Comparative study between tuberculin skin test and serum albumin level in patients with active pulmonary tuberculosis

Ahmad A. Mohammad[a], Osama E. Mohammad[a], Abeer A. Shoman[b]

Background Tuberculosis is difficult to diagnose and is an important cause of death among adults in developing countries. There is an urgent need for low-cost diagnostic markers in resource-limited settings.

Aim The aim of the study was to investigate the relationship between the intensity of the tuberculin test and serum albumin level in patients with active pulmonary tuberculosis.

Patients and methods Forty patients with active pulmonary tuberculosis before treatment were classified into two groups: group A and group B. Group A included 20 patients (17 men and three women; age 23–70 years) with serum albumin level below 3.5 g/dl. Group B included 20 patients (16 male and four female patients; age 15–68 years) with serum albumin level of 3.5 g/dl or more. Patients were subjected to full clinical evaluation. Comorbidities that may affect tuberculin reaction, such as HIV infection, alcoholism, chronic renal failure, and neoplasms, were excluded. Laboratory tests included complete blood count, evaluation of erythrocyte sedimentation rate, liver and kidney function tests, plain chest radiography, tuberculin skin test using the Mantoux technique, sputum test for acid fast bacilli by means of Ziehl–Neelsen staining for three consecutive days, and serum albumin level at the same time as the tuberculin test.

Results There was a statistically significant difference between the two groups as regards serum albumin level. The mean tuberculin skin test diameter in group A was 7.5 ± 3.94 mm and in group B was 20.9 ± 5.51 mm, which revealed statistically significant difference between the two groups. There was a statistically significant positive correlation between the intensity of tuberculin skin reaction at 72 h and serum albumin levels in both groups.

Conclusion Patients with active pulmonary tuberculosis and lower serum albumin levels have weaker skin responses to tuberculin test. *Egypt J Broncho* 2015 9:188–191

Egyptian Journal of Bronchology 2015 9:188–191

Keywords: active pulmonary tuberculosis, serum albumin levels, tuberculin skin test

Departments of [a]Chest Diseases and Tuberculosis, [b]Physiology, Benha University, Benha, Egypt

Correspondence to Ahmad Abdelsadek, MD, Department of Chest Diseases and Tuberculosis, Benha University, Benha, 13511, Egypt
Tel: +20 122 275 8380; fax: 0133227491 - 0133213511;
e-mail: ahmadabdelsadek@yahoo.com

Received 02 Febuary 2015 **Accepted** 07 March 2015

Introduction

Tuberculosis (TB, short for tubercle bacilli) is a common and often deadly infectious disease caused by various strains of mycobacteria, usually *Mycobacterium tuberculosis* in humans. Tuberculosis usually attacks the lungs but can also affect other parts of the body [1].

The tuberculin skin test (TST) is a useful diagnostic test for evaluating individuals who have symptoms of tuberculosis or who are suspected of being infected with *M. tuberculosis* [2].

The TST is the standard test for the diagnosis of asymptomatic tuberculous infection. Tuberculin, a broth culture filtrate of tubercle bacilli, was first prepared by Robert Koch in 1891. Subsequently, a standardized version of tuberculin, the purified protein derivative, was introduced in 1934 [3].

Serum albumin is the most abundant protein in human plasma. Albumin is synthesized in the liver as preproalbumin. The rate of synthesis is dependent on protein intake, subjected to feedback regulation by plasma level, oncotic pressure, inflammation, and hormones. During times of increased albumin loss, the liver can increase the rate of synthesis [4].

Hypoalbuminemia is a common problem among individuals with acute and chronic medical conditions; malnutrition is observed frequently in patients with pulmonary tuberculosis because of anorexia [5].

Aim of the work

The aim of the study was to investigate the possible relationship between the intensity of the TST reaction and serum albumin level in patients with active pulmonary tuberculosis.

Patients and methods

The study included 40 patients with active pulmonary tuberculosis just before initiation of treatment who were selected from the chest outpatient clinic, Benha University Hospital, during the period from March 2010 to December 2011. They were classified into two groups.

 DOI: 10.4103/1687-8426.158086

Group A: This group included 20 patients with serum albumin level below 3.5 g/dl and included 17 men (85%) and three women (15%), their ages ranging from 23 to 70 years.

Group B: This group included 20 patients with serum albumin level of 3.5 g/dl or more and included 16 male (80%) and four female (20%) patients, their ages ranging from 15 to 68 years.

Inclusion criteria

Patients suffering from active pulmonary tuberculosis (smear positive), defined as one or more initial sputum smear examinations positive for acid fast bacilli by microscopy, were eligible for inclusion into the study [6].

Exclusion criteria

(1) Previous antituberculosis treatment.
(2) HIV infection.
(3) Alcoholism and drug abuse.
(4) Chronic renal failure.
(5) Neoplasmic diseases.
(6) Chronic use of corticosteroids.

All patients were subjected to the following:

(1) Full history taking and physical examination.
Special attention was paid to fever, cough, loss of weight and appetite, night sweats, weakness, and malaise, as well as to physical signs, such as pallor and weight loss, rales, and bronchial breathing.
(2) Laboratory tests.
   (a) Complete blood count.
   (b) Erythrocyte sedimentation rate.
   (c) Liver and kidney function tests.
(3) Plain chest radiography posterior anterior view.
A chest radiograph was taken for radiological classification according to the extent of the disease and to exclude an associated lung disease.
(4) TST using the Mantoux technique.
A volume of 0.1 ml (five tuberculin units) of purified protein derivative RT tween 80 was administered intradermally into the volar surface of the forearm. Results were read after 48–72 h. A positive reaction is indicated by induration of more than 10 mm in size.
(5) Sputum for acid fast bacilli by Ziehl–Neelsen staining.
Three first morning sputum specimens of 5–10 ml were taken after a deep productive cough for three consecutive days by asking the patients to cough into a sterile screw cap [7]. The specimens were kept at 4°C before processing with *N*-acetyl-l-cysteine-NaOH (NALC-NaOH), for liquefaction, decontamination, and concentration [8].
(6) Serum albumin level at the same time as the tuberculin test.

Statistical analysis

Data were statistically analyzed using SPSS, version 16. Quantitative data were analyzed using mean and SD, whereas frequency and percentage were used for qualitative data. The Student *t*-test was used to compare means of different groups, and the χ^2-test and the *Z*-test were used to compare frequencies. Pearson's correlation was used to ascertain relationships.

Statistical significance was set at *P* values less than 0.05 [9].

Discussion

The TST is a useful diagnostic test for evaluating individuals who have symptoms of tuberculosis or who are suspected of being infected. A positive TST only indicates infection and by itself is not diagnostic of tuberculosis disease as it fails to distinguish between active disease and prior sensitization by contact with *M. tuberculosis* [10].

Malnutrition and tuberculosis are both problems of considerable magnitude. These two problems tend to interact with each other, and the link between them has long been recognized. Malnutrition can lead to secondary immunodeficiency, which increases the host's susceptibility to the development of clinical disease. In patients with tuberculosis, it leads to reduction in appetite, nutrition malabsorption, and altered metabolism [11].

In the present study 40 patients with active pulmonary tuberculosis were divided into group A and group B. Patients in group A had serum albumin level below 3.5 g/dl and their ages ranged from 23 to 70 years, with a mean of 44.25 ± 15.55 years. Patients in group B had serum albumin level of 3.5 g/dl or more and their ages ranged from 15 to 68 years, with a mean of 35.3 ± 14.77 years. There was no statistically significant difference between the two groups as regards age distribution (Table 1).

Group A included 17 male patients (85%) and three female patients (15%) and group B included 16 male patients (80%) and four female patients (20%), revealing no statistically significant difference (Table 2).

Table 1 Age distribution in the studied groups

Variable	Groups	Range	Mean ± SD	Student's *t*-test	*P* value
Age	A	23–70	44.25 ± 15.55	1.87	0.07 (NS)
	B	15–68	35.3 ± 14.77		

NS, nonsignificant.

The radiological classification of the extent of the disease was as follows: in group A – minimal disease in 10 patients (45%), moderately advanced disease in seven patients (35%), and far advanced disease in three patients (15%); in group B – minimal disease in eight patients (40%), moderately advanced disease in eight patients (40%), and far advanced disease in four patients (20%). The results revealed no statistically significant difference between the two groups (Table 3).

In this study serum albumin level in group A ranged from 1.5 to 3.4 g/dl, with a mean of 2.6 ± 0.48, and in group B it ranged from 3.5 to 4.5 g/dl, with a mean of 3.85 ± 0.33. These results showed statistically significant difference between the two groups (Table 4). This result was in accordance with those of Michaelides *et al.* [12]. Their study included 48 patients with active pulmonary tuberculosis who were divided into group A, with low serum albumin (mean serum albumin level 2.95 ± 0.91) and group B, with normal serum albumin level (mean serum albumin level 3.92 ± 0.6).

Tuberculosis can cause diverse laboratory abnormalities such as anemia, increased erythrocyte sedimentation rate, and low serum albumin. Malnutrition *per se* has a more pronounced effect on serum albumin concentration in tuberculosis patients. Thus, all chronic infections such as tuberculosis can cause decreased production of serum albumin [13]. In the present study, TST diameter in group A ranged from 5 to 15 mm, with a mean of 7.5 ± 3.94 mm, and from 12 to 30 mm with a mean of 20.9 ± 5.51 mm in group B, which showed statistically significant difference between the two groups (Table 5). This result was in agreement with those of Michaelides *et al.* [12]. In their study group A had low serum albumin and their mean TST diameter was 11.3 ± 2.1, and group B had normal serum albumin and their mean TST diameter was 18.4 ± 3.9, revealing statistically significant difference between the two groups.

Table 2 Sex distribution in the studied groups

Sex	Group A [*N* (%)]	Group B [*N* (%)]	Total [*N* (%)]	FET	*P* value
Male	17 (85.0)	16 (80.0)	33 (82.5)	0.173	1.0 (NS)
Female	3 (15.0)	4 (20.0)	7 (17.5)		
Total	20 (100.0)	2 (100.0)	40 (100.0)		

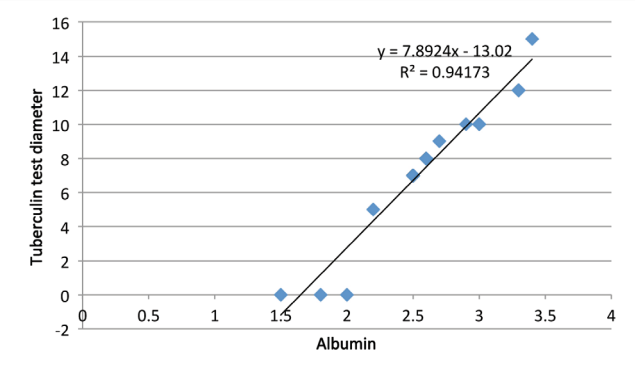
NS, nonsignificant.

In our study there was a statistically significant positive correlation between intensity of tuberculin skin reaction at 72 h and serum albumin levels in both groups (Figs 1 and 2). This result was in accordance with those of Kardjito and Donosepoetro [14], who studied the Mantoux test in tuberculosis. The result showed a statistically significant positive correlation between intensity of tuberculin skin reaction and serum albumin levels.

This result was in accordance with those of Michaelides *et al.* [15], who studied the relationship between tuberculin hypersensitivity and serum albumin level in patients with pulmonary tuberculosis. Their study included 42 patients (35 males and seven females) aged 33.04 ± 15.7 years. The diameter of induration was 17.8 ± 6.01 mm and the serum albumin level was 7.27 ± 0.86 g/dl. Analysis showed a statistically significant positive correlation between intensity of tuberculin skin reaction and serum albumin levels.

These findings indicated that tuberculous patients with lower albumin levels have weaker skin responses to tuberculin compared with those with normal albumin levels, which could be attributed to malnutrition, which causes suppression of delayed hypersensitivity reaction; false negative tuberculin reactions are very common in cases of advanced malnutrition, and malnutrition has been linked to decreased immune function [16].

Fig. 1



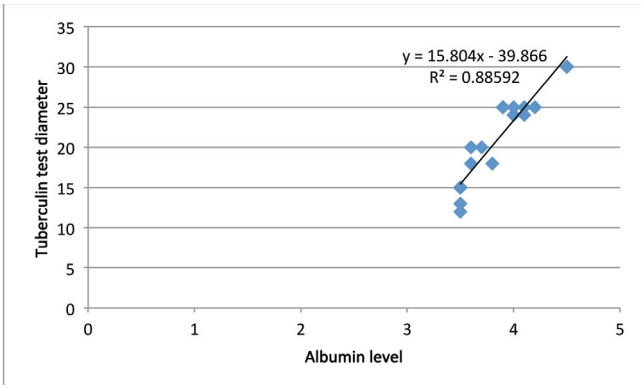
Correlation between intensity of tuberculin skin reaction after72 hours and serum albumin levels in group A

Table 3 Radiological classification according to extent in the groups

Radiographic finding	Group A [*N* (%)]	Group B [*N* (%)]	Total [*N* (%)]	FET	*P* value
Minimal	10 (45.0)	8 (40.0)	17 (42.5)	0.243	0.89) NS)
Moderate advanced	7 (35.0)	8 (40.0)	15 (37.5)		
Far advanced	3 (15.0)	4 (20.0)	7 (17.5)		
Total	20 (100.0)	20 (100.0)	40 (100.0)		

NS, nonsignificant.

Fig. 2



Correlation between intensity of tuberculin skin reaction after 72 hours and serum albumin levels in group B

Table 4 Serum albumin levels in the studied groups

Variable	Groups	Range	Mean ± SD	Student's *t*-test	*P* value
Albumin	A	1.5–3.4	2.6 ± 0.48	9.51	0.001 (S)
	B	3.5–4.5	3.85 ± 0.33		

This table shows that there is a statistically significant difference between groups A and B as regards serum albumin ($P = 0.001$); S, significant.

Table 5 The diameter of induration in the tuberculin skin test of the studied groups after 72 h

Variable	Groups	Range	Mean ± SD	Student's *t*-test	*P* value
Tuberculin test	A	5–15	7.5 ± 3.94	8.84	0.001 (S)
	B	12–30	20.9 ± 5.51		

This table shows that there is a significant tendency for the 72 h reaction to be greater in group B ($P = 0.001$); S, significant.

Conclusion

(1) Malnutrition is known to cause suppression of delayed hypersensitivity reaction.
(2) Tuberculous patients with lower serum albumin levels have weaker skin responses to tuberculin.

Acknowledgements

Conflicts of interest
None declared.

References

1 Kumar V, Abbas AK, Fausto N,Mitchell R *Robbins basic pathology*. 8th ed. Philadelphia, PA: Saunders Elsevier; 2007.516–522.

2 Castelo-Filho A, Kritski AL, Barreto AW, *et al.* Consenso Brasileieiro de Tuberculose. *J Bras Pneumol* 2004a; **30**:557–586.

3 Chan ED, Heifets L, Iseman MD Immunologic diagnosis of tuberculosis: a review. *Tuber Lung Dis* 2000; **80**:131–140.

4 Jacobs JM, Adkins JN, Qian WJ, Liu T, Shen Y, Camp DG 2nd, Smith RD. Utilizing human blood plasma for proteomic biomarker discovery. *J Proteome Res* 2005; **4**:1073–1085.

5 Finfer S, Bellomo R, McEvoy S, Lo SK, Myburgh J, Neal B, Norton R, SAFE Study Investigators Effect of baseline serum albumin concentration on outcome of resuscitation with albumin or saline in patients in intensive care units: analysis of data from the saline versus albumin fluid evaluation (SAFE) study. *BMJ* 2006; **333**:1044.

6 World Health Organization Library Cataloguing in Publication Data. *Implementing the WHO stop TB strategy: a hand book for national tuberculosis control programmes*. Geneva, Switzerland: WHO/HTM/2008; 2008. 401.

7 Yassin MA, Cuevas LE. How many sputum smears are necessary for case finding in pulmonary tuberculosis? Trop Med Int Health 2003; **8**:927-932.

8 Topley WW, Wilson GS. *Principles of bacteriology, virology and immunity*. 8th ed. London, UK: Arnold; 1990.

9 Dodge Y. *The oxford dictionary of statistical terms*. Oxford, UK: Oxford University Press; 2003.

10 Castelo-Filho A, Kritski AL, Barreto AW, *et al.* The diagnosis of tuberculosis. *Clin Chest Med* 2005 2004b; **26**:247–271.

11 Gupta KB, Gupta R, Atreja A, Verma M, Vishvkarma S Tuberculosis and nutrition. *Lung India* 2009; **26**:9–16.

12 Michaelides S, Chandrinos V, Hatzimanolis I, *et al. Tuberculosis: metabolic insights, tuberculin hypersensitivity and its relation to nutritional status in patients with active tuberculosis*. Attiki, Greece: 1st Department of Thoracic Medicine, School of Medical Assistants and Nursing; 2010.

13 Paton NI, Chua YK, Earnest A, Chee CB Randomized controlled trial of nutritional supplementation in patients with newly diagnosed tuberculosis and wasting. *Am J Clin Nutr* 2004; **80**:460–465.

14 Kardjito T, Donosepoetro M, Grange JM. The Mantoux test in tuberculosis: correlations between the diameters of the dermal responses and the serum protein levels. *Tubercle* 1981; **62**:31–35.

15 SA Michaelides, J Vrioni, A Tsarouha, *et al.* Relationship between tuberculin hypersensitivity and serum albumin level in patients with active tuberculosis. *Am Coll Chest* J 2005; **128**:142s.

16 Cegielski JP, McMurray DN. The relationship between malnutrition and tuberculosis: evidence from studies in humans and experimental animals. *Int J Tuberc Lung Dis* 2004; **8**:286–298.