Leptin hormone in obese and non-obese stable and exacerbated cases of chronic obstructive pulmonary disease

Ahmad Elsayed Mahmoud a,*, Magdy Mohammed Omar a, Nabil A. Abdelghaffar Hibah a,*, Hisham Ali Issa b

a Chest Department, Faculty of Medicine, Benha University, Egypt
b Clinical and Chemical Pathology Department, Faculty of Medicine, Benha University, Egypt

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Keywords
Serum leptin; Stable COPD; COPD exacerbation; Obese; Non-obese; BMI

Abstract Objectives: The aim of this study was to assess the level of serum leptin hormone in chronic obstructive pulmonary disease patients during acute exacerbation and in stable conditions and also, to determine if these changes correlate with changes in the ventilatory functions.

Methods: Sixty cases were included in this prospective study (40 COPD patients and 20 age related smokers without symptoms or signs of COPD and within normal pulmonary functions as a control). Patients and control were divided according to their BMI into obese (BMI ≥ 30) and non-obese (BMI = 18.5–25). Subjects were submitted to full history taking, thorough physical examination, plain chest X-ray, complete blood count, erythrocyte sedimentation rate, liver and kidney functions, fasting and post prandial blood sugar, ventilatory functions, and serum leptin level measurement.

Results: Serum leptin level (ng/ml) was significantly higher (P < 0.001) in stable obese COPD (mean ± SD = 23.85 ± 4.47) patients than obese controls (mean ± SD = 20.9 ± 2.7) and stable non-obese COPD (mean ± SD = 5.63 ± 1.05) and stable non-obese COPD cases had significantly higher (P < 0.05) serum leptin level than non-obese controls (mean ± SD = 6.53 ± 1.19). Serum leptin level was significantly higher (P < 0.001) in obese COPD cases during exacerbation (mean ± SD = 67.59 ± 9.8) than in non-obese COPD cases during exacerbation.

Abbreviations: BMI, body mass index; COPD, chronic obstructive pulmonary disease; SI, smoking index; PFT, pulmonary function tests; FEV1, forced expiratory volume in first second; FVC, forced vital capacity

* This work was primarily carried out in: Benha University Hospitals, Benha, Egypt.
* Corresponding authors at: Benha university hospitals, Chest department, Benha city 13512, Egypt. Tel./fax: +20 13 3227518, mobile: +20 1016940428 (N.A. Abdelghaffar Hibah).
E-mail address: nabil.hibah@yahoo.com (N.A. Abdelghaffar Hibah).
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Introduction

Chronic obstructive pulmonary disease (COPD) is a preventable and treatable disease with some significant extra pulmonary effects that may contribute to the severity in individual patients, its pulmonary component is characterized by airflow limitation that is not fully reversible, the airflow limitation is usually progressive and associated with an abnormal inflammatory response of the lung to noxious particles or gases [1]. Tobacco smoking is a common risk factor for multiple co-morbidities, including coronary heart disease, heart failure and lung cancer. Co-morbidities such as pulmonary artery disease and malnutrition are directly caused by COPD. These extrapulmonary manifestations are mostly caused by chronic systemic inflammation. All of these co-morbidities potentiate the impact of COPD on health and lead to increased hospitalizations and healthcare costs [2–5].

Obesity is defined as a body mass index (BMI) greater than 30 kg/m²; Over 1.6 billion adults worldwide are overweight, of which 400 million are obese. The World Health Organization predicted that 10% of the global population will be obese by 2015; In the United States of America, the annual health care costs are 36% greater for an obese patient compared with a patient with a normal BMI [6].

Leptin is a 167 amino acid peptide made exclusively in adipose tissue in a wide range of animal species, including humans. The (ob) gene encoding leptin is located on the mouse chromosome and the human homolog of the ob gene has been mapped to chromosome 7q31. Northern blot or RT-PCR analysis of the messenger ribonucleic acid (mRNA) for the ob gene showed that it was expressed only in adipose tissue [7–9].

Aim of the work

The aim of this study was to assess the level of serum leptin hormone in chronic obstructive pulmonary disease patients during acute exacerbation and in stable conditions and also, to determine if these changes correlate with changes in the ventilatory functions.

Methods

Sixty cases were included in this prospective study (40 COPD patients and 20 age related smokers without symptoms or signs of COPD and within normal pulmonary functions as a control). All COPD cases were in acute exacerbation and were admitted in El-Fayuom Chest hospital and Chest Department in Benha University from October 2010 to October 2011 and the diagnosis of COPD was established on the basis of Global Initiative for Chronic Obstructive Lung Disease [1]. All participants were divided according to their body mass index (BMI) values into non-obese (BMI < 25 > 18.5) and obese (BMI ≥ 30). Participants were classified into 4 groups: group-1 (G1) contained 20 obese COPD cases, Group-2 (G2) contained 20 non-obese COPD cases, control-1 (C1) contained 10 control subjects and control-2 (C2) contained 10 control subjects.

Exclusion criteria for participants:

- The presence of a co-morbidity can affect the levels of leptin hormone in cardiovascular disease, cerebral vascular diseases, Diabetes mellitus, arthritis, liver cirrhosis, end-stage renal disease, Tuberculosis, bronchiectasis, malignancy and connective tissue disorders [10].

All participants were subjected to the following:

1. Thorough history taking and clinical examination including:
   - Measuring of smoking index (number of packs/day x number of years smoking).
   - History of co-morbidities that may affect the level of the leptin hormone as ischemic heart diseases, hypertension, diabetes mellitus, tuberculosis, malignancy, end-stage renal disease, rheumatoid arthritis and any systemic infection or inflammation [10].

2. Body mass index (BMI): was calculated for all cases (the weight in kg divided by height²).
3. Laboratory investigations: complete blood picture, erythrocyte sedimentation rate, fasting and 2 h post-prandial blood glucose, kidney and liver function tests.
4. Radiological examination: plain postero-anterior and lateral chest x-rays were done to exclude any chest lesion if present.
5. Pulmonary function tests (spirometry): before and after bronchodilatation using Sensor-medics V max series, 2130 Spirometer, V6200 Autobox, 6200DL. Ambient temperature and pressure were entered with the patient data (age in years, weight in kilograms, height in centimeters and sex) so that all results were calculated as percent of predicted (% predicted) except for FEV1/FVC. Pulmonary functions were done pre and post bronchodilatation during acute exacerbation of the disease and pre and post bronchodilatation after management of cases during stability.
6. Serum leptin hormone measurement:

Serum leptin hormone level (ng/ml) was significantly higher in obese COPD cases than in controls and non-obese cases and during exacerbation than in stability which indicates that leptin plays a role in the systemic inflammatory process. Serum leptin hormone level positively correlated with BMI (kg/m²).
Sampling:
The leptin hormone level was measured twice in all COPD patients [in acute exacerbation (AECOPD) and after stability] and once in all control subjects. All samples were collected at 9 AM and all patients were in fasting state for at least 8 h. Four-five milli liter of blood was collected into an
appropriately labeled tube and all samples centrifuged and carefully the layer was removed then the serum samples were stored at (–70) degree till analyzed.

**Principles of the test:**
Quantitative analysis of the serum leptin level was done using an enzyme immunoassay. The approximate leptin concentration in the patient sample was calculated (leptin Titer in ng/ml) and a Reference value of 3.8 ng/ml [range (2–5.6 ng/ml) in normal weight non-obese male patient] was determined.

**Serum leptin measurement procedure:**
The kit components:
- Anti leptin monoclonal antibody coated Microwell plate-break apart wells.
- Monoclonal anti leptin antibody conjugated to biotin in a protein based buffer with a non mercury preservative in a bottle 10 ml.
- Streptavidin conjugated to horseradish peroxidase in protein based buffer with a non mercury preservative in a bottle 0.4 ml.
- Six bottles of leptin calibrators containing leptin in a protein based buffer with non mercury preservative.
- One bottle of control solution containing leptin in a protein based buffer with non mercury preservative.
- One bottle of wash buffer concentrate containing buffer with non-ionic detergent and non mercury preservative.
- One bottle of assay buffer containing protein based buffer with non mercury preservative.
- One bottle of TMB substrate (tetramethylbenzidine) and hydrogen peroxide in non DMF or DMSO containing buffer.
- One bottle of stopping solution containing sulfuric acid.

**The procedure:**
- Working solution of streptavidin HRP conjugate and wash buffer was prepared.
- 20 μl of each calibrator, control and serum sample was pipetted into correspondingly labeled wells in duplicate.
- 80 μl of the monoclonal anti-leptin-biotin conjugate was pipetted into each well.
- Incubated on a shaker for 1 h at room temperature.
- The wells were washed 3 times with prepared wash buffer.
- 100 μl of prepared streptavidin HRP conjugate was pipetted into each well.
- Incubated on a plate shaker for 30 min at room temperature.

- 100 μl of TMB substrate was pipetted into each well.
- Incubated on a plate shaker for 15 min at room temperature.
- 50 μl of stopping solution was pipetted into each well.
- The plate was read on the Microwell plate reader at 450 nm in 20 min.

**Statistical analysis**
Results are given as mean ± SD. Differences between groups were statistically analyzed using an unpaired Student’s *t* test. In the patients with leptin values below the detection limit (0.25 ng/ml); the value 0.25 ng/ml is used in the analysis. After curve estimation, linear, exponential or logarithmic Pearson product moment correlation will be calculated. After the simple correlations, a regression model will be fitted to the data to select the variables that contributed to the explained variation in plasma leptin concentration. Significance will be determined at the 5% level. Data were analyzed using SPSS (Statistical Package for the Social Sciences, version 14.0 for Windows).

**Results and discussion**
Researchers have speculated that a potential link between obesity and COPD subsists since low BMI and weight loss are associated with increased mortality in patients suffering from COPD [11].

The aim of this study was to assess the level of serum leptin hormone in chronic obstructive pulmonary disease patients during acute exacerbation and in stable conditions and also, to determine if these changes correlate with changes in the ventilatory functions.

Regarding the statistical comparison in demographic data between all groups in this study there were no statistically significant differences in different values except BMI between obese and non-obese groups (Table 1).

In this study pre and post-bronchodilator spirometry was done among 40 patients known to have COPD during exacerbation and stability and showed partial reversibility in the FEV1% predicted (less than 12%) confirming the diagnosis of COPD.

Regarding pulmonary function parameters, there was no statistically significant difference between obese and non-obese COPD cases during stability regarding FVC% predicted,

<table>
<thead>
<tr>
<th>Group</th>
<th>State</th>
<th>Range</th>
<th>Mean ± SD</th>
<th><em>P</em> value</th>
<th>Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>G1</td>
<td>Exacerbation</td>
<td>49–83</td>
<td>64.59 ± 9.8</td>
<td>&lt;0.001</td>
<td>HS</td>
</tr>
<tr>
<td>Stable</td>
<td></td>
<td>17–31</td>
<td>23.85 ± 4.47</td>
<td></td>
<td></td>
</tr>
<tr>
<td>G2</td>
<td>Exacerbation</td>
<td>11.6–29</td>
<td>11.6–29</td>
<td>&lt;0.001</td>
<td>HS</td>
</tr>
<tr>
<td>Stable</td>
<td></td>
<td>4.1–7.4</td>
<td>4.1–7.4</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

G1 = obese COPD, G2 = non-obese COPD. HS = highly significant

There was a statistically highly significant difference in leptin concentration during acute exacerbation and during stability in obese COPD cases and a highly significant difference in leptin concentration during acute exacerbation and during stability in non-obese COPD cases.

Table 3 Statistical comparison in serum leptin (ng/ml) in obese and non-obese COPD cases during exacerbation and stability.
FEV1% predicted, FEV1/FVC and FEF25–75%. There were statistically significant differences between obese and non-obese COPD cases during exacerbation regarding FVC% predicted, FEV1% predicted and FEV1/FVC (Table 2).

Similar results were reported by [12] who studied 97 men aged 67–78 y with body mass index (BMI; in kg/m$^2$) ranging from 19.8 to 37.1. Body composition was evaluated by using dual-energy X-ray absorptiometry and fat distribution was evaluated by using waist and hip circumferences, waist-to-hip ratio, and sagittal abdominal diameter (SAD). Spirometry was done in all subjects and the distance walked by each subject during a 6-min walking test was evaluated as leg strength and found a significant negative correlation between adiposity, fat distribution indexes, forced vital capacity (FVC), and forced expiratory volume in 1 s (FEV$_1$).

This was also in agreement with work done by [13] who examined the combined effects of obesity and COPD on dyspnea and exercise tolerance by comparing dyspnea intensity ratings and ventilatory responses (breathing pattern, operating lung volumes and gas exchange) during symptom-limited incremental cycle exercise in well characterized groups of 18 obese (BMI = 35 ± 4 kg/m$^2$; mean ± SD) and 18 normal-weight (BMI = 22 ± 2 kg/m$^2$) patients with moderate to severe COPD. Groups were well matched for FEV1 (mean 49% predicted) and diffusing capacity (means > 70% predicted) but resting lung hyperinflation [end-expiratory lung volume (EELV)] was significantly reduced in association with increasing BMI ($p < 0.005$).

Regarding the serum leptin level (Tables 3–6), there was a statistically highly significant difference in serum leptin concentration between obese and non-obese COPD cases during acute exacerbation and stability.

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**Table 4** Statistical comparison of serum leptin (ng/ml) between obese and non-obese COPD cases during exacerbation and during stability.

<table>
<thead>
<tr>
<th>Group</th>
<th>Range</th>
<th>Mean ± SD</th>
<th>$P$ value</th>
<th>Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Exacerbation</td>
<td>G1 49–83</td>
<td>64.59 ± 9.8</td>
<td>&lt;0.001</td>
<td>HS</td>
</tr>
<tr>
<td></td>
<td>G2 11.6–29</td>
<td>18.14 ± 4.1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stability</td>
<td>G1 17–31</td>
<td>23.85 ± 4.47</td>
<td>&lt;0.001</td>
<td>HS</td>
</tr>
<tr>
<td></td>
<td>G2 4.1–7</td>
<td>5.63 ± 1.05</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

G1 = obese COPD, G2 = non-obese COPD, C1 = obese controls, C2 = non-obese control, HS = highly significant, S = significant, NS = non-significant.

There was a statistically highly significant difference in serum leptin concentration between obese and non-obese COPD cases during acute exacerbation and stability.

**Table 5** Serum leptin (ng/ml) in obese COPD cases during exacerbation and in stable state in comparison with obese control cases.

<table>
<thead>
<tr>
<th>State</th>
<th>Group</th>
<th>N</th>
<th>Range</th>
<th>MEAN ± SD</th>
<th>$P$ value</th>
<th>Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Exacerbation</td>
<td>G1 20</td>
<td>49–83</td>
<td>67.59 ± 9.8</td>
<td>&lt;0.001</td>
<td>HS</td>
<td></td>
</tr>
<tr>
<td></td>
<td>C1 10</td>
<td>16–25</td>
<td>20.9 ± 2.7</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stable</td>
<td>G1 20</td>
<td>17–31</td>
<td>23.8 ± 4.47</td>
<td>&lt;0.05</td>
<td>S</td>
<td></td>
</tr>
<tr>
<td></td>
<td>C1 10</td>
<td>16–25</td>
<td>20.9 ± 2.7</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

G1 = obese COPD, C1 = obese controls, HS = highly significant, S = significant.

There was a statistically highly significant difference in serum leptin concentration (ng/ml) in obese COPD cases during exacerbation and obese control cases and a statistically significant difference in serum leptin concentration in obese COPD cases during stability and obese control cases.

**Table 6** Serum leptin (ng/ml) in non-obese COPD cases during exacerbation and in stable state in comparison with non-obese control cases.

<table>
<thead>
<tr>
<th>State</th>
<th>Group</th>
<th>N</th>
<th>Range</th>
<th>MEAN ± SD</th>
<th>$P$ value</th>
<th>Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Exacerbation</td>
<td>G2 20</td>
<td>11.6–29</td>
<td>18.14 ± 4.15</td>
<td>&lt;0.001</td>
<td>HS</td>
<td></td>
</tr>
<tr>
<td></td>
<td>C2 10</td>
<td>4.7–8.12</td>
<td>6.53 ± 1.19</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stability</td>
<td>G2 20</td>
<td>4.1–7.4</td>
<td>5.63 ± 1.05</td>
<td>&lt;0.05</td>
<td>S</td>
<td></td>
</tr>
<tr>
<td></td>
<td>C2 10</td>
<td>4.7–8.12</td>
<td>6.53 ± 1.19</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

G1 = obese COPD, G2 = non-obese COPD, C1 = Obese controls, C2 = non-obese control, HS = highly significant, S = significant, NS = non-significant.

There was a statistically highly significant difference in serum leptin concentration between non-obese COPD cases during exacerbation and non-obese control cases and also a statistically significant difference between non-obese COPD cases during stability and non-obese control cases.
During acute exacerbation (mean ± SD = 64.59 ± 9.8 ng/ml) and during stability (mean ± SD = 23.85 ± 4.47 ng/ml) in obese COPD cases and a high significant difference in leptin concentration during acute exacerbation (mean ± SD = 18.14 ± 4.1 ng/ml) and during stability (mean ± SD = 5.63 ± 1.05 ng/ml) in non-obese COPD cases. Both comparisons indicated that the level of serum leptin hormone (ng/ml) elevated during COPD exacerbation than during stability. There was a statistically high significant difference in serum leptin concentration between obese and non-obese COPD cases during acute exacerbation and stability. There was a statistically high significant difference in serum leptin concentration (ng/ml) in obese COPD cases during exacerbation and obese control cases and a statistically significant difference in serum leptin concentration in obese COPD cases during stability and obese control cases. There was a statistically high significant difference in serum leptin concentration between non-obese COPD cases during exacerbation and non-obese control cases and also a statistically significant difference between non-obese COPD cases during stability and non-obese control cases.

This finding was in agreement with work done by Calikoglu et al. [14] that reported malnourished patients experiencing exacerbation, exhibit significantly higher leptin levels, compared to normal-weight stable COPD patients, an observation not replicated when compared to malnourished stable COPD patients.

Also in agreement with a study done by Kythreotis et al. [15] and measures plasma leptin and insulin-like growth factor I levels during acute exacerbations of chronic obstructive pulmonary disease and indicated that leptin values were significantly elevated in COPD patients during acute exacerbation versus controls and leptin concentrations gradually decreased throughout the exacerbation, but, remain significantly elevated during hospitalization. The normal feedback regulation of leptin preserved on day 7 of the exacerbation, although dissociation has been reported on day 1, is possibly due to a temporary dysfunction related to the event.

Similar results were also obtained by Creutzberg et al. [16] who indicated that the disturbances in leptin metabolism were related to energy imbalance during acute exacerbations of chronic obstructive pulmonary disease and indicated that there was transient elevation in serum leptin concentration (ng/ml) during acute exacerbation.

On the other hand, these results were not matched with the results of the work done by Yang et al. [17] who measured the role of serum leptin hormone and tumor necrosis factor-alpha in malnutrition of male chronic obstructive pulmonary disease patients and indicated that there was a statistically non-significant difference in serum leptin levels (ng/ml) between COPD patients without malnutrition during acute exacerbation, COPD patients without malnutrition during stable state and controls.

All these findings demonstrated that serum leptin hormone increased in obese subjects than non-obese subjects as it is a hormone secreted from adipose tissue and elevated in obese and non-obese during exacerbation than in obese and non-obese controls and also elevated in obese COPD cases during stability than in obese controls as it is an inflammatory marker increased during systemic inflammation; but it decreases in non-obese COPD cases than in non-obese controls.

This was in agreement with work done by Takabatake et al. [20] who investigated serum leptin levels, along with circulating tumor necrosis factor (TNF) and soluble TNF receptor (sTNF-R55 and -R75) levels, in 31 patients with COPD and 15 age-matched healthy controls. The body mass index (BMI) and percent body fat (%fat) were significantly lower in the COPD patients than in the healthy controls and serum leptin levels were significantly lower in the COPD patients than in the healthy controls.

A study done by Figen et al. [21] who measured plasma leptin concentrations in thirty-two patients with COPD (all males) with stable chronic obstructive pulmonary disease indicated that patients with COPD had significantly lower leptin, albumin and CKr levels than did the control subjects. COPD patients also had decreased arterial PO2, and increased arterial PCO2 values. The levels of FEV1 (% predicted) and FVC (% predicted) were significantly lower in COPD patients than in healthy controls. Serum TNF-α level in COPD patients was significantly higher than those in the healthy controls.

In the present study the correlations between serum leptin concentration (ng/ml) and pulmonary function tests in obese

<table>
<thead>
<tr>
<th>Group</th>
<th>R</th>
<th>p value Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>C1</td>
<td>0.945</td>
<td>&lt;0.001 HS</td>
</tr>
<tr>
<td>C2</td>
<td>0.970</td>
<td>&lt;0.001 HS</td>
</tr>
<tr>
<td>G1 Exacerbation</td>
<td>0.812</td>
<td>&lt;0.001 HS</td>
</tr>
<tr>
<td>G1 Stable</td>
<td>0.774</td>
<td>&lt;0.001 HS</td>
</tr>
<tr>
<td>G2 Exacerbation</td>
<td>0.876</td>
<td>&lt;0.001 HS</td>
</tr>
<tr>
<td>G2 Stable</td>
<td>0.799</td>
<td>&lt;0.001 HS</td>
</tr>
</tbody>
</table>

G1 = obese COPD, G2 = non-obese COPD, C1 = obese controls, C2 = non-obese control, HS = highly significant.
control subjects were done as shown in Table 10 and indicated that there was a statistically non-significant positive correlation between BMI (kg/m²) and FEV1/FVC-L (r = 0.245 and p > 0.05), FEV25–75% predicted (r = 0.259 and p > 0.05) and significant negative correlation with FEV1% predicted (r = −0.664 and p < 0.05) and highly significant negative correlation with FVC% predicted (r = 0.830 and p < 0.01).

A correlation between BMI (kg/m²) and pulmonary function tests in non-obese controls was done and indicated in Table 11 and showed that there was a statistically non-significant negative correlation between BMI (kg/m²) and FVC% predicted (r = −0.128 and p > 0.05) and FEF25–75% predicted (r = −0.391 and p > 0.05), significant negative correlation with FEV1/FVC L (r = −0.714 and p < 0.05) and high significant negative correlation with FEV1% predicted (r = −0.916 and p < 0.001).

These findings were in agreement with study done by Santana et al. [12] who measured the relation between body composition, fat distribution, and lung function in elderly men in 97 men aged 67–78 years with body mass indexes (BMIs; in kg/m²) ranging from 19.8 to 37.1 and body composition was evaluated by using dual-energy X-ray absorptiometry and fat distribution was evaluated by using waist and hip circumferences, waist-to-hip ratio, and sagittal abdominal diameter (SAD). Spirometry was done in all subjects and the distance walked by each subject during a 6-min walking test was evaluated as leg strength and indicated that there was a significant negative correlation between adiposity, fat distribution indexes, forced vital capacity (FVC), and forced expiratory volume in 1 s (FEV1).

These results also were in agreement with work by Lazarus et al. [22] who measured the effects of obesity and fat distribution on ventilatory function showed that the ratio of abdominal circumference to hip breadth and sub-scapular skin-fold thickness was negatively associated with FVC% predicted.

Table 8 Correlation between change in serum leptin (ng/ml) and change in P.F.T from acute exacerbation to stability in obese COPD cases.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>r</th>
<th>p value</th>
<th>Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>FVC% predicted</td>
<td>0.191</td>
<td>&gt;0.05</td>
<td>NS</td>
</tr>
<tr>
<td>FEV1% predicted</td>
<td>−0.523</td>
<td>&gt;0.05</td>
<td>NS</td>
</tr>
<tr>
<td>FEV1/FVC</td>
<td>−0.541</td>
<td>&gt;0.05</td>
<td>NS</td>
</tr>
<tr>
<td>FEF25–75%predicted</td>
<td>−0.135</td>
<td>&gt;0.05</td>
<td>NS</td>
</tr>
</tbody>
</table>

NS = non-significant.

In the present study, we measured the correlation between the change of serum leptin hormone concentration (which is serum leptin in ng/ml during exacerbation – serum leptin in ng/ml during stable state) and changes in the pulmonary function tests (which is pulmonary function value during exacerbation – pulmonary function value during stable state) in obese COPD and non-obese COPD patients.

In obese COPD cases as shown in Table 8 a significant negative correlation was found between change in serum leptin (ng/ml) and change in pulmonary function parameters [change in FEV1% predicted (r = −0.523 and p < 0.05) and change in FEV1/FVC L (r = −0.541 and p < 0.05)] and non-significant negative correlation [change in FEF25–75% predicted (r = −0.135 and p > 0.05)] and non-significant positive correlation [change in FVC% predicted (r = 0.191 and p > 0.05)].

In non-obese COPD cases as shown in Table 9 there was no correlation between change in serum leptin (ng/ml) and change in pulmonary functions parameters [FVC% predicted (r = −0.176 and p > 0.05), FEV1% predicted (r = −0.009 and p > 0.05), FEF25–75% predicted (r = −0.129 and p > 0.05), FEV1/FVC L (r = 0.057 and p > 0.05)].

Little or no researches were found that study the correlation between change in leptin concentration and change in PFT.

In this study, correlation between serum leptin (ng/ml) and body mass index (kg/m²) in the different studied groups was done and shown in Table 7 and demonstrated that there was a highly significant positive correlation between leptin (ng/ml) and BMI (kg/m²) of different groups (P < 0.01) and in obese control (r = 0.945), non-obese control (r = 0.970), obese COPD in exacerbation (r = 0.812), obese COPD in stable state (r = 0.774), non-obese COPD exacerbation (r = 0.876) and non-obese COPD in stable state (r = 0.799).

The results in Table 7 demonstrated that there was direct proportion between BMI (kg/m²) and leptin levels (ng/ml) and that leptin increased by increasing BMI and vice versa, and it was also increased during exacerbation than during the stable state but still higher in COPD during stability than in control obese.

This indicates that leptin hormone plays a role in systemic and local inflammatory process in COPD during acute exacerbation and in stable state.

These results were in agreement with a study done by Cooper et al. [23] who measured serum leptin levels in obese males during over and underfeeding in eight obese (BMI 30–40 kg/m²), but otherwise healthy, males aged 19–42 who participated in this study. Subjects were normo-lipemic (cholesterol < 2 g/l, triglycerides < 1.55 g/l), and had normal thyroid function as determined by thyroid-stimulating hormone levels (0.4–3.6 mU/l). Due to the large volume of blood

Table 10 Correlation between BMI (kg/m²) and pulmonary function tests in obese controls.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>r</th>
<th>p value</th>
<th>SIG</th>
</tr>
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<tbody>
<tr>
<td>FVC% predicted</td>
<td>−0.830</td>
<td>&lt;0.001</td>
<td>HS</td>
</tr>
<tr>
<td>FEV1% predicted</td>
<td>−0.664</td>
<td>&lt;0.05</td>
<td>S</td>
</tr>
<tr>
<td>FEV1/FVC</td>
<td>0.245</td>
<td>&gt;0.05</td>
<td>NS</td>
</tr>
<tr>
<td>FEF25–75%predicted</td>
<td>0.295</td>
<td>&gt;0.05</td>
<td>NS</td>
</tr>
</tbody>
</table>

In non-obese COPD cases as shown in Table 9 there was no correlation between change in serum leptin (ng/ml) and change in pulmonary functions parameters [FVC% predicted (r = −0.176 and p > 0.05), FEV1% predicted (r = −0.009 and p > 0.05), FEF25–75% predicted (r = −0.129 and p > 0.05), FEV1/FVC L (r = 0.057 and p > 0.05)].
being drawn, inclusion criteria included normal iron stores as determined by serum iron (0.5–1.6 mg/l) and serum ferritin (15–200 μg/l), and normal total iron binding capacity (2.5–4.0 mg/l) in conjunction with normal hemoglobin (135–175 g/l). Exclusion criteria included a history of metabolic disease, use of prescription medication or over-the-counter substances such as melatonin. Subjects who exercised regularly or did not eat three meals a day (including breakfast or an early morning meal) were also excluded. The study was approved by the institutional review board at the University of Chicago and all subjects provided written informed consent. The study was performed at the Clinical Research Center at the University of Chicago Hospital; and indicated that during the initial eucaloric or baseline period, the serum leptin level averaged 6.0 ± 1.1 ng/ml for the underfeeding treatment group and 15.5 ± 2.5 ng/ml for the overfeeding treatment group. As expected, these leptin levels correlated with body weight (r = 0.91, P = 0.01 and r = 0.96, P = 0.01), percent body fat (r = 0.84, P = 0.01 and r = 0.79, P = 0.02), and trended with BMI (r = 0.62, P = 0.08 and r = 0.69, P = 0.06) and fat mass (r = 0.57, P = 0.18 and r = 0.50, P = 0.16), for treatment groups, respectively.

These results were also in agreement with work done by Lazzer et al. [24] who investigated leptin changes in 26 obese adolescents (12 boys and 14 girls) during and after a 9-month weight-reduction program in a specialized institution with lifestyle education, moderate energy restriction and regular three meals a day (including breakfast or an early morning meal). After 9 months, the adolescents had lost 19% body weight, reduced by 33% while the levels of circulating leptin declined by 52%. Leptin levels strongly and persistently correlated with body mass index (BMI) during the study and, compared to admission, Log leptin, adiponectin and L/A ratio were significantly associated with variables of systemic inflammation, after proper adjustments, both on admission and in stable condition.

Leptin and Leptin-receptor expressing cells in normal subjects, smokers without COPD and COPD subjects were investigated by Bruno et al. [27] concluded that leptin expression increased in bronchial mucosa of chronic obstructive pulmonary disease patients, associated with airway inflammation and airflow obstruction.

Conclusion

Serum leptin hormone level (ng/ml) was significantly higher in COPD cases than in controls, significantly higher in obese than non-obese cases during exacerbation and in stable state and significantly higher in COPD cases during exacerbation than during stable state which indicates that leptin plays a role in systemic inflammatory process. Serum leptin hormone level (ng/ml) correlated positively with BMI (kg/m²) and a negative correlation was found between the change in serum leptin (ng/ml) and the change in some pulmonary function parameters (FEV1% predicted and FEV1/FVC).

This work was primarily carried out at Benha University Hospitals, Benha, Egypt.

Disclosure of financial support

Nil (none to be declared).

Conflict of interest

No conflicts of interest to be declared.

References


Table 11 Correlation between BMI (kg/m²) and pulmonary function tests in non-obese controls.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>R</th>
<th>P value</th>
<th>SIG</th>
</tr>
</thead>
<tbody>
<tr>
<td>FVC% predicted</td>
<td>−0.128</td>
<td>&gt;0.05</td>
<td>NS</td>
</tr>
<tr>
<td>FEV1% predicted</td>
<td>−0.916</td>
<td>&lt;0.001</td>
<td>HS</td>
</tr>
<tr>
<td>FEV1/FVC</td>
<td>−0.714</td>
<td>&lt;0.05</td>
<td>S</td>
</tr>
<tr>
<td>FEF25–75% predicted</td>
<td>−0.391</td>
<td>&gt;0.05</td>
<td>NS</td>
</tr>
</tbody>
</table>

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