

Study of correlation of serum protein levels with tuberculosis

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Abstract

Background: It is well established that changes in levels of serum proteins occur in response to both acute and chronic infections. This is especially true of immunoglobulins and acute phase proteins. Serum protein levels change in an infection like tuberculosis, however, its role in diagnosis and prognosis is not clear. In the present study an effort has been made to explore the correlation of serum proteins levels with the severity of tuberculosis. **Material and Methods:** The study subjects included 100 patients above 12 years of age without HIV co-infection of newly diagnosed cases of pulmonary and extrapulmonary tuberculosis diagnosed. Serum total protein was measured by biuret method, whereas serum albumin was measured by dye-binding technique and the globulin fraction was determined by subtracting the albumin from the total protein. **Results:** Out of the 100 cases of tuberculosis collected from our hospital, 55 patients were PTB, and 45 were of extra-pulmonary tuberculosis. Total protein levels were found to be decreased in 23% of cases. While it was normal in mild cases, 20% of patients with moderate lung involvement and 44% with severe involvement had decreased protein level. Hypoalbuminaemia was found more frequently, the levels decreasing as the severity of the disease increased. Thus the decrease in total protein and albumin levels was proportionate to the extent of the disease. **Discussion:** Significant changes in the levels of several serum proteins have been observed to be associated with tuberculosis. Though they may not be of diagnostic value, they do, however, indicate the response of the body to the infection and recovery after treatment.

Keywords: Tuberculosis, serum protein, hypoalbuminaemia, prognosis.

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INTRODUCTION

Despite the advances and the fact that nearly all cases can be cured, TB remains one of the world's biggest threats. In 2014, TB killed 1.5 million people including non-HIV infected people. The toll comprised 890000 men, 480000 women and 140 000 children¹. Various biochemical changes act as marker for the diagnosis, prognosis and

response to therapy. In pulmonary tuberculosis biochemical abnormalities such as, low serum albumin level and increased serum bilirubin and alkaline phosphatase are common and they are valuable aids to diagnosis². It is well established that changes in levels of serum proteins occur in response to both acute and chronic infections. This is especially true of immunoglobulins and acute phase proteins. In an infection like tuberculosis, such changes in serum protein levels are expected. In a survey of the literature, a number of reports on inconsistent changes in the levels of various serum proteins in pulmonary tuberculosis were found³⁻⁷. However, it is not clear if the changes in serum protein concentrations have any aetiological significance or prognostic value. In the present study an effort has been made to explore the correlation of serum proteins levels with the severity of tuberculosis.

MATERIAL AND METHODS

The study subjects included 100 patients of newly diagnosed active cases (defined as up to two weeks after the start of antituberculous treatment) of pulmonary and extra-pulmonary tuberculosis diagnosed between October 2006 to October 2008 in the Medicine and Chest TB department of Mahatma Gandhi Mission’s Medical College, New Mumbai. The inclusion criteria were patients first time diagnosis, no current or previous anti-tuberculous drug treatment, and not to be suffering from any other chronic disease. The exclusion criteria included past history of pulmonary TB, currently on antituberculous drug or any other drugs which affected bone marrow or peripheral blood, and known at the time of study to have a chronic disease which will adversely affect the body systems including the bone marrow and the peripheral blood. Depending on the site/s involved, TB was classified as pulmonary or extra-pulmonary as per WHO guidelines [8] and disseminated if the patient had miliary TB or involvement of two or more organ systems. Detailed clinical history and physical examination was done of all the enrolled patients. Pulmonary TB patients were diagnosed on the basis of

positive sputum smears for acid fast bacilli (AFB), and /or radiographic reports, skin tests and positive culture reports. For extra pulmonary TB, detection of AFB in the samples, radio-imaging reports, skin tests and positive culture reports were taken into account. For estimation of serum proteins, about 3-4 ml peripheral venous blood was drawn aseptically with the help of sterile syringe in a plain bulb. Serum total protein was measured by biuret method, whereas serum albumin was measured by dye-binding technique and the globulin fraction was determined by subtracting the albumin from the total protein.

RESULTS

A total of 100 patients newly diagnosed as pulmonary and extra pulmonary TB were enrolled in this present study. Of the 100 patients, 63 (63%) were under 40 years of age (range 12 to 39), whereas, 37 (37%) were more or equal to 40 years of age (range 40 to 78). Mean age of young adults (below 40 years) was 32.71±3.7 years and elderly (more than or of 40 years) was 67.57±1.03 respectively.

Table 1: Correlation of Serum Protein Levels with Tuberculosis

		Decreased Total protein	Decreased Serum Albumin	Increased Serum Globulin	A/G (<1)
Pulmonary TB	MILD	0	2	1	2
	MOD	2	15	8	16
	SEV	8	16	8	15
Pleural effusion		3	12	3	4
Miliary / Disseminated		5	9	1	7
Abdominal		1	1	1	1
Lymph node		0	0	0	0

Decreased albumin levels were seen in 33 out of 43 patients of pulmonary TB and 25 out of 41 patients of extra-pulmonary TB. It was seen in 2 out of 5 patients with mild, 15 out of 19 patients of moderate and 16 out of 18 patients with severe lung involvement. Protein levels were normal with mild involvement. 2 patients with moderate and 8 patients showed decreased s. proteins. The albumin by globulin (A/G) ratio of less than 1 were decreased in 2 mild, 16 moderate and 15 cases with severe lung disease. Even in EPTB decrease in albumin was seen commonly. It was seen in 12 out of 26 cases of pleural effusion, 5 out of 10 cases of miliary/disseminated and 1 case of abdominal T.B. Protein levels were decreased in 3,5 and 1 case of pleural, disseminated and abdominal TB. While albumin by globulin ratio was altered in 4 of 26 cases of effusion, 7 out of 10 cases of disseminated TB and in 1 case of abdominal TB. None of the 2 cases of LN tuberculosis had altered protein levels.

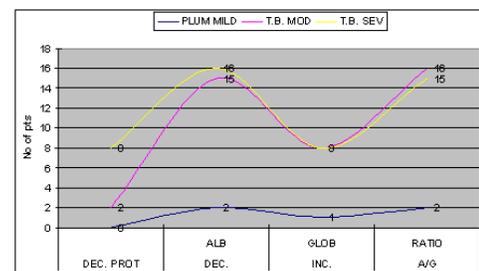


Figure 1: Correlation of Serum protein levels with severity of pulmonary TB

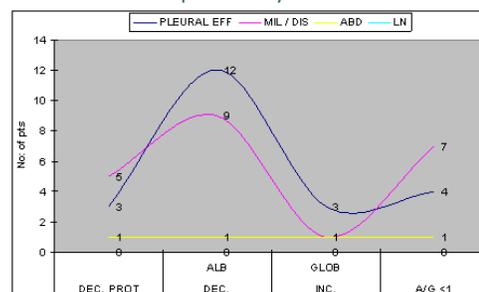


Figure 2: Correlation of Serum protein levels with extra-pulmonary TB

Table 1 and graph 2 and 3 have been illustrated to see the magnitude of alteration in protein levels and compare it with study by Mhiita *et al*^{10,3}. The average protein levels decreased with increasing severity of lung disease, from 6.9 gm% with mild to 5.9gm% with severe involvement. Average albumin levels also decreased from 3.5 gm% in mild to 2.7 gm% in severe lung involvement. In pleural effusions, the average protein and albumin were 5.6 gm% and 6.6 gm%, and 2.7 gm% and 3.7 gm% with and without lung involvement respectively. While in miliary/disseminated TB the average protein, albumin and globulin was 6 gm%, 2.8 gm% and 3 gm% respectively. In abdominal TB the average protein and albumin was 7 gm% and 3.7 gm% respectively; and in LN tuberculosis the corresponding values were 6.7 gm% and 3.8gm%.

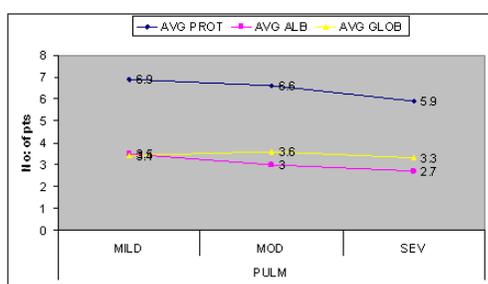


Figure 3: Average serum protein levels in pulmonary TB cases

DISCUSSION

Haematological and biochemical abnormalities in pulmonary tuberculosis are common and may be valuable aids in diagnosis. Total protein levels were found to be decreased in 23% of patients. While, it was normal in mild cases, 19% of patients with moderate involvement and 44% with severe involvement had decreased protein level. Hypoalbuminemia was found most frequently, the levels decreasing as the severity of the disease increased. From 40% in mild disease, the percentage of patients with hypoalbuminemia increased to 88% in those with moderate and severe lung involvement. This can further be evaluated from graph 3, where the average albumin levels decreased from 3.5 gm% in mild to 2.7 gm% in severe lung involvement and the total protein decreased from 6.9 gm% in mild to 5.9 gm% in severe lung involvement. Though, the globulin levels were increased in 9/42 or 21% of patients with PTB, the albumin by globulin (A/G) ratio of less than 1, indicative of relative increase in globulin when compared with albumin levels were decreased in 78% of patients. This has been shown by various studies earlier. Gupta *et al*⁹, Gaitonde *et al*¹⁰, Vyas *et al*¹¹ and Koul *et al*¹², have consistently found a decrease in the values of total proteins and serum albumin, which was more marked in advanced cases. Mhiita VK *et al*¹³, found the decrease of 17% below

normal in average total protein levels, again the decrease being proportionate to the extent of the disease. Serum albumin values were found to be decreased by 45%. Morris *et al*¹⁴, found hypoalbuminemia in 72% of PTB. This is similar to our study where 66% of patients had hypoalbuminemia. In pleural effusions, the levels were lower if there was a concomitant lung parenchymal lesion. The average protein and albumin levels were 5.6/6.6 gm%, and 2.7/3.7 gm% with/without lung involvement respectively. In miliary/disseminated TB, the albumin levels were decreased in 90% of cases, as is the case in the study by Hussain *et al*¹⁵, where it was decreased in 92% of patients. Marteen *et al*¹⁶, have linked the hypoalbuminemia to the severity of the miliary disease. In conclusion, significant changes in the levels of several serum proteins have been observed to be associated with tuberculosis. Though they may not be of diagnostic value, they do, however, indicate the response of the body to the infection and recovery after treatment.

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