ADA AND CRP: NOVEL DIAGNOSTIC MARKERS FOUND IN TB PATIENTS

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ABSTRACT

In present study some tuberculous cases were investigated for biochemical parameters such as ADA and CRP, it is found that, the sensitivity and specificity for serum concentration is 98% and 100% of serum ADA concentration and CRP, respectively.

After the study, the result confirms the high sensitivity and specificity of ADA test for really diagnosis of TB in cases of serous effusion. The selective enzyme increase in tuberculous peritonitis strongly supports the concept that the study of ADA activity is of great value for identifying the tuberculosis etiology of ascites.

ADA has been proposed to be a useful surrogate marker for TB in pleural, pericardial and peritoneal fluids. High levels of serum CRP indicate that it is also a good indicator of the severity and progress of the tuberculosis.

Cytological examination of suspected malignant pleural effusion can result in false-negative rates of up to 40%. Diagnostic difficulties have led to the search of novel markers. Pleural fluid ADA and CRP levels were established to be significantly higher in tuberculous and parapneumonic effusions (PPES) when compared with other pleural effusions. Pleural fluid ADA and CRP levels can be a useful combination in the differential diagnosis of pleural effusions of malignant, tuberculous, and parapneumonic nature.

Keywords: *Pleural, Serum, Effusions, Parapneumonic, ADA, CRP*

INTRODUCTION:

Tuberculosis is a common prevalent infectious disease and is a major health problem in all world especially in developing countries. TB is one of the dreadful diseases affecting number of people in developing countries including India. It is one the most common diseases causing a high mortality and morbidity (Maher et al. 1997). Another emerging issue is widespread dissemination of multiple drug resistant cases of TB, which has raised the eyebrows of public health experts because it not only makes the disease condition more lethal, it also required very high cost to cure the condition. This disease, which is caused by bacteria of the *Mycobacterium tuberculosis* (Rothschild et al. 2001) complex, usually affects the lungs, although other organs are involved in up to one-third of cases.

BCG vaccination to prevent TB is highly practiced with some success. The governments in developing countries then greatly ignored the serious consequences of this very less sensitive vaccination. Moreover, the case detection process was also slow because culture of TB bacteria took weeks before diagnosed and the x-ray, despite being sensitive was not very specific. However, after the introduction of sputum cytology for (acid fast bacilli) AFB detection of TB became very sensitive, specific and relatively easy. Also, the curative drugs became available, but none of them are completely curing and required dose is for months (Shah and Asian 1992)

In the present study, biochemical studies in blood and body fluids of tubercular patients are studied which included mainly two parameters which are as follows:

(i) Adenosine Deaminase (ADA)

(ii) C-Reactive Protein (CRP).

Adenosine Deaminase (ADA) is an enzyme which catalyses the deamination of Adenosine into Inosine and Ammonia. It helps in maturation and proliferation of T-cells. ADA level has been found to be elevated in TB and typhoid fever (Galanti et al. 1981, Mishra et al. 1994), where cell mediated immunity is enhanced. The ADA level is significantly raised in TB and helps to differentiate tubercular from non- tubercular disease (Jhamaria and Runayan 1988). The ADA level has been found to be elevated in serum and pleural fluid in

patients of tubercular pleural effusion (Piras and Gokhi 1978, Ocana et al. 1986, Sigura et al.1989, Gakis 1996, Sharma and Mohan 1996, Shibagaki et al. 1996), tubercular ascites (Dwivedi and Mishra 1990, Sather et al. 1995) and tubercular pericardial effusion (Sigura et al 1989).

The ultimate aim is to evaluate ADA activity (Giusti and Galanti 1974) as a diagnostic as well as a prognostic marker. The ADA analysis is simple, inexpensive, standard diagnostic test that can be performed on body fluids. Diagnosis of TB is often overlooked during the initial investigation due to non specific clinical presentation. If pleural fluid sample stored properly then ADA determination can still be made several weeks later.

C-Reactive Protein (CRP) (Kidmark 1972) synthesized in the liver. Its rate of synthesis increases within hours of acute injury or the onset of inflammation and may reach as high as 20 times the normal levels. A rapid fall in CRP level indicates recovery.

At present, CRP analysis is predominantly employed to monitor the extent of activity of such as diseases and effect of treatment. CRP analysis is a useful test for supporting the diagnosis of infection and has been proven as a valuable tool in follow-up and differential diagnosis such as in case of cancer, connective tissues diseases, heart attack), inflammatory bowel disease(IBS), lupus, pneumonia, rheumatoid arthritis, rheumatic fever and TB. Low level of CRP does not always mean that there is no inflammation present, more sensitive CRP test is called high sensitive CRP (HS-CRP).

Use of CRP as a marker for detection of TB has emerged up as a most promising upcoming technique now days although many other techniques are in practice too, but this helps us not only in diagnosis but also helps us to evaluate progression & effectiveness of drugs used to cure it.

The test is now used in many laboratories and is widely been used as its cost is under the common man's pocket. As mentioned earlier, the mycobacterium culture though it is definite method however is a time consuming (4-6 weeks at least) and requires a lot of manual work and stringent conditions. Thus, CRP estimation is easy simple test to support diagnosis of TB infection. It also reflects the course of diseases and effectiveness of drug.

PROCEDURE

The present study "Biochemical studies in blood and body fluids of tubercular patients" was carried out in Department of Pathology of SAAII College of Medical Science & Technology, Kanpur from December 2010 to October 2012.

The patients suffering from pulmonary TB as well as TB of various organs of body are the subject of study.

Group A: 100 normal healthy age and sex matched controls.

Group B: 100 authentic pulmonary TB patients

Group C: 100 cases of non- tubercular diseases

The clinical features and detailed history of each case is recorded in a standard format including exposure to infection, physical examination and chest radiography.

Blood samples of the control and study group was collected for various biochemical analyses by vein puncture and transferred to EDTA vacutainer and used for haematological tests and serum for the analysis of ADA and CRP.

Haematological Tests as:

(1) Total WBC Count by Automated Cell Counter.

(2) Differential Leukocyte Count by Stain Blood Film,

(3) ESR by Wintrobe' Method

(4) Ziehl Neelsen's(Z-N) Staining For AFB

Biochemical tests:

(1) Serum ADA carried out by ADA hydrolysis with biochemical reactions.

(2) Serum CRP estimated by CRP-UV (a turbidometric immunoassay).

Considering biochemistry regarding serum ADA, CRP test estimated for the specific diagnosis of the tubercular infection.

RESULT:

Serum ADA were estimated in all the three group and it was found that in group B the serum ADA is (19.32±2.151 u/l) were significantly higher than the group A (10.11± 0.39 u/l) and group C(10.55± 0.901 u/l) . Similarly, the serum CRP levels when estimated in all entire three group, it was found that the serum CRP levels were significantly higher in group B (2.00± 0.39 mg/l) as compared with group A (0.40 ± mg/dl).

The result obtained shows that there was significant increase ADA in group B subjects in pleural fluid (29.61±3.93mg/dl), pericardial fluid (28.53±1.86 mg/dl), as compared with group C and subjects in pleural fluid(10.33±1.28 mg/dl) and CSF (101.07± 88mg/dl).

Similarly, CRP level in body fluids from group B subjects were compared with group C body fluids. It was found that there was significant increase in CRP levels of group B subjects in pleural fluid (2.05 ± 0.04 mg/dl), pericardial fluid (1.79±0.04 mg/dl), peritoneal fluid (1.74± 0.08mg/dl) and CSF (0.67±0.032 mg/dl) than the group C subjects in pleural fluid (0.69± 0.03 mg/dl) and CSF(0.49±0.02 mg/dl).

Thus, to calculate the diagnostic importance of the parameters studied here a cut-off value for each of the parameter accordingly the sensitivity and specificity for each of the parameters was calculated. By considering the cut-off value of 15 IU/L for serum ADA the sensitivity is 98% and specificity is 100%. And the cut-off value of 1.5mg/dl for serum CRP the sensitivity is 95% and specificity is 100%. Patients with more than the serum values are tuberculous and rest are non-tuberculous.

CONCLUSION:

Thus, the present study suggests that a significantly change is seen in the biochemical parameters studied and a careful correlation may help in the diagnosis as well in understanding the course of the disease. The parameter studied here could be considered as reliable indicator for the diagnosis of Tubercular infection. However, further studies are required to find out the more usefulness of new parameters like serum ADA and CRP so as to improve the management and control of the tuberculosis as they are found to be novel diagnostic biomarkers in TB patients.

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