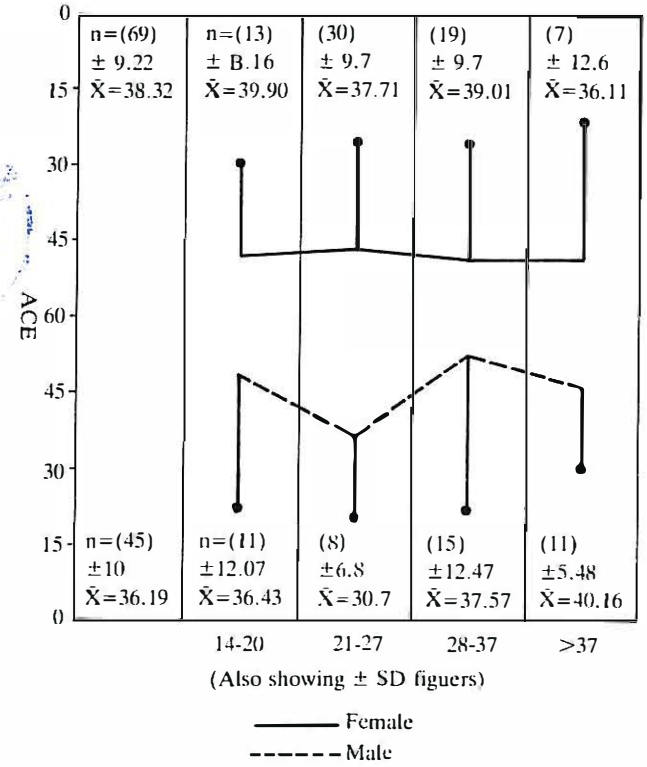


Fig.1. SACE levels in variable age and sex groups in normal controls.

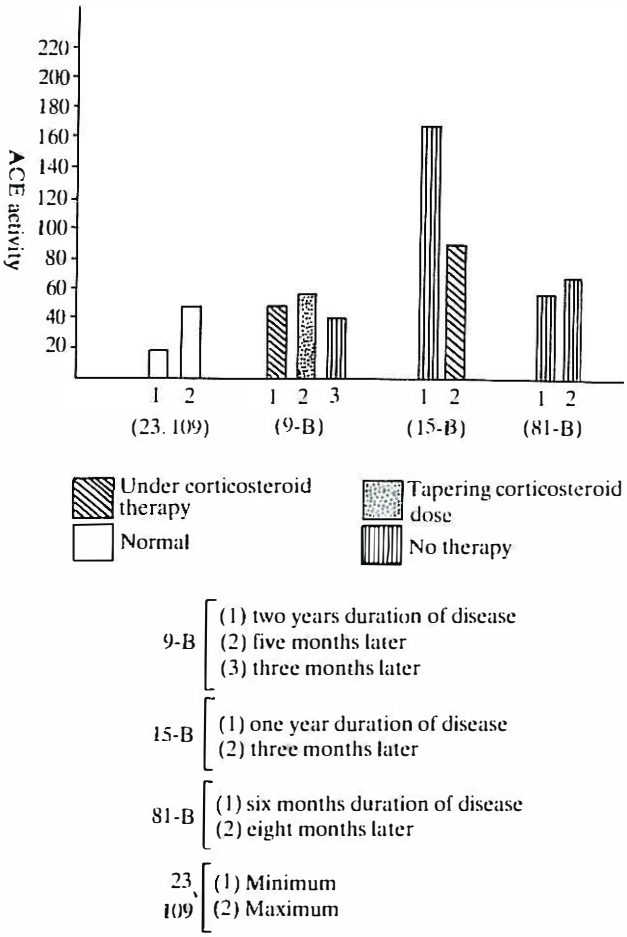


Fig.2. A comparison of sarcoidosis patients with and without corticosteroid therapy.

cytes and epithelioid cells within the granuloma.[7] The concentration of ACE in the lung parenchyma is thirty times more than other tissues and it therefore is the best site for the conversion of angiotensin I to angiotensin II.

MATERIALS AND METHOD

Proper handling of serum for ACE assay requires either prompt testing or storage at 5°C, where it can be preserved for more than six months. Serum ACE activity can be measured by using a refractometer or UV spectrophotometer. In this study, we choose to use the UV spectrophotometer (Bechman). The method used to determine the ACE activity level was that of Cushman and Cheung- modified by Liberman.[6,8-10]

The sera were obtained from patients suspected for sarcoidosis or tuberculosis. A final diagnosis was reached using a combination of chest- X-ray, direct smear and culture for mycobacterium, a gallium scan, a Kveim test, and tissue biopsy.

The normal control group was chosen from medical students and laboratory personnel who showed no evidence of disease after a complete physical examination and laboratory work-up, including a chest-X-ray.

RESULTS

The mean sera ACE activity in 108 of 114 normal controls was 35.56± 10.5. Out of 275 cases suspected for sarcoidosis, only 82 cases were confirmed. In these 82 patients (having pulmonary, ophthalmic, or dermatologic manifestations; some also with lymph node, renal, or posterior pituitary involvement) the SACE level was on the avarage 77.76± 21.8. In 29 proven cases of tuberculosis from 30 patients, the mean SACE was29.58 ± 8.35; which on the average was even below the normal range.

The (P) value in patients with tuberculosis compared to that in the normal control group was significant (P<0.01). From 114 normal controls, 9.64% showed a false increase in serum ACE activity while in the tuberculosis group, false positivity was noticed in 6.66%.

In the normal control group, males of 14-27 years of age had a higher ACE activity compared to females in

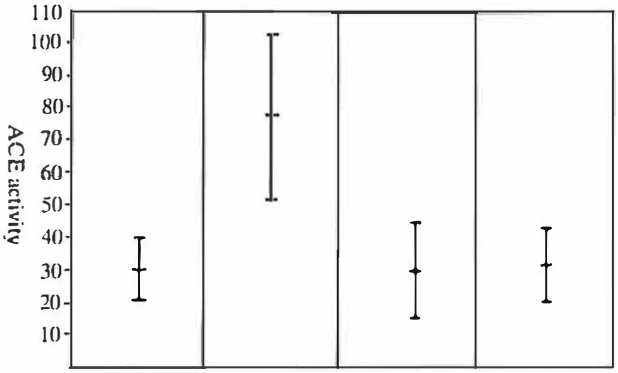
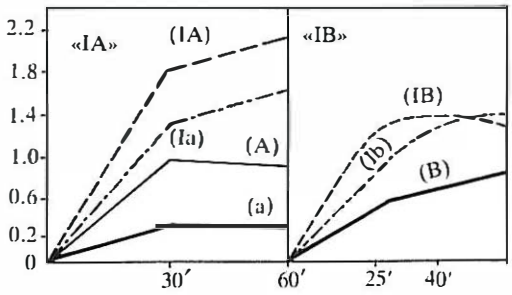


Fig.3. Comparison of SACE values in normal individuals and various pulmonary disease states.



A-Upper limit of SACE in normal controls.
1A-Upper limit of SACE in sarcoidosis of two years duration.
a-Lower limit of SACE in normal controls.
1a-Lower limit of SACE in sarcoidosis of less than 6 months duration.
B-SACE levels in normal controls.
1B-SACE levels in sarcoidosis of one year duration.
1b-SACE levels in sarcoidosis of five years duration.

Fig.4. SACE level in normal controls and sarcoidosis patients at several time intervals.

the same age group, which could be due to the effect of male sex hormones. On the other hand, females over 37 years of age had higher levels than age- matched males in the normal control group (Fig. 1).

Maximum activity of SACE was also observed in the normal group during the fasting and resting state; therefore, the best time for blood sampling is while the patient is at rest.

In those patients with proven sarcoidosis, serum ACE activity in males was higher on the average than in females; whereas the number of affected females was greater. The extent of the disease showed to be an important factor in raised SACE levels, rather than the duration of the disease (Fig. 4). Patients in stage II of the disease had higher levels than those in stage I. Following corticosteroid therapy, there was a 50% decrease in serum ACE activity in eight out of 14 patients (Fig. 2, 15-B). Only one patient showed an increase of ACE activity after five months of therapy (Fig. 2, 9-B). In those later proven to be sarcoidosis, ten cases had normal serum ACE activity at first trial. All showed increased levels upon repeating the assay after 2-4 months. There was a drop of SACE in five out of six patients with spontaneous remission. Only one patient had persisting elevated levels, even after eight months (Fig. 2, 81-B).

DISCUSSION

Measurement of serum ACE activity could differentiate sarcoidosis from other pulmonary diseases such as tuberculosis, because it usually increases in sarcoidosis as opposed to a decrease seen in tuberculosis (Fig. 3). This difference in ACE activity is due to different secretory products of the granuloma. Some epithelioid cells of a sarcoid granuloma secrete mainly ACE. There is evidence that the bradykinin released from sarcoid tissue may also stimulate ACE secretion from the endothelium of pulmonary vessels.

Increased activity of ACE in sarcoidosis correlates well with the activity of the disease. This seems to be due to the number of epithelioid cells which increase up to stage II of the disease and is replaced by fibrosis in stage III. Likewise SACE levels begin elevating from stage I, peak at stage II, and decline in stage III (Fig. 4). Therefore enzyme activity can also be correlated with roentgenographic findings.

In this survey, six cases of proven sarcoidosis showed a raise in serum ACE of more than 2U/ml, which was probably due to involvement of organs in addition to the lung. In those with a concomittant granulomatous disease, such as a fungus infection, the SACE was not higher that those with sarcoidosis-alone, confirming that ACE is predominantly secreted by the epithelioid cells of sarcoid tissue.

ACE measurement can also be used to assess the effect of corticosteroid therapy or become aware of a self- healing process. When the enzyme activity falls below 70 u/ml, drug therapy can be discontinued. As

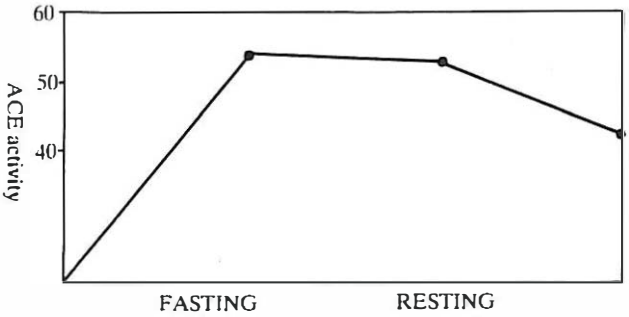


Fig.5. Daily pattern of SACE levels. Maximum activity of SACE levels in normal controls during a state of fasting or resting.

shown in Fig 2. (9-B), there is a rebound increase in serum ace activity when drug dosage is suddenly reduced. This emphasizes the need for gradual tapering of cortico- steroids following treatment of sarcoidosis.

This study of SACE, the first done in Iran, shows a higher incidence of sarcoidosis among Iranian females; whereas the SACE levels are on the average higher in affected males.

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