

# Clinical Significance and Precision analysis of Angiotensin converting enzyme (ACE) in suspected and Confirmed cases of sarcoidosis

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## 1. Abstract:

**Background:** Angiotensin converting enzyme (ACE) is known to be elevated in cases of Sarcoidosis. **Aim:** The present study described the precision analysis of ACE and clinical correlation with different groups of patients either suspected of sarcoidosis or confirmed cases, waiting for or undergoing treatments. **Materials and Methods:** Study covered the period of Dec 2013 to Dec 2015. Data of 100 patients that were either suspected cases of sarcoidosis or confirmed were retrieved, reviewed and classified into Group I, II, III (groups of suspected cases) according to their ACE levels and IV-that were confirmed cases of sarcoidosis. ACE was analyzed in serum of patients according to the established standard methods. For precision analyses, samples from each group, that were analyzed simultaneously in two instruments of Randox Monza (Randox UK), were plotted using regression correlation methodology to retrieve R<sup>2</sup>. ACE levels of each group I, II, III and IV were compared with each other and with healthy control subjects using student's t-test and level of significance as P < 0.05. **Results:** Precision analysis of ACE levels in group I showed R<sup>2</sup> of 0.99 depicting instrument to instrument precision of 99% for ACE analyte ranges of 15-30 U/L. Similarly ACE precision comparison of groups II and III showed R<sup>2</sup> of 0.98 and 0.99, exhibiting significant correlation of analytical precision. Comparison of ACE of Group I = 22.7 ± 4.60 U/L with groups II (36.6 ± 7.75 U/L) and III (47.6 ± 6.15 U/L) exhibited P < 0.01, whereas with group IV (55.10 ± 8.90 U/L) as P < 0.001. **Conclusion:** Data depicted significant correlation of ACE level (P < 0.001) in patients with sarcoidosis as compared to those with suspicion of initial stages of the same. Precision analysis also manifested R<sup>2</sup> of 0.98 to 0.99, suggesting significant instrument to instrument accuracy and precision.

**Key words:** Angiotensin converting enzyme (ACE), Sarcoidosis, precision

**Short title:** Clinical significance of ACE

## 2. Introduction:

Angiotensin converting enzyme (ACE) is known to be elevated in cases of Sarcoidosis [1,2]. Sarcoidosis is characterized by non-necrotizing granuloma in various organs especially locating in lungs [1]. However, etiology of sarcoidosis is unknown or related to autoimmune disarray [3]. Since the initial discoveries of correlation of ACE with sarcoidosis by Lieberman in 19754 and his further studies on chest roentgenograms and pulmonary function tests [2], ACE remains a prime investigative tool to diagnose sarcoidosis and earlier studies reported its sensitivity

upto 40% to 60% and specificity as 80% to 99% [5,6]. It has been suggested that ACE analysis be done readily after initial

diagnosis or suspicion of the disease to assess the longitudinal pattern in ACE levels [2].

The present study described the precision analysis of ACE and clinical correlation with different groups of patients either suspected of sarcoidosis or confirmed cases, waiting for or undergoing treatments.

## 3. Materials and Methods:

**3.1 Patient's selection and Study design:** Patients were selected retrospectively on the basis of their ACE data from archives of department of Biochemistry lab services and department of pathology, Govt Lyari General Hospital, Karachi. The study covered the period of Dec 2013 to Dec 2015. Files and data of 100 patients that were either suspected cases of sarcoidosis or confirmed were retrieved and reviewed. They were then classified into Group I, II, III (groups of suspected cases) according to their ACE levels and IV-that were confirmed cases of sarcoidosis. Details of number of patients in each group and ACE ranges were provided in Table I and Figures 1, 2 and 3. ACE was also determined from 15 healthy control subjects of either gender and used as comparative data for level of significance study.

**3.2 Analytical methods and precision analysis:** ACE was analyzed in serum of patients according to the methods described by Maguire *et al* [7] and Burtis and Ashwood [8]. The principle is dependent on ACE present in the serum that converts Furylacrylphenylalanyl-glycylglycine (FAPGG) to Furylacrylphenylalanine (FAP). The subsequent decrease in absorbance at 340nm is directly proportional to the activity of ACE.

For precision analyses, samples from each group, that were analyzed simultaneously in two instruments of Randox Monza (Randox UK), were plotted using regression correlation methodology to retrieve R<sup>2</sup>

**3.3 Statistical Analysis:** ACE levels of each group I, II, III and IV were compared with each other and with healthy control subjects using student's t-test. The data were considered significance when P < 0.05

## 4. Results:

Results are summarized in Table I and Figures 1,2 and 3. Precision analysis of ACE levels in group I showed R<sup>2</sup> of 0.99 depicting instrument to instrument precision of 99% for ACE

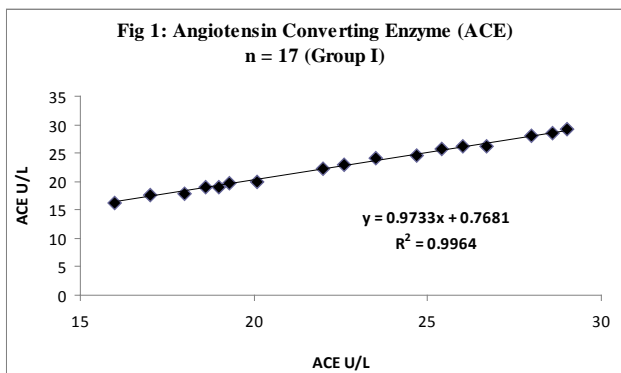
analyte ranges of 15-30 U/L (Fig 1). Similarly ACE precision comparison of groups II and III showed R2 of 0.98 and 0.99, exhibiting significant correlation of analytical precision. Clinical significance of ACE, when compared with each other in groups I, II and III where patients were suspected of sarcoidosis and group IV which includes confirmed cases, under-treatment or waiting for treatment, the outcome and level of significance noted to be variable (Table I). Comparison of ACE of Group I = 22.7 ± 4.60 U/L with groups II (36.6 ± 7.75 U/L) and III (47.6 ± 6.15 U/L) exhibited P < 0.01, whereas with group IV (55.10 ± 8.90 U/L) as P < 0.001. However G III and group IV showed no significance when compared with each other. On the other hand, when ACE levels of group IV compared with Group I (Table I), it exhibited significance level of p<0.001.

Table 1: Clinical significance of Angiotensin converting enzyme ACE levels in patients suspected of Sarcoidosis

Groups	ACE levels U/L	P < 0.05
Patients Group I	22.7 ± 4.60	0.01 [Group I vs Groups III, IV]
Patients Group II	36.6 ± 7.75	0.01 [Group II vs Controls, Group IV]
Patients Group III	47.6 ± 6.15	NS [Group III vs Group IV]
Sarcoidosis Group IV	55.10 ± 8.90	0.001 [Group IV vs Groups I & controls]
Controls	15.10 ± 2.30	-- --

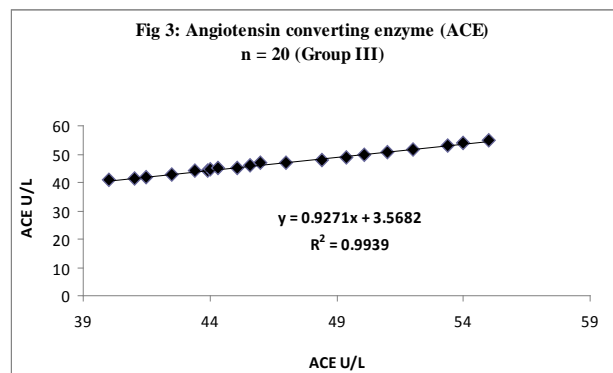
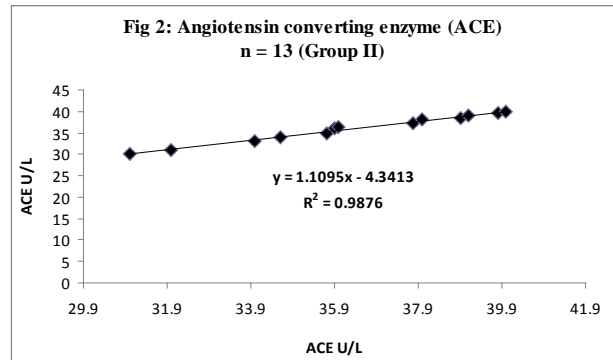
### 5. Discussion:

Previous studies on correlation of ACE levels in patients suffering from Sarcoidosis and siliconism in comparison with healthy individual showed elevated concentrations [9,10]. Similarly, sensitivity and specificity of ACE in diagnosis of sarcoidosis and frequency of false positive results were studied, depicting sensitivity and specificity of 58.1% and 83.8%, respectively [10]. Moreover, sensitivity levels were noted to be more risen upto 85.9% in patients who were suspected of sarcoidosis and 92.1% in confirmed cases of the same [10]. Both findings are in agreement with our study wherein patients with diagnosed sarcoidosis showed higher level of significance (P< 0.001) as compared to those with suspicion of it (P <0.01) or related anomalies.



Studies and reviews as early as 1970s and 1980s related to the clinical significance of ACE in sarcoidosis [3,11,12,13]. ACE as

a useful diagnostic tool was first identified by Liebermann [5] who suggested that serial measurement might help in clinical management of sarcoidosis. Studies that proceeded also confirmed Liebermann postulation and suggested that ACE is significantly elevated and facilitates early in diagnosis and management of early and advanced cases of sarcoidosis [3]. However few studies argued that ACE levels didn't correlate with radiological staging of sarcoidosis at the initial staging of the disease [1]. Arguably, most of the studies concluded earlier and thus referred henceforth, in patients with early and advanced stages of sarcoidosis, did exhibited considerably elevated levels of ACE that can be regard as clinical significant.



### 6. Conclusion:

Present study described the clinical significance and precision analysis of ACE in patients with suspected or initial stages of sarcoidosis and its confirmed/advanced stage cases. Data depicted significant correlation of ACE level (P< 0.001) in patients with sarcoidosis as compared to those with suspicion of initial stages of the same. Precision analysis also manifested R2 of 0.98 to 0.99, suggesting significant instrument to instrument accuracy and precision.

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