et al., we did not find any association between adiponectin and serum concentrations of albumin, a marker of protein malnutrition. However, an association between adiponectin and serum lipids was demonstrated.

The third finding was that malnourished CF patients had significantly higher percentage of VAT in comparison to patients without malnutrition, despite the significantly decreased body fat (absolute amount and percentage). Both groups had comparable fat free mass, which was lower to that of healthy controls. Moriconi et al., also found increased central fat in CF patients in comparison to healthy controls, attributed to CF-related factors (chronic inflammation, corticosteroids, physical inactivity, anabolic hormones or relative growth hormone deficiency). [16] In the present study, VAT was measured with CT-scan only in CF patients; therefore comparisons were only possible between patients with and without malnutrition. None of our patients received corticosteroids. Finally, although central fat is associated with insulin resistance, HOMA-IR and FGIR did not differ between patients with and without malnutrition.

The fourth observation of the study was that adiponectin levels were increased among CF patients with biliary cirrhosis. They were normal among patients without liver disease. The presence of malnutrition did not affect adiponectin concentrations in this patient group. Elevated adiponectin has been described among patients with cirrhosis. Tacke et al., demonstrated elevated adiponectin in chronic liver disease, attributed to liver damage and inflammation. High adiponectin levels after bile duct ligation in mice and in human bile from patients

having cholestasis suggest that biliary secretion is involved in adiponectin clearance and that adiponectin could serve as a novel marker indicating cholestasis in liver cirrhosis. [41] Tietge et al., also found that adiponectin levels were significantly elevated in cirrhosis. They did not correlate with parameters of body composition or metabolism. They correlated exclusively with reduced liver function and altered hepatic hemodynamics. They concluded that the liver was a major source of adiponectin extraction. [42] Our findings are in accordance with these data and were taken into consideration in the interpretation of the results.

Limitations of our study include the small number of subjects, its cross-sectional design as well as the fact that CF patients had a varying degree of disease severity, making it a heterogeneous population.

In conclusion, our study revealed elevated adiponectin levels among young CF patients with normal nutrition which may be attributed to the energy deficit inherent to the disease and low adiponectin levels among malnourished CF patients probably attributed to lipodystrophy-like body fat reduction. It also revealed that CF patients with biliary cirrhosis had increased adiponectin levels. Patients with malnutrition tended to have a more central fat distribution with increased visceral adipose tissue. More studies are warranted to further elucidate the role of adiponectin as a marker of liver disease and also of energy deficiency and imminent malnutrition among growing CF patients.

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