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Research Article

Diagnostic Value of Ferroxidase Activity of Ceruloplasmin in Extra Pulmonary Tuberculosis

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Abstract: The aim of this study is to assess the diagnostic level of Ferroxidase activity of ceruloplasmin in tuberculousserosal effusion. The study was carried out on 50 patients suffering from tuberculous pleural and peritoneal effusion and 50 patients suffering from non- tuberculous pleural and peritoneal effusion. Mean ± SD of ferroxidase in tuberculous pleural effusion was 1042 ± 112 IU/L and the sensitivity and specificity was 100% and 95% respectively. Mean ± SD of ferroxidase in tuberculous peritoneal effusion was 968 ± 94 IU/L and sensitivity and specificity was 100% and 94% respectively. Serosal fluid ferroxidase estimation is a simple and rapid test with high degree of sensitivity and specificity. Hence Ferroxidase activity of ceruloplasmin may be used as a surrogate marker for tuberculousserosal effusion.
Keywords: Ferroxidase, Ceruloplasmin,Pleural and Peritoneal effusion

INTRODUCTION

Tuberculosis, one of the oldest diseases known to affect humans, is a major cause of death worldwide.This disease, which is caused by Mycobacterium tuberculosis complex, usually affects the lungs, although other organs are involved upto one-third of cases [1].

Involvement of the pleura, which accounting for of extra pulmonary cases is common in primary tuberculosis and may result from either contiguous spread of parenchymal inflammation or, as in many cases of pleurisy accompanying post primary disease, actual penetration by tubercle bacilli into the pleural space.

The diagnosis of tuberculous pleural effusion requires investigation of pleural fluid biochemistry, cytology and pleural biopsy. Positivity for AFB and histopathologicalstudy of pleura is very low and culture is very time consuming.

Molecular assays play important role in the diagnosis of extra-pulmonary MTb infections, such as pleuritis, peritonitis, pericarditis or meningitis, because these infections can be very difficult to diagnose by traditional methods [2].But molecular assays are very expensive test.

Ascites is the predominant finding and it is present in about 78 percent of patients with tuberculous peritonitis [3]. Because of low sensitivity of the current methods which are ascites total protein, serum-ascites albumin gradient, Ziehl-Neelson staining and culture [4, 5], a better test for diagnosis of tuberculous peritonitis is needed.

In the present study, serosal fluid ferroxidase activity of ceruloplasmin has been proposed to be a useful surrogate marker for diagnosing extra-pulmonary tuberculosis.

MATERIAL AND METHODS

The present study was carried out on 100 patients suffering from serosal effusion (pleural and peritoneal effusion)who were admitted in TB-sanatorium and in our hospital medicine ward. Among them 50 were tuberculousserosal effusion (pleural and peritoneal effusion) patients and another 50 were non-tuberculousserosal effusion (pleural and peritonealeffusion) patients with various etiologies.

Sample collection

From the study subjects appropriate serosal fluid (pleural or peritoneal fluid) aspirated and blood

sample for appropriate investigation was collected after getting written informed consent.

Detailed clinical history, physical examination and investigations like AFB staining, cytological examination, biochemical analysis and wherever possible biopsy, histopathological examination, USG, X-ray chest were done.

The serosal fluids (pleural and peritoneal fluid) were then analyzed for Ferroxidase activity of Cp by the method of Ozcan erel [6] using spectrophotometry.

Inclusion criteria

Tuberculous and non-tuberculousserosal effusion (pleural and peritoneal effusion) patients of both male and female between 20 to 60 years were included in the study.

Exclusion criteria

Cases with HIV infection, hepatocellular or renal damage, malignancies such as leukemia, lymphoma, breast carcinoma etc., enteric fever, leprosy, viral hepatitis, infectious mononucleosis and those patients not willing to give written informed consent were excluded from the study.

RESULTS

Table 1: Mean±SD values of serosal fluid Ferroxidase activity of Cp (IU/L)

Type of Fluid		Mean ± SD (IU/L)
Pleural Fluid	Tuberculous	1042±112
	Non-tuberculous	562±86
Peritoneal Fluid	Tuberculous	968±94
	Non-tuberculous	460±70

Student independent t test was used to find the P value between tuberculous and non-tuberculousserosal effusion patients.Serosal fluid Ferroxidase level ranges between 930-1154 IU/L in Tuberculous pleural effusion and 874-1062 IU/L in Tuberculous peritoneal effusion patients. In cases of non-tuberculous pleural effusion, serosal fluid ferroxidase level ranges between 476-648 IU/L and in non-tuberculous ascites it ranges between 390-530 IU/L.

In both males and females, there was highly significant P value ($P<0.001$) on comparison of the mean levels of pleural fluid ferroxidase level between tuberculous and non-tuberculous cases. Also P value was significantly high ($p<0.001$) when the mean ferroxidase level of tuberculous and non-tuberculous ascites was compared.

DISCUSSION

Pleural effusion is a common medical condition with many possible underlying etiologies like tuberculosis, pneumonia, pulmonary infection, malignant disease etc. [7]. Pleural fluid analysis and pleural biopsy are integral parts in the investigative work up of an exudative pleural effusion. For diagnosis of tuberculous pleural effusion, the yield of pleural fluid culture for MTb is low [8]. Joint sensitivity of biopsy tissue samples is as high as 90% [8], but pleural biopsy is a relatively invasive procedure and involves a long waiting time for mycobacteria culture results. Pleural fluid ferroxidase activity of Cp has thus become an important diagnostic tool in the evaluation of exudative pleural effusions.

In response to MTB infection, alveolar macrophages, neutrophils and granulocytes secrete pro-inflammatory cytokines into the blood stream. The liver responds to these cytokines release by producing acute phase proteins [9]. Ceruloplasmin (Cp) being positive acute phase protein, its level gets elevated in MTB infection. This is in accordance with studies carried out by Shinghvi and Maitra [10] and Sudha *et al*.[11].

Cp is an α2-globulin that contains 95% of the total copper found in serum [12]. Cp is an important extracellular antioxidant and free radical scavenger [13]. The study by Lee *et al*. shows that Cp by acting as a ferroxidase catalyzes the enzymatic oxidation of ferrous iron to ferric iron [14]. Thereby it facilitates iron binding with transferrin and inhibits iron uptake by bacilli [15].

Tuberculous pleural effusion (TPE) cases shows highly significant increase in pleural fluid ferroxidase level compared to non-tuberculous cases. The sensitivity and specificity for TPE was 100% and 95% respectively.

Ascites cases due to tuberculosis etiology show significantly high level of ferroxidase when compared to non-tuberculosis cases. The sensitivity and specificity for tuberculous ascites was 100% and 94% respectively.

The method of ferroxidase estimation is simple, rapid, inexpensive and highly sensitive and specific for diagnosis of tuberculousserosal effusion (Pleural and Peritoneal effusion). Hence estimation of feroxidase activity of Cp should be employed routinely to differentiate between tuberculosis and non-tuberculosis etiology in patients of pleural and peritoneal effusion.

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