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# Serum Leptin Level in Patients with Cystic Fibrosis †

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**Abstract:** Introduction: Along with the significant increase in the average life expectancy of patients with cystic fibrosis (CF), there are still significant differences in the height, weight, and body mass index (BMI) of patients compared to healthy controls. The association between leptin and fat mass might be an additional factor in weight loss or poor weight gain in CF patients. Aim: Our objective was to estimate serum leptin concentrations in CF patients aged 10–39 years as well as to assess correlations between leptin and the clinical characteristics of CF. Materials and methods: Leptin serum concentrations after an overnight fast were measured using an enzyme-linked immunosorbent assay in 38 CF patients and 16 controls. In all participants' height, weight, BMI, and forced expiratory volume in 1 s ($FEV_1$) were estimated. In addition, fasting serum C-reactive protein (CRP) concentrations were also analyzed. Results: Fasting leptin levels in CF were significantly higher in patients with CF patients (13.9 ± 6.9 vs. 6.5 ± 2.6 ng/mL, $p < 0.001$) compared to controls. There were no differences in leptin concentration between female and male CF participants (15.7 ± 7.8 vs. 12.2 ± 5.6 ng/mL, $p = 0.13$). Leptin was correlated with age ($R = 0.64$, $p < 0.001$), BMI ($R = 0.65$, $p < 0.001$), $FEV_1$ ($R = -0.49$, $p < 0.01$), and CRP ($R = -0.73$, $p < 0.001$). Conclusion: An increased serum leptin level was positively associated with age and nutritional status, as well as negatively associated with $FEV_1$ and CRP in patients with CF. The results of our study suggest that reduced pulmonary function in CF may be related to an elevated level of leptin, while weight loss may be associated with a decreased level of leptin.

**Keywords:** body mass index; cystic fibrosis; leptin

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## 1. Introduction

Cystic fibrosis (CF) is a multi-system disease caused by mutations in a gene that leads to a defective or missing CF transmembrane conductance regulator. With the increase in survival time, technological advancement and improved quality of medical care, there are still significant differences in the height, weight, and body mass index (BMI) of patients compared to healthy controls [1,2]. Approximately 70% of CF patients suffer from malnutrition, and in some patients, additionally, body weight deficiency, growth deficiency, reduced brachial fold thickness and reduced lean tissue mass are also observed [3]. In addition, fat-soluble vitamin deficiencies are common [4]. Due to the fact that the nutritional status of the CF patient is closely correlated with the functioning of the respiratory system, systematic monitoring of the patient and the prevention of nutritional disorders are recommended [5]. Leptin is a peptide hormone secreted by adipocytes that helps regulate energy balance by inhibiting hunger. However, current data on circulating leptin levels in CF are inconsistent and indicate decreased, increased, or unchanged levels of this hormone [6,7].

Our objective was to estimate serum leptin concentrations in patients with CF, as well as to assess any correlations between leptin and the clinical characteristics of CF.

## 2. Methods

A single-center study was carried out in a sample of 38 CF patients, as well as 16 control subjects. Participants were recruited from the Department of Allergology and Cystic Fibrosis, Provincial Hospital No 2, Rzeszów, Poland. The study protocol was approved by the local Bioethics Committee of the University of Rzeszów. Blood samples were taken between 8 am and 10 am after overnight fasting, into blood collection tubes and centrifuged, and the obtained serum was aliquoted and frozen at −80 °C until further analysis. Leptin serum concentrations after an overnight fast were measured using the enzyme-linked immunosorbent assay (Wuhan Fine Biotech Co., Ltd., Wuhan, China), according to the manufacturer's protocol. In all participants' height, weight, body mass index (BMI), and forced expiratory volume in 1 s ($FEV_1$) were measured using a standard spirometry device (Lungtest 1000 MES SJ, Poland) according to recommendations [8]. Furthermore, fasting serum C-reactive protein (CRP) concentrations were also analyzed using the dry chemistry immunological method on a VITROS 250 analyzer (Ortho Clinical Diagnostics, Johnson and Johnson, USA). Statistical analysis of the data was performed using the STATISTICA software package (version 13.1, StatSoft Inc. 2016, Tulsa, OK, USA). Data are presented as mean ± SD and range. Comparisons of the groups were performed with the Mann-Whitney U test. Spearman's rank correlation coefficient analysis was used to estimate the relationships between the studied parameters, assuming linear dependence.

## 3. Results

Baseline characteristics, clinical laboratory values, and indices of pulmonary function for patients with CF and healthy controls are presented in Table 1. Weight, BMI and $FEV_1$ were significantly lower, whereas the number of white blood cells and the CRP concentration were significantly elevated in CF adolescents compared to controls.

**Table 1.** Demographic data of the participants at enrolment *.

| | | CF | Healthy Controls | *p* |
|---|---|---|---|---|
| Sex (F/M) | | 17/21 | 10/6 | |
| Age (years) | mean ± SD | 19.58 ± 7.9 | 19.25 ± 7.3 | *0.855* |
| | range | 10–39 | 10–38 | |
| Height (cm) | mean ± SD | 157.56 ± 18.1 | 160.56 ± 15.1 | *0.598* |
| | range | 124–188.5 | 130–180 | |
| Weight (kg) | mean ± SD | 50.03 ± 13 | 58.75 ± 13.9 | ***0.038*** |
| | range | 22.1–76 | 34–82 | |
| BMI ($kg/m^2$) | mean ± SD | 19.89 ± 2.8 | 22.47 ± 2.5 | ***0.003*** |
| | range | 14.4–25.9 | 18.7–25.6 | |
| Clinical laboratory markers | | | | |
| WBC ($10^3/\mu L$) | mean ± SD | 9.95 ± 3.6 | 7.46 ± 2.3 | ***0.022*** |
| | range | 5.1–19.3 | 4.3–10.5 | |
| NEU (%) | mean ± SD | 61.01 ± 15.3 | 59.12 ± 6.1 | *0.605* |
| | range | 25.1–82.3 | 50.6–68.6 | |
| CRP (mg/L) | mean ± SD | 5.32 ± 4.8 | 1.92 ± 1.2 | ***0.001*** |
| | range | 0.5–22 | 0.3–4.2 | |
| Pulmonary function | | | | |
| $FEV_1$ (% predicted) | mean ± SD | 86.35 ± 27 | 102.4 ± 8.2 | ***0.006*** |
| | range | 35–142 | 97–127 | |

***** BMI—body mass index, WBC—white blood cells, NEU—neutrophils, CRP—C-reactive protein, $FEV_1$—forced expiratory volume in 1 s. Statistically significant differences are in bold.

Fasting leptin levels in CF were significantly higher in patients with CF patients (13.9 ± 6.9 vs. 6.5 ± 2.6 ng/mL, $p < 0.001$) compared to controls (Figure 1).

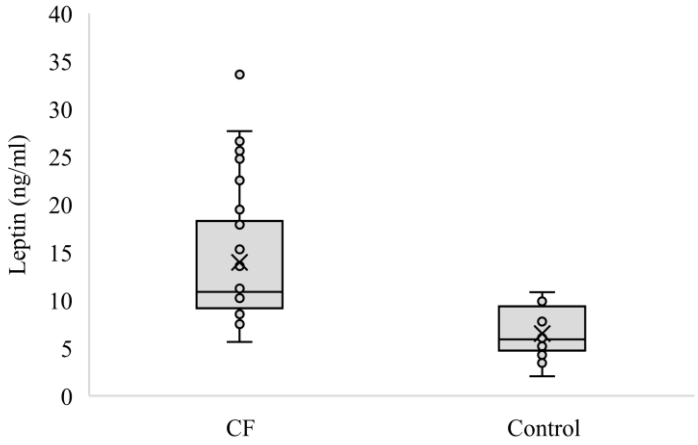


**Figure 1.** Leptin concentration in CF and control participants.

There were no differences in leptin concentration between female and male CF participants (15.7 ± 7.8 vs. 12.2 ± 5.6 ng/mL, $p = 0.13$, Figure 2).

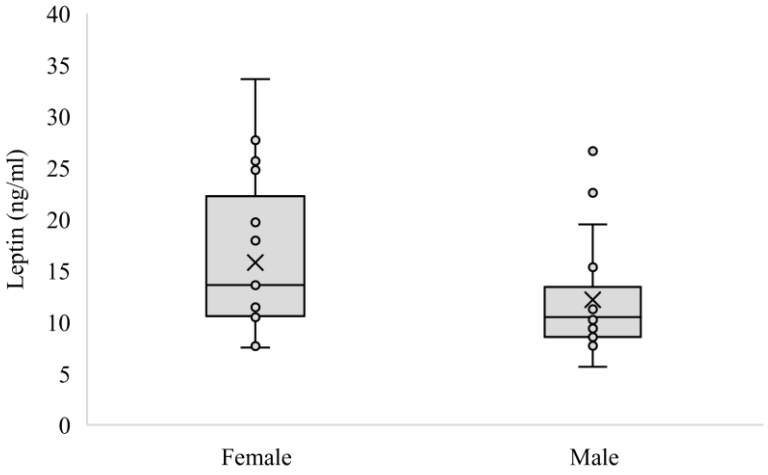


**Figure 2.** Leptin concentration in female and male participants with CF.

Table 2 presents the correlation of leptin with the clinical features of the studied patients. We found a positive significant correlation of leptin with age (R = 0.64, $p < 0.001$), BMI (R = 0.65, $p < 0.001$). Leptin was negatively correlated with $FEV_1$ (R = −0.49, $p < 0.01$), and CRP (R = −0.73, $p < 0.001$).

**Table 2.** Correlation coefficients between leptin concentration and clinical features of studied patients.

| **Age** | | **Height** | | **Weight** | | **BMI** | |
|---|---|---|---|---|---|---|---|
| *R* | *p* | *R* | *p* | *R* | *p* | *R* | *p* |
| 0.643 | **0.0004** | 0.002 | 0.99 | 0.344 | **0.046** | 0.649 | **0.0002** |
| **WBC** | | **NEU** | | **CRP** | | **$FEV_1$** | |
| *R* | *p* | *R* | *p* | *R* | *p* | *R* | *p* |
| −0.071 | 0.691 | −0.048 | 0.786 | −0.731 | **0.0008** | −0.494 | **0.003** |

* BMI—body mass index, WBC—white blood cells, NEU—neutrophils, CRP—C-reactive protein, $FEV_1$—forced expiratory volume in 1 s. Statistically significant differences are in bold.

## 4. Discussion

Leptin levels may reflect the amount of body fat that may be decreased in anorexia or increased in obesity [9,10]. In the literature there are conflicting data regarding the leptin concentration CF patients, which indicates that there is dysregulation of leptin synthesis among CF patients. Similarly to our results, Stylianou et al. also reported significantly higher leptin level in CF adolescents than healthy controls ($p = 0.03$), as well as elevated hormone level in CF females than CF males [6]. Moreover, a higher level of leptin was observed among pediatric CF patients [11,12]. These results could provide an explanation and could also be an additional factor in the decreased appetite and poor weight gain observed in CF patients [13]. On the other hand, serum leptin concentration was similar in CF and controls (5.3 ± 4.1 ng/mL vs. 4.4 ± 3.6 ng/mL) in the study by Arumugam et al. [14]. However, they also observed a significantly lower leptin level in CF males than females. Nevertheless, decreased leptin concentration was noted in severe CF patients ($FEV_1$ < 45%) compared to controls and other CF subjects [7]. Likewise, pediatric and youth patients with CF had lower leptin levels compared to the control group [15–17]. A higher proportion of body fat and an increased rate of leptin synthesis per unit mass of adipose tissue may explain the higher level of serum leptin in women than in men [18]. Leptin was lower in children, as could be expected and described previously [19].

The current study demonstrates a positive association between BMI and leptin concentrations as previously described [7,11]. Nonetheless, we found a negative correlation between $FEV_1$ and leptin concentration which is different from that described earlier in CF patients aged 22–48 years [7]. A study on human coronary artery smooth cells showed that hypoxia increased leptin expression, with earlier expression of angiotensin II and reactive oxygen species [20].

It should be noted that a negative correlation between $FEV_1$ and serum leptin has also been described in healthy obese and non-obese children, adults, and asthmatic subjects [21–23]. It should be noted that direct comparisons of reports may be difficult because of small numbers of patients and different CF and control populations of different ages, geographic regions and ethnic groups.

## 5. Conclusions

Increased serum leptin level was associated positively with age and nutritional status, as well as negatively with $FEV_1$ and CRP in patients with CF. The results of our study suggest that reduced pulmonary function in CF may be related to an elevated level of leptin, while weight loss may be associated with a decreased level of leptin.

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