Original Article

Serum Concentration of IL-6 Level in Patients with Pulmonary Tuberculosis

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Abstract:

Background and Aim: Mycobacterium tuberculosis is the causative agent of tuberculosis (TB). Bangladesh is one of the nations with a high TB burden, and the number of cases and fatalities from the disease are rising constantly. Analyzing the serum levels of IL-6 of TB patients may be helpful to track the development of infection and determine the likelihood that the disease will progress to an active phase. The goal of the current study was to assess the serum level of IL-6 in tuberculosis patients.

Methods: This case control study was conducted at the Department of Biochemistry, National Medical College and Hospital, Dhaka during November 2017 to November 2020. This study contained two groups, one with 50 controls who had no active infections and another with 50 patients who had been diagnosed with active pulmonary tuberculosis. Serum levels of IL-6 were assessed prior to, during, and after anti-tubercular therapy in patients with active pulmonary TB and also in control individuals. Chemiluminescence assay was used to evaluate the serum levels of IL-6 in all subjects.

Results: In contrast to patients undergoing therapy, patients completing treatment, and control subjects, patients with active TB had mean serum levels of IL-6 which were significantly higher ($p < 0.01$). On top of that, it was found that IL-6 levels in TB patients both during and after therapy were significantly higher than in controls ($p < 0.05$).

Conclusion: A strong biomarker of tuberculosis may be IL-6, which appears to be a predominant cytokine produced during mycobacterial infection and which also plays a part in clinical symptoms and pathological outcomes of this disease.

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Introduction

As a single infectious agent, *Mycobacterium tuberculosis* causes the greatest number of fatalities worldwide. Bangladesh has an estimated 221 cases of TB per 100,000 people, which accounts for 3.6% of all TB cases worldwide. Pulmonary TB accounts for over 80% of all TB cases in Bangladesh. According to the Global TB Report 2020, multi –drug resistant TB (MDR-TB) is identified in 0.7% of new cases and 11% of cases that have already been treated with an incidence rate of 2.0 per 100,000 people in Bangladesh.[1]

Neutrophils, macrophages, natural killer cells, and dendritic cells are the immune effector cells that play key roles in the mycobacterium tuberculosis-infected cells and act as the main reservoir of the organism. A number of inflammatory cytokines released by host immune cells which are involved in modulating the interaction of infected macrophages with T lymphocytes, can also play significant roles in the initiation and modulation of the immune response at the various stages of the disease development.[2,3] Although it has long been recognized that IL-6 interferes with the gamma interferon (IFN-γ) generated signal, the importance of IL-6 formation in tuberculosis is still not entirely understood. Although interleukin-6 (IL-6) is regarded as a type 2 cytokine, current research indicates that IL-6 is necessary for the activation of a protective T-cell response against *M. tuberculosis*.[4,5]

The immunological signaling mediated by inflammatory cytokines released during TB infections is right now only partially understood. At different phases of disease progression, it is essential to maintain the amounts of these particular cytokines and to create an appropriate balance between pro- and anti-inflammatory cytokine signaling.

The goal of this study was to evaluate the contribution of IL-6 in active pulmonary tuberculosis and compare those levels to those in TB patients before, during, and after therapy as well as in healthy individuals.

Methodology

In this case-control study, 50 healthy human volunteers and 50 patients with active pulmonary tuberculosis served as the subjects. Samples were taken from all patients both before and after treatment, as well as from controls, and then serum IL-6 levels were measured.

Patients attending the National Medical College Hospital's outpatient department (OPD) who were of either gender and older than 18 but under 60 were included in the study as subjects. Patients who refused to participate in the study or were uncooperative were not included in it. Prior to the study, informed consent and patient information were obtained with the approval of the National Medical College Hospital's institutional ethics committee.

Simple vacutainers were used to collect blood samples, which were subsequently centrifuged to extract the serum. Then, using an automated Maglumi 1000 Chemiluminescence Immunoassay System (CLIA) instrument, serum IL-6 levels were determined. The statistical analysis was performed using SPSS version 27.0.

Results

Demographic characteristics of study subjects (Table-1) showed no significant differences between active pulmonary TB patients with healthy controls in terms of age and sex. However, active pulmonary TB patients had significantly lower BMI than healthy controls.

Table I: Demographic characteristics of study subjects (n=100)			
	Groups		
	Active PTB (n=50)	Controls (n=50)	*p* value
Age (in years)			
20-29	5	4	
30-39	25	21	
40-49	12	14	
50-59	8	11	
mean ± SD	37.29 ± 10.32	40.31 ± 9.63	0.133[a]
Gender			0.057b
Male, n (%)	31 (62%)	24 (48%)	
Female, n (%)	19 (38%)	26 (52%)	
BMI (in kg/m²)	19.36±2.35	21.45±1.63	<0.001[a]

In this study, IL-6 levels were measured in all study subjects and mean IL-6 levels were significantly higher in active pulmonary TB patients than healthy controls (Table II).

Table II: IL-6 level of study subjects (n=100)			
	Groups		
	Active PTB (n=50)	Controls (n=50)	*p* value
IL-6 (pg/ml)	472.35±14.86	49.67±4.39	<0.001

We also measured IL-6 levels in patients with pulmonary TB six months after treatment and compared the results with the same patients before undergoing therapy and found significant decrease in IL-6 levels.

Table III: IL-6 level of PTB patients before and 6 months after therapy (n=50)			
	PTB patients		
	Before therapy	After therapy	*p* value
IL-6 (pg/ml)	472.35±14.86	154.69±28.79	<0.001

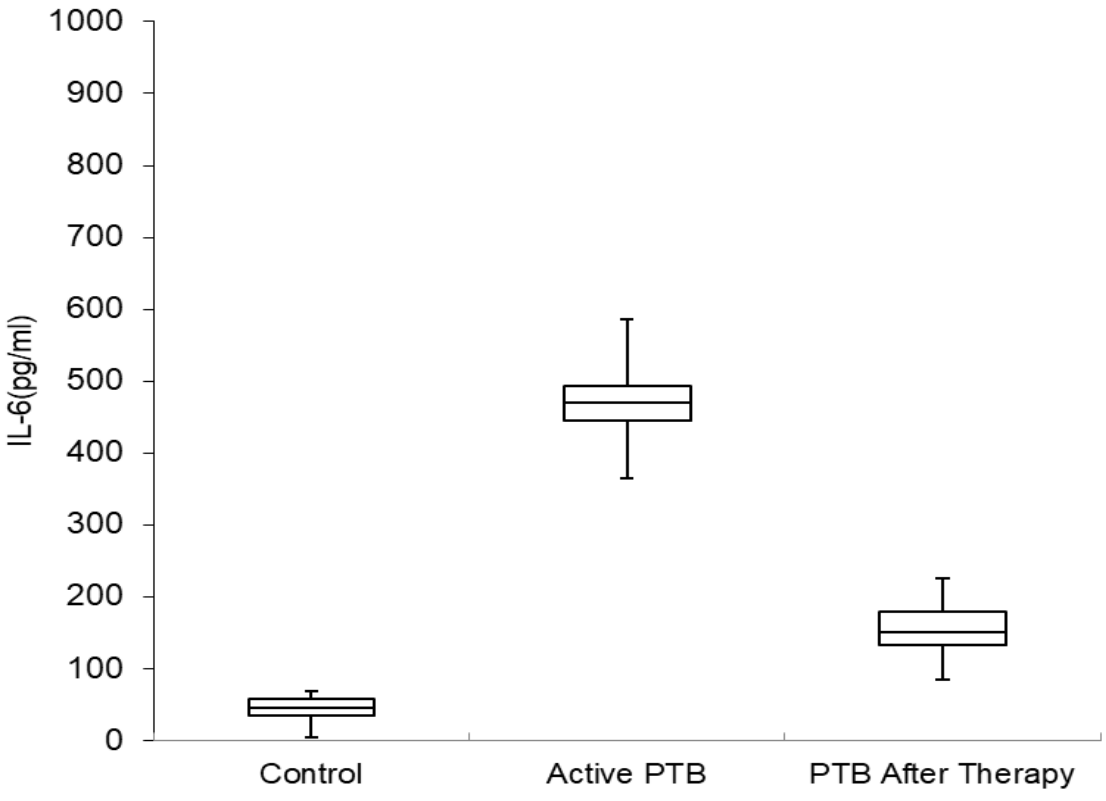

Figure 1: Box plots showing comparison among healthy controls, active PTB patients and PTB patients after therapy.

Discussion

In the course of the progression of TB, cytokines play a pivotal role. Even though it was previously established that IL-6 stimulates mycobacteria to grow intracellularly in monocytes, it was additionally discovered that IL-6 appears to be essential in maintaining resistance to TB.

In our study, active PTB patients had a mean age of 37.29 ±10.32 years, whereas healthy controls had a mean age of 40.31 ± 9.63 years. There were no significant differences regarding ages between these two groups. In a similar study, Chowdhury et al. also found no significant differences in terms of ages between active PTB patients with healthy subjects.[6]

In this study, the genders of the two groups were also matched. While the group of active PTB patients had 31 (62%) males and 19 (38%) females, the group of healthy controls comprised 24 (48%) males and 26 (52%) females respectively. In a related study, Dalvi et al. used gender-matched groups as well.[7]

Active PTB patients in our study had a BMI that was significantly lower (19.36±2.35 kg/m^2) than that of healthy controls (21.45±1.63 kg/m^2) and the findings were in accordance with the findings by Chowdhury *et al.*[6]

In comparison to healthy controls (49.67±4.39 pg/ml), individuals with active PTB had significantly ($p < 0.001$) higher mean serum levels of IL-6 (472.35±14.86 pg/ml). When compared to their prior active PTB stage, the mean serum IL-6 levels in the same patient group significantly ($p < 0.001$) decreased (154.69±28.79 pg/ml) after six months of therapy.

In a study by Verbon et al. discovered that the mean IL-6 serum level was considerably greater in patients with active TB than it was during therapy, after treatment, in contacts, and in control subjects ($p < 0.001$).[8]

According to the research by Chowdhury et al., active PTB patients had considerably higher ($p < 0.001$) serum IL-6 levels than healthy individuals, and these levels gradually decreased after starting anti-tubercular therapy.[6]

Conclusion

The study found highly elevated IL-6 in active PTB patients compared to healthy individuals also a reduction in the serum levels of IL-6 after anti-tubercular therapy. These findings indicate, anti TB therapy may have a significant impact on the immune system's ability to protect the host from Mycobacterium tuberculosis infection. As a result, the serum IL-6 level may be a useful marker for assessing the effectiveness of treatment in patients.

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