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.
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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 χ²-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.

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].

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.

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.
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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.

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