Research Journal of Pharmaceutical, Biological and Chemical Sciences

Serum Ceruloplasmin Albumin Ratio as a Biochemical Marker to Assist the Diagnosis, Treatment and Prognosis of Pulmonary Tuberculosis Patients

Ramesh [1*], Rakesh Mudaraddi[2], Ravindra Maradi[3]

[1]Department of Biochemistry, Raichur Institute of Medical Sciences, Raichur.
[2] Department of Biochemistry, SDM College of Medical Sciences and Hospital, Dharwad.
[3]Deparment of Biochemistry, Kasturba Medical College, Manipal, Manipal university.

ABSTRACT

Pulmonary tuberculosis (PTB) is a global disease affecting about one third of the world's population with its attendant mortality and morbidity. Acute phase proteins have been used in monitoring the progress of infection. In the present study serum ceruloplasmin and albumin levels were determined in 75 patients of tuberculosis, of which 25 were freshly diagnosed tuberculosis patients (group I), 25 were those who were taking treatment from 1-2 months from the day of diagnosis (group II), 25 were completely treated patients (group III). 25 age and sex matched healthy controls were selected for the study. Mean $\pm$ SD of serum ceruloplasmin levels in controls, group I, group II, group III was found to be (31.896$\pm$7.122) , (61.32$\pm$ 5.744), (50.400$\pm$5.058), (33.920$\pm$6.700) respectively. Mean $\pm$ albumin levels in controls, group I, group II, group III was found to be (4.502$\pm$0.451) , (3.098$\pm$ 0.881), (3.384$\pm$0.593), (4.488$\pm$0.646) respectively. Serum ceruloplasmin albumin ratio in group I increases (0.025$\pm$0.017) p(0.001) than group II (0.015$\pm$0.003) and group III (0.008$\pm$0.002) and it was significantly lower in group II and group III. Therefore serum ceruloplasmin albumin ratio can be used as marker to assist the diagnosis, treatment and prognosis of pulmonary tuberculosis patients.
Keywords: Pulmonary tuberculosis, Ceruloplasmin, Albumin, Biochemical markers

*Corresponding author:
Email: ramesh07ainoli@gmail.com

INTRODUCTION

Pulmonary tuberculosis is communicable disease of global importance .It is caused by mycobacterium tuberculosis .Today one third of world's population is infected with tubercle bacilli,one million of these develop the disease and almost two million die out of these curable disease[1].

Inflammatory response that is usually determined by the acute phase proteins in PTB .acute phase reaction is a collective designation for change in serum protein profile and cellular immune response encompassing symptoms like fever, tiredness and general malaise induced by infection ,inflammation or trauma [1].

Albumin is one of the most important serum proteins produced in the liver.It represents 50 to 60% by weight of all plasma proteins . Recent evidence indicates that albumin may provide antioxidant protection by functioning as a serum peroxidase in the presence of reduced glutathione, which is an intracellular antioxidant [2]. Epidemiological data consistently show that reduced levels of serum albumin, is associated with increased mortality [3].

Ceruloplasmin is an acute phase protein which is normally synthesized in the liver [4]. Ceruloplasmin is an α_2- globulin that contains approximately 95% of the total serum copper, giving it a blue colour [5]. Ceruloplasmin is an important extracellular antioxidant. It also acts as a host defense mechanism by its radical scavenging an copper donar activity . Increased plasma ceruloplasmin levels are associated with generation of oxidant products ie, $^{.}O^{-}_2$ & H_2O_2. Oxidation of ferrous ion leads to superoxide ion leads to peroxidative damage.Cerculoplasmin due to its ferroxidase activity can catalyze the oxidation of Fe $^{2+}$ with concomitant production of H_2O from O_2 and acts as an acute phase reactant [6].

Aim of the present study was to determine the serum ceruloplasmin,albumin and ceruloplasmin albumin ratio to assist in the diagnosis, treatment and prognosis in the PTB patients.

MATERIAL AND METHODS

Present study was conducted in the department of biochemistry Kasturba Medical College Mangalore(KMC) .The ethical committee of the KMC approved the study .75 pulmonary TB Patients were taken for the present study ,of which 25 were freshly diagnosed pulmonary TB Patients(Group I).25 pulmonary TB Patients ,those who were taking the treatment from 1-2 months from the day of diagnosis (Group2) and 25 patients of PTB who had completed their treatment and recovered. The patients with other active medical conditions like HIV,liver , renal disease, extra pulmonary TB patients and asthma were excluded from the study .

25 age and sex matched healthy controls were selected for the study. Serum albumin was estimate by Biuret method [7] and serum ceruloplasmin was estimated by method of F.Willian et al [8].

Statistical analysis was carried out using software package for social sciences -16 version.

RESULTS

TABLE 1 Values of Ceruloplasmin, Albumin, and Ceruloplasmin to   Albumin Ratio In Controls, Group I, Group II And Group III.

Subject	Ceruloplasmin mg/dl	Albumin g/dl	Cerulopasmin/ Albumin ratio
Controls	31.896±7.122 (21-40)	4.502±0.457 (3.50-5.30)	0.007±0.002 (0.004-0.011)
Group I	61.320±5.744 (51.19-71.10)	3.098±0.881 (1.70-4.95)	0.025±0.017 (0.009-0.299)
Group II	50.400±5.058 (43-60)	3.384±0.593 (3-4.5)	0.015±0.003 (0.011-0.021)
Group III	33.920±6.700 (23-43)	4.488±0.646 (3.2-5.5)	0.008±0.002 (0.004-0.011)

Values are mean ±SD, Values in paranthesis indicate range.

1. In the present study, the mean ± SD of ceruloplasmin levels in controls, Group I, Group II and Group III were found to be (31.896 ± 7.122), (61.320 ± 5.744) and (50.400 ± 5.058). This showed that serum ceruloplasmin level increases significantly (p=0.001) in Group I as compared to normal and decreases near to normal during treatment and reaches to normal levels after complete treatment.

2. Mean ± SD of serum albumin levels in controls, Group I, Group II and Group III were found to be (4.502 ± 0.451), (3.098±0.881), (3.384±0.593) and (4.488±0.646) respectively indicating significant decrease in serum albumin levels in Group I as compared to controls and increases to near to normal during the treatment and reached to normal level after complete treatment.

3. Mean ±SD of Ceruloplasmin albumin ratio in controls, Group I, Group II and Group III were found to be (0.007±0.002),(0.025±0.017),(0.015±0.003)and (0.008±0.002) respectively ,indicating highly significant increase in the ratio(p =0.001) was found in Group I when compared to controls and during treatment ratio was near to normal and on complete treatment ratio was reverted back to normal levels.

DISCUSSION

Levels of certain proteins in plasma increase during acute inflammatory state or secondary to certain types of tissue damage. These proteins are called acute phase proteins or reactants [9].

In the present study serum ceruloplasmin level was increases in PTB patients (GroupI) as compared to normal and decreases near to normal during treatment and reaches to normal level after complete treatment .

Mean±SD of ceruloplasmin levels in controls , Group I, Group II and Group III were found to be (31.896±7.122),(61.320±5.744)and (50.4±5.058),(33.92±6.70) respectively. This showed that serum ceruloplasmin increases significantly (p=0.001)as compared to normal and decreases near to normal during treatment and reaches to normal level after complete treatment .This was in agreement with Chandra Immanuel et al, who reported C –reactive protein (CRP) and ceruloplasmin, haptoglobin and α - acid glycoprotein were significantly rised in pulmonary TB, abdominal TB and meningeal TB [10].

T. Wong [11] and J.M. Grange [12] were reported that significant increase in ceruloplasmin, α -1 antitrypsin and haptoglobulin in pulmonary TB patients as compared to normals.

P .O. Motiani et al observed that significant rise of ceruloplasmin in sputum positive pulmonary TB, as compared to sputum negative with radiological extent of disease [13]. According to Boloursaz Mohammed Reza et al, copper is mainly transported in blood by binding to ceruloplasmin and there was significant rise in serum copper in children infected with pulmonary TB and also significant rising copper/zinc ratio in TB patients than normal controls [14].

Following stimulus through infection or injury, the macrophage release a monokine, interleukin-1, which stimulates the hepatocyte to secrete a number of acute phase proteins. These acute phase reactants have been shown to serve a variety of functional roles during tissue repair of infection or inflammation and in several host immune defence mechanisms. CRP has been shown to cause bacterial capusular swelling, promotion of agglutination, complement fixation and enhancement of phagocytosis. Ceruloplasmin known to possess significant ferroxidase activity and capable of scavenging superoxide radicals is probably responsible for limiting the damage caused by these radicals [10].

In the present study Mean ±SD of serum albumin levels in controls, Group I, Group II and Group III were found to be (4.502±0.451),(3.098±0.881),(3.384±0.593) and (4.488±0.646) respectively . This showed that serum albumin significantly decreases in Group I (p=0.001) as compared to controls and increases near to normal during the treatment and reached to normal level after complete treatment .

This observation was in agreement with Adedapo k.s et al [15], Kuppamuthu Ramakrishan, etal [16]. They reported significantly decreased in albumin level in pulmonary TB as compared to normal before the treatment and level was significantly increased after treatment.

According to Elvina Karyadi et al, albumin concentration was 10% lower in TB patients than in controls. They also found that serum albumin concentration was much significantly lower in malnourished TB patients than well nourished healthy controls, malnourished healthy controls and well nourished TB patients [17].

Albumin concentration was much lower in older tuberculosis patients as compared to younger TB patients. This could be due to older persons suffering from malnutrition more frequently than younger people and also poor personal care received by older persons [18].

Infection induces a reduction in plasma albumin level in human beings as well as experimental animals. In the present study, plasma albumin levels were significantly decreased as compared to healthy controls. The possible cause for the low albumin in pulmonary TB patients were considered to be nutritional factors, enteropathy and acute phase reactions. The hepatic synthesis of acute phase proteins is induced by cytokines such as interleukin - 6 and tumor necrosis factor-α, which inhibit the production of serum albumin and cause dramatic shifts in the plasma concentration of certain essential micronutrients and albumin [16].

In the present study Mean ±SD of ceruloplasmin albumin ratio in controls, Group I ,Group II and Group III were found to be (0.007±0.002).(0.025±0.017),(0.015±0.003),and (0.008±0.002) respectively . Highly significant increase in the ratio(0.025±0.017),(p =0.001) more than the double was found in Group I when compared to controls and during treatment ratio was near to normal and on complete treatment ratio was reverted back to normal levels. This was in agreement of Hitender Singh Batra et al [19] who reported instead of ferroxidase, which increases significantly in Group I, if the ferroxidase albumin ratio is used by measuring the decreased albumin to assist in the diagnosis and therapy of pulmonary TB, then statistically significant changes were observed.

CONCLUSION

Inspite of recent in vitro nucleic acid direct amplification tests and culture of the mycobacteria in a specimen for diagnosis and prognosis of pulmonary tuberculosis, there is a definite requirement of biochemical parameters in assisting the diagnosis and follow up of pulmonary tuberculosis. Therefore ceruloplasmin albumin ratio used as a marker to assist diagnosis, treatment and prognosis of pulmonary tuberculosis patients.

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