A Clinical Study on Active Pulmonary Tuberculosis Using Cancer Antigen-125 as a Diagnostic and Prognostic Tool

Tirupati S Rajasekhar
Associate Professor, Department of Medicine, Kannur Medical College, Kannur, Kerala, India

Abstract

Background: Cancer antigen-125 (CA-125) is produced by coelomic epithelium. Its levels are increased in malignant diseases, like ovarian cancer but also in other medical conditions, such as pulmonary and extra-pulmonary tuberculosis (PTB). TB is usually diagnosed using conventional methods such as smear microscopy, culture, and chest radiography. The other methods used are the detection of immunological response and the search for biochemical markers. CA-125 was evaluated mainly in patients with extra-PTB.

Aim of the Study: This study aims to use CA-125 in differentiating PTB from other pulmonary infections; also to determine its value as an indicator of response to antituberculous drugs.

Materials and Methods: Group A consisted of 42 patients with active PTB, Group B consisted of 23 patients with extra-PTB, and Group C consisted of 21 healthy volunteers. CA-125 levels were estimated in all the groups. It was reassayed 4 months after antituberculous medication in Group A.

Observations and Results: The CA-125 values of Group A were higher at significant levels than the other groups. The sensitivity and specificity of CA-125 were found to be 79.34% and 91.30%, respectively, at a 34.6 U/ml cutoff point.

Conclusions: CA-125 was a useful tool in differentiating PTB from extra-PTB. It was also useful in assessing the response to antituberculous drugs in patients.

Key words: Cancer antigen-125, Malignancy and immunological response, Tuberculosis

INTRODUCTION

Even today, tuberculosis (TB) represents an important health problem worldwide that was declared by the World Health Organization to be global emergency,[1] the most common form of clinical form of presentation with TB is pulmonary type. 95% of TB cases reported from developing countries.[2] It is estimated that 12 million patients are coinfected with HIV and mycobacterium TB, with the majority living in Africa and Southeast Asia.[3] Microscopic examination and demonstration of acid-fast stained sputum smears is the most useful diagnostic method.

If it is positive, the initiation of TB therapy and respiratory isolation could be started immediately. However, in few patients, positive acid-fast bacillus in sputum samples may be negative or respiratory specimens may not be available, and other methods have to be used to establish the diagnosis of TB. In addition to microbiological molecular diagnostic tests, certain biochemical parameters are being used as helpful tools for this purpose, including various markers of cellular activity, acute phase reactants, and enzymes.[4-8] Cancer antigen-125 (CA-125) tumor marker also was proposed as a useful diagnostic tool for TB. CA-125 serum concentrations are known to rise in some benign and malignant diseases.[9,10] High serum levels of CA-125 are reported in patients with pulmonary and extra-pulmonary TB (PTB), including pleural, peritoneal, pelvic, miliary, and intra-abdominal TB. However, the diagnostic value of CA-125 to help differentiate PTB from other pulmonary infections has been poorly studied.[11-13] CA-125 antigen or carbohydrate antigen-125 is a high-molecular-weight glycoprotein (200 KDa) which was identified on the surface...
of the ovarian carcinoma cell line OVCA 433 by Bast et al.,[14] in 1981. High levels of CA-125 have been reported in patients with pulmonary and extra-PTB, including pleural, peritoneal, pelvic, miliary, and intra-abdominal disease.[11-13] The present study was conducted to assess the specificity and accuracy of serum CA-125 levels in differentiating PTB and non-PTB; to use its levels as a prognostic tool to know the effect of antituberculous chemotherapy.

### Institution of Study
This study was conducted at Kannur Medical College, Anjarakandy, Kannur.

### Period of Study
This study was from May 2010 to April 2013.

### MATERIALS AND METHODS

A total of 86 subjects were included in the present study. They were divided as Group A consisted of 42 patients with active PTB, Group B consisted of 23 patients with extra-PTB, and Group C consisted of 21 healthy volunteers. An ethical committee clearance was obtained before commencing the study. An ethical committee cleared consent form was used to collect the data.

#### Inclusion Criteria
1. Patients aged above 18 years were included in all groups
2. Patients with active PTB were included in Group A
3. Patients with non-PTB diseases were included in the Group B
4. Healthy subjects were taken as control
5. Patients with typical symptoms of TB such as cough, expectoration, fever, chills, evening rise in temperature, night sweating, loss of weight, and appetite were included.

#### Exclusion Criteria
1. Patients non-TB lung diseases were excluded.
2. Patients with acute pyrexia of unknown origin were excluded.
3. Patients with COPD were excluded.
4. Patients with rheumatic fever or carditis were excluded.
5. Patients with malignancies, cirrhosis of liver, renal diseases, and gynecological tumors were excluded.
6. Patients with heart failure (left-sided heart failure) were excluded.

All the patients in Group A (42 patients) were elicited about their illness and symptoms of TB. All the patients were subjected to TC, DC, ESR, and Mantoux test, sputum for AFB, X-ray chest, and serum CA-125 levels. All patients in Group A received antituberculous drugs in the form of 2 months of intensive therapy of rifampicin, isoniazid, pyrazinamide, and ethambutol followed by 4 months of rifampicin and isoniazid. After 2 months of treatment, sputum smears were repeated and conversion into sputum smear-negative occurred in all patients. Radiological signs of PTB were noted in the data. In Group B, patients (23 patients) with non-PTB were included. Patients in this group were those who had cervical TH lymphadenitis, TB osteomyelitis, and renal TB and dermatological TB diseases. All the patients in this group were negative for sputum AFB staining. All patients in group A received antituberculous drugs in the form of 2 months of intensive therapy of rifampicin, isoniazid, pyrazinamide, and ethambutol followed by 4 months of rifampicin and isoniazid. After 2 months of treatment, serum CA-125 levels were estimated. Group C subjects were healthy individuals without respiratory symptoms or TB symptoms. They also were subjected to all the tests on special consent.

5 ml of venous blood was drawn from each subject. Blood samples were left to clot for 15–20 min at 37°C, and then centrifuged at 3000 rpm for 20 min. Expressed serum was frozen at 40°C until the time of CA-125 assay. The results were automatically calculated by the instruments and the concentrations were expressed in U/ml. Another assessment of serum CA-125 was detected among Group (A) only after 4 months of antituberculous drugs. All the data collected were analyzed using standard statistical methods; P < 0.05 was taken as significant.

### OBSERVATIONS AND RESULTS

In the Group A 42 patients, there were 28 males and 14 female patients. The age group was between 20 and 60 years with a mean age of 38.42 ± 2.68 years. In the Group B 23 patients, there were 15 males and 08 female patients. The age group was between 20 and 60 years with a mean age of 38.42 ± 2.68 years. In the Group C 21 patients, there were 11 males and 10 female patients. The age group was between 20 and 60 years with a mean age of 39.10 ± 2.68 years [Table 1]. The data are not significant in regards with the formation of groups (P = 0.601) but significant in regards with the mean age (P = 0.041), [Table 1].

The mean CA-125 levels in Group A were 91.6 U/ml, in Group B, it was 61.4 U/ml, and in Group C, it was 12.6 U/ml. The CA-125 levels were significant.

<table>
<thead>
<tr>
<th>Gender</th>
<th>Group A</th>
<th>Group B</th>
<th>Group C</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>28</td>
<td>14</td>
<td>11</td>
<td>0.601</td>
</tr>
<tr>
<td>Female</td>
<td>15</td>
<td>08</td>
<td>10</td>
<td></td>
</tr>
<tr>
<td>Mean</td>
<td>38.42±2.68</td>
<td>36.35±3.47</td>
<td>39.10±2.68</td>
<td>0.041</td>
</tr>
</tbody>
</table>

CA-125: Cancer antigen-125
Higher among Group A compared to normal subjects in Group C (P = 0.006) [Table 2]. The CA-125 values are compared between Groups B and C and found to be significant (P = 0.028). Similarly, the CA-125 values compared between A and B groups were not significant (P = 0.061) (P < 0.05).

Serum CA-125 levels were reassayed after 4 months of antituberculous treatment among Groups A and B patients. CA-125 levels were significantly lower after treatment than before in Group A patients; it was 32.7 U/ml, and in Group B, it was 27.4 U/ml with P = 0.008 [Table 3].

The radiological signs before and after treatment in Group A patients were correlated with the C-125 levels and found that there was statistical significance with P = 0.042 [Table 4].

The sensitivity and specificity of CA-125 values in the diagnosis and as a tool of prognostic assessor in the study were calculated from the data and found to be 81.4% and 95%, respectively.

**DISCUSSION**

CA-125 levels in the serum as a tumor marker although used in the diagnosis and assessing the prognosis of ovarian and other malignant tumors in the literature, later, it was found to be useful in diagnosing the benign conditions also. It was also found that CA-125 levels were significantly higher than normal in patients with pulmonary and extra-PTB and that serum CA-125 level may be a useful marker for discriminating between patients with active TB and those with inactive disease. In the present study, serum CA-125 levels were significantly higher in Group A patients with active PTB when compared to healthy subjects as well as Group B patients with non-PTB and healthy subjects of Group C [Table 2]. The mean CA-125 values in a study by Yilmaz et al. among patients with PTB were ([109.7] 86.9 U/ml), while it was ([118.46] 248.41 U/ml) in Ozsahin et al. study, which are closer to the values in the present study (91.6 U/ml). On the other hand, Kim et al. study showed a lower mean value of CA-125 in patients with active PTB (54.5) 22.4. The difference may be due to the different methods of diagnosis used for tuberculous; they depended on sputum culture while in this study sputum examination of acid-fast bacillus was used. The authors Ronay et al. determined that CA-125 was immunohistochemically localized and sharply demarcated around tubercular granuloma with peritoneal TB; they concluded that the inflammatory mesothelial cell proliferation was the source for secretion of CA-125 in patients with TB. In the present study, there was a significant positive correlation between serum CA-125 levels and incidence of positive radiological signs of PTB [Table 4]. Similar results are in agreement with those reported by Kanagarajan et al., who found that levels of CA-125 being highest in cavitory PTB and in miliary TB. Kim et al. also found that CA-125 levels appeared to be highest in patients with cavitary rather than nodular type and this may reflect the level or extent of the infection. In the present study, there was an insignificant correlation of age and sex to CA-125 among the entire studied Table 1. The sensitivity and specificity of CA-125 values in the diagnosis and as a tool of prognostic assessor in the study were calculated from the data and found to be 81.4% and 95%, respectively.

**REFERENCES**

7. Taha RA, Kotsimbos TC, Song YL, Menzies D, Hamid Q. IFN-gamma and IL-12 are increased in active compared with inactive tuberculosis. Am J Respir Crit Care Med 1997;155:1135-9.

How to cite this article: Rajasekhar TS. A Clinical Study on Active Pulmonary Tuberculosis Using Cancer Antigen-125 as a Diagnostic and Prognostic Tool. Int J Sci Stud 2017;5(8):1-4.

Source of Support: Nil, Conflict of Interest: None declared.