

Assessment of Adiponectin as a Marker for Severity of Pulmonary Tuberculosis

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Abstract

Background: To evaluate the serum levels of adiponectin in patients with both active and old pulmonary Tuberculosis (TB) and their possible relation with the severity of the disease, forty patients of both sexes suffering from pulmonary TB (20 cases active and 20 cases old) were matched with 20 healthy control volunteers in this study from February 2014 to June 2014. Body mass index (BMI) and serum levels of adiponectin were measured in all subjects.

Results: Both BMI and serum levels of adiponectin were significantly different between active TB patients and control. Comparing old TB patients with controls also have the same results. No correlation between BMI and serum adiponectin level in old TB patients was found, while adiponectin levels in active TB patients show a significant negative correlation.

Conclusion: Increased adiponectin in serum of TB patients may be a promising marker for severity of the disease independent of BMI.

Key words: adiponectin pulmonary tuberculosis

Introduction:

Pulmonary tuberculosis (TB) occurs due to infection of the lungs with *Mycobacterium tuberculosis* (MTB). It is a major health problem throughout the world and remains to be the single most infectious disease causing high mortality in humans. Cell mediated immunity can control the infection in most of the cases. It is still a major health problem, and although the disease seems to be limited in the developed countries, it still remains a major problem in developing countries. It is a major infectious cause of death around the world, with most of the 1.5 million deaths per year attributable to the disease occurring in developing countries. Negative energy balance and wasting in chronic inflammation has been recognized as a prominent feature of TB and one of the major obstacles to manage the patients.⁽¹⁾

The early diagnosis and adequate treatment of infected patients with pulmonary TB is considered necessary to reduce transmission of *Mycobacterium TB* and to achieve the goal of disease elimination and diagnosis, also, treatment of individuals with latent TB infection, who are at high risk to develop active infection, is crucial for disease control. There is an urgent need for rapid and accurate diagnostic methods in order to achieve higher sensitivity and specificity compared to traditional methods i.e., microscopic examination and culture of sputum.⁽¹⁾

Adiponectin (APN) is a secretory protein synthesized by adipocytes and plays a potential role in regulating the inflammatory response by many of autocrine or paracrine. Adipokines have both pro-inflammatory and anti-inflammatory properties. Adiponectin is a protein produced exclusively in adipose tissue that appears to play a critical role in mediating physiological effects such as insulin sensitivity, inflammatory response, and cell proliferation. Adiponectin levels are inversely associated with obesity and are thought to decrease in individuals with increased adiposity through down-regulation of adiponectin.^(2,3)

Adiponectin has an endocrine effect (as a circulating hormone acting on blood vessels, liver and skeletal muscles) and an auto/paracrine effect (differentiation of preadipocytes to adipocytes), adiponectin also with all of the known receptors for adiponectin such as AdipoR1, AdipoR2, T-cadherin and calreticulin are expressed on multiple cell types in the lung and APN has been isolated from Bronchoalveolar lavage fluids (BAL).⁽⁴⁾

Patients with pulmonary TB disease often suffer from weight loss. Body mass index is known to be inversely correlated with adiponectin.⁽⁵⁾ Thus, increased adiponectin may be a promising marker for severity of the disease independent of the BMI.

Adipokines may play a role in the immune response to *M. tuberculosis*, and TB may impair the expression of inflammatory adipokines, such as leptin and adiponectin. ⁽⁶⁾

Aim of the work:

The objective of this study is to evaluate the serum levels of adiponectin in patients with both active and old pulmonary TB and their possible relation with the severity of the disease in order to be used as a diagnostic marker.

Subjects & Methods:

Forty patients of both sexes 28 male & 12 female, their age ranged from 46 to 65 years suffering from pulmonary TB and 20 healthy control volunteers (who were matched as regard age & sex) were included in this study [from February 2014 to June 2014].

The patients were divided into two groups:

The first group included 20 patients with active TB; (with typical symptoms as: cough lasting >3 weeks, weight loss, night sweats, fever and abnormal chest x-ray)

The second group included 20 patients with old TB; (Patient usually don't feel sick with normal X ray).

Exclusion criteria:

Patients with other chest infections, hypertension and diabetes were excluded

Body mass index was calculated as weight (kg) divided by the square of the height (m²). ⁽⁷⁾

All patients and healthy control subjects gave their written, informed consent to participate in the study. Data of these three groups were compared and analyzed.

Blood sampling and analysis:

Venous blood samples were collected after 12 hours fasting from each participant.

Serum levels of adiponectin were measured in all subjects using AviBion Human Adiponectin ELISA kits. ⁽⁸⁾

Statistical analysis:

Results were expressed as mean \pm SD with a 95% confidence interval (95% CI). The mean values of the groups were compared using Student's unpaired t-test. Statistical significance was set at $P < 0.05$. Correlation between variables was evaluated using Pearson's correlation coefficient and regression analysis.

Results:

As seen in table 1, comparison between active TB patients and control group reveals that; both BMI and serum levels of adiponectin are significantly differ between the two groups (p-value; <0.001 & <0.0001 respectively).

The same results were observed when comparing old TB patients and controls; however, the difference was less statistically significant. BMI was significantly less in old TB patients than controls ($p < 0.05$). Serum adiponectin levels were significantly higher in old TB group than control group (9.72 ± 3.13 $\mu\text{g/ml}$, versus 7.17 ± 2.92 $\mu\text{g/ml}$; $P < 0.05$) (table 2).

No correlation between BMI and serum adiponectin level in old TB patients. While adiponectin levels in active TB patients show a significant negative correlation ($r = -0.47$ & $p < 0.05$) with their BMI (table 3).

Discussion:

In the present study, we showed that serum adiponectin levels in patients with active pulmonary tuberculosis were very significantly higher than in healthy subjects, while it is only significantly higher in old TB patients in comparison to healthy subjects. In active TB patients the serum adiponectin levels were inversely correlated with BMI.

Our data provide the basis for speculating that the elevated serum adiponectin level was associated not only with decreased BMI but also with active inflammation due to pulmonary tuberculous infection.

In obese subjects, the adiponectin level is decreased and inversely correlated with both body weight and fat mass. ⁽⁹⁾ In contrast, it has been reported that plasma adiponectin levels are elevated in underweight subjects such as patients with anorexia nervosa. ⁽¹⁰⁾ and cachexia ⁽¹¹⁾

The results of this study were in agreement with the results of **Keicho et al.** ⁽¹⁾ who studied the circulating levels of adiponectin, leptin, fetuin-a and retinol-binding protein in patients with TB and concluded that increased adiponectin, may be a promising marker for severity of the tuberculous disease independent of BMI.

Our results were consistent with those of **Tomoda et al.** ⁽¹²⁾ who reported that plasma levels of adiponectin were elevated in

patients with COPD and correlated with body weight loss and lung hyperinflation, and also the results of this research were in accordance with those of **Cohen *et al.*** ⁽¹³⁾ who studied serum adiponectin in relation to BMI and other correlates in black and white women and found that adiponectin has consistently been found to be negatively correlated with obesity in white and Asian populations.

Our results were explained by **Perna *et al.*** ⁽⁶⁾ she measured plasma leptin, soluble leptin receptor and adiponectin, weight and body mass index in nineteen patients with diagnosed pulmonary TB before and six months after treatment and suggested that impaired immune response in tuberculosis patients seems to be related to weight loss that coexists with an immunoendocrine imbalance suggesting that wasting is well-recognized prominent feature of tuberculosis (TB), which may not be reversed even after six months of treatment, concluding that active TB infection may affect the expression of leptin, in addition to the wasting that may occur in these patients, and that effective TB treatment increases circulating leptin levels, probably restoring normal immunological competence.

Conclusion:

In conclusion, serum adiponectin levels are elevated in patients with pulmonary TB and inversely correlated with BMI. Although adiponectin is known to have anti-inflammatory effects on obesity-associated inflammation, the inappropriately secreted adiponectin in pulmonary TB might have pro-inflammatory effects as in other chronic inflammatory diseases that are not associated with obesity and play a role in the pathophysiology of these diseases. Increased adiponectin in serum of TB patients may be a promising marker for severity of the disease independent of BMI.

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Table (1): Demographic and biochemical parameters in active TB patients and controls.

Parameters	Active TB patients (n = 20)	Controls (n = 20)
Ages (years) Mean ± SD p-values	54.2 ± 11.9	54.4 ± 5.2 NS
Weight (kg) Mean ± SD p-values	56.3 ± 3.4	72 ± 3.5 <0.0001***
BMI (kg/m ²) Mean ± SD p-values	21.1 ± 1.33	25.6 ± 2.91 0.001**
Serum adiponectin (µg/mL) Mean ± SD p-values	12.50 ± 3.08	7.17 ± 2.92 0.0001***

NS: is considered non-significant.

P<0.001 **: is considered highly significant.

P<0.0001***: is considered very highly significant.

Table (2): Demographic and biochemical parameters in old TB patients and control.

Parameters	Old TB patients (n = 20)	Controls (n = 20)
Ages (years) Mean ± SD P-values	55.1 ± 12.1	54.4 ± 5.2 NS
Weight Mean ± SD p-values	68.3 ± 3.8	72 ± 3.5 < 0.05*
BMI (kg/m ²) Mean ± SD p -values	22.8 ± 2.1	25.6 ± 2.91 < 0.05*
Serum Adiponectin (µg/mL) Mean ± SD p -values	9.72 ± 3.13	7.17 ± 2.92 <0.05*

NS: is considered non significant.

p < 0.05 *: is considered significant

Table (3): Correlations of BMI and serum adiponectin levels in active and old TB patients.

	Adiponectin of active TB	Adiponectin of old TB
BMI	r = - 0.47	r=- 0.39
	p< 0.05	p = NS

NS: is considered non significant.

p < 0.05 *: is considered significant