

## HEMATOLOGICAL AND BIOCHEMICAL ABNORMALITIES IN CASE OF PULMONARY TUBERCULOSIS PATIENTS IN MALWA REGION (INDORE)

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### ABSTRACT

Malwa is a natural region in west-central northern India occupying a plateau of volcanic origin. Tuberculosis is an epidemiological problem which is associated with changing pattern of RBC indices. At least thousand deaths occur from tuberculosis each year in Indore alone. The Present study was carried out at Shri Aurobindo Institute of Medical Sciences, Manorma Raje Tuberculosis Hospital & from different DOTS Centers of Indore between March 2009 to March 2010. Hematological abnormalities were observed in study group and were significant ( $p < 0.001$ ) when the data were compared to control. The Present study concluded that alteration in RBC indices takes place due to rise in CRP level resulting anemia in PTB Patients.

### KEY WORDS

Malwa region, Hematological abnormalities, RBC Indices, pulmonary tuberculosis patients, Anemia.

### INTRODUCTION

Malwa is a natural region in west-central northern India occupying a plateau of volcanic origin. Tuberculosis (TB) is the world's second most common cause of death from infectious disease, after HIV/AIDS. Every year, approximately 2 million persons in India develop tuberculosis (TB), accounting for one fourth of the world's new TB cases. Hematological abnormalities have been associated with tuberculosis [1]. Tuberculosis is a chronic infectious disease, so anemia of inflammation may contribute significantly [2, 3, 4]. A number of studies have documented anemia in patients with TB[5,6]. The comprehensive investigations on hematological changes and abnormalities associated to tuberculosis are still lacking[7]. The Present study objective is to assess the changing patterns in biochemical parameters during tuberculosis which leads to abnormalities in RBC indices resulting anemia in such patients.

### MATERIAL AND METHOD

The Present study consists of 63 pulmonary tuberculosis (PTB) patients and 35 control subjects having 20 to 58 years age group. All newly diagnosed Pulmonary Tuberculosis Patients falling in DOTS (CAT I) were selected from the Out Patient Department (OPD) of Medicine in Shri Aurobindo Institute of Medical Sciences, Manorma Raje Tuberculosis Hospital & from different DOTS Centers of Indore and control subjects were selected from staff and students of SAIMS Medical College. We excluded patients with any other medical conditions that can cause anemia. Prior to start of study Informed consent was taken from each subject. Blood Samples were collected from each subjects and analyzed for: complete Haemogram (RBC, Hb, PCV, MCV, MCH, MCHC and RDW) values were measured by Automated Cell Counter (Sysmex KX- 21). This was based on principle of Electrical Impedance Counters. Serum C- reactive protein (by solid phase

immunoenzymatic by using kit acquired from USA), serum ferritin by the method of Ronald H et al [8], Serum iron by the method of Siedel J. et al [9] and Serum Total Iron Binding Capacity (TIBC) by the method of Tietz NW [10]. Anemic & Non-anemic Patients were selected as per WHO criteria [11].

**Statistical Analysis:** Unpaired t- test were used for statistical assessments with SPSS Version 10 to evaluate mean levels of variables in study groups. Values were expressed as Mean  $\pm$  SD.

## OBSERVATION & RESULTS

**TABLE 1: Comparison of Hematological Parameters between control Group & PTB Patients**

Parameter	Control (n = 35)	PTB Patients (n = 63)	t -value	p-value
RBC ( $\times 10^{12}/L$ )	4.78 $\pm$ 0.36	4.18 $\pm$ 0.37	6.682	< 0.001**
Hb (g/dL)	14.46 $\pm$ 1.61	11.25 $\pm$ 1.12	9.742	< 0.001**
HCT (%)	39.37 $\pm$ 3.61	32.57 $\pm$ 3.66	7.872	< 0.001**
MCV (fL)	83.09 $\pm$ 1.73	77.18 $\pm$ 5.68	5.883	< 0.001**
MCH (pg)	28.18 $\pm$ 3.59	26.96 $\pm$ 2.69	1.621	> 0.05
MCHC (g/dL)	36.30 $\pm$ 2.08	34.12 $\pm$ 2.40	4.069	< 0.001**

Values are in Mean  $\pm$  SD      \*\*highly Significant p < 0.001      p > 0.05 not significant      **DF = 96**

**Table 1:** A highly significant decrease (p < 0.001) was noted in RBC, Hb, HCT, MCV & MCHC but there was no significant change (p > 0.05) was observed in MCH.

**TABLE 2: Comparison of Biochemical Parameters between control Group & PTB Patients**

Parameter	Control (n = 35)	PTB Patients (n = 63)	t -value	p-value
Serum Iron ( $\mu\text{mol/l}$ )	16.35 $\pm$ 3.65	6.43 $\pm$ 3.47	18.54	< 0.001**
TIBC ( $\mu\text{g/dL}$ )	295.21 $\pm$ 32.2	188.20 $\pm$ 46.05	11.43	< 0.001**
Ferritin (ng/mL)	170.25 $\pm$ 30.5	325.58 $\pm$ 68.23	12.45	< 0.001**
CRP ( $\mu\text{g/mL}$ )	2.87 $\pm$ 2.34	40.55 $\pm$ 10.67	23.23	< 0.001**

Values are in Mean  $\pm$ SD      \*\*highly Significant p < 0.001      p > 0.05 not significant      **DF = 96**

**Table 2:** A highly significant decrease was noted in Serum Iron & TIBC but Ferritin & CRP levels were significant increased (p < 0.001), when these values were compared with control group.

**TABLE 3: Percentage changes in levels of biochemical & hematological parameter in PTB Patients in comparison to control subjects**

Parameter	Percentage (%) change
Serum Iron ( $\mu\text{mol/l}$ )	60.67 % decreased
TIBC ( $\mu\text{g/dL}$ )	36.24 % decreased
Ferritin (ng/mL)	91.23 % increased
CRP ( $\mu\text{g/mL}$ )	1312.89 % increased up to 1000 fold
Hb (g/dL)	22.19 % decreased

**Table 3:** The above table showed percentage increase in the level of C - reactive protein (CRP), and Ferritin whereas the level of Serum iron, TIBC and Hemoglobin (Hb) were decreased.

CHART

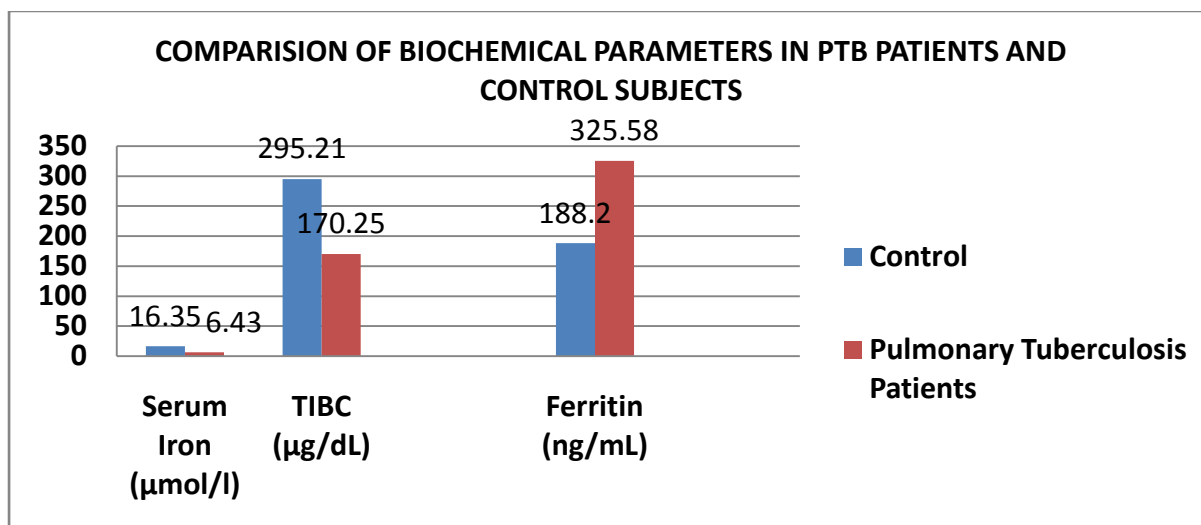


CHART 1. Comparisons of Biochemical parameters in Pulmonary Tuberculosis Patients and control subjects

**DISCUSSION**

**Comparison of Hematological parameters of PTB with control**

The mean hematological parameter (RBC, Hb, HCT, MCV, MCH & MCHC) in the study groups were lower and statistically significant ( $p < 0.001$ ) except MCH ( $p > 0.05$ ), as compared to control group (Table 1). Most of the study group showed anemic parameters. Anemia is a highly common hematologic complication among TB patients and is a strong risk factor for mortality. The previous report also showed the fall in hemogram levels in PTB Patients [1, 5, 12].

In the present study majority of PTB Patients had normocytic normochromic anemia (86 %) and few cases were of normocytic & hypochromic anemia (14 %). The present study 22.19 % reduction in percentage hemoglobin was observed in PTB Patients (Table 3). Normocytic and normochromic pattern in most of the TB patients were observed by others researchers earlier [6, 13].

**Comparison of Biochemical parameters of PTB with control**

The present study showed that there was a significant decrease in Serum iron, Hemoglobin and Total iron binding protein whereas a significant increase in the level of CRP and Ferritin (Table No. 2 and 3). The reduced level of Hemoglobin is inversely correlated with C - reactive protein in PTB patients The finding

concludes that elevated level of CRP is responsible for decline in Hemoglobin level in PTB patients. Significant & positive correlation was found between Hb & Serum iron in PTB Patients. Increased level of CRP was negatively correlated with increased level of FRT in PTB Patients. Previous report suggests that in pulmonary tuberculosis ferritin synthesis is stimulated by the inflammatory process [6, 14, 15]. It is well established that nutritional deficiency is associated with impaired immune functions [16].

In PTB Patients, a highly significant rise was noted in serum levels of C-reactive proteins (CRP), and Ferritin (FRT) as compared to control group. Elevated level of serum C- reactive protein in pulmonary tuberculosis patients has been also reported by previous study [17, 18, 19]. Various pathogenesis have been suggested in TB-associated anemia, but most studies have shown suppression of erythropoiesis by inflammatory mediators [20, 21]. Anemia due to inflammation as well as that of Iron deficiency has been reported earlier by other scientists [22]. The reason for low serum iron & TIBC in PTB patient was due to the disturbances in iron homeostasis due to alteration in C- Reactive Proteins (Table 2 & 3). The decreased level of TIBC might have been due to acute phase response and also reported low iron in patients of pulmonary tuberculosis [23, 24, 25].

On the basis of previous and present study we conclude that inflammation and the acute phase response interact with iron metabolism at several levels. Since anemia of pulmonary tuberculosis is multifactorial in origin as like anemia of chronic disease which affect iron metabolism directly and indirectly, depending upon the severity of disease condition. In PTB patients, more rise in acute phase protein leads to blunted erythropoietin resistance which is responsible for anemic condition. The subnormal values of hematological parameters were found in PTB patients, which might be associated with the underlying chronic disease condition which slowly progress in the TB patients due to poor nutrition, anorexia, increased acute phase response and severity of the disease that causes blunted erythropoietin response which in turn causes iron deregulation and anemia.

#### REFERENCES

- Singh KJ; G Ahuwalla SK; R Saxena; V.P.Chaudhary and T. Anant; Significances of hematological manifestation in patients with tuberculosis. J.Assoc. Physicians India. 2001; 49: 790-794.
- Bullen JJ; Rogers HJ & Griffiths E; Role of iron in bacterial infection. Curr. Top Microbiol Immunol 1978; 80, 1–35.
- Weinberg E; Iron and infection. Microbiol Rev 1978; 42, 45–66.
- Jurado RI; Iron, infection, and anemia of inflammation. Clin Infect Dis 1997; 25, 888–895.
- Baynes RD; Flax H; Bothwell TH; Bezwoda WR; MacPhail AP; Atkinson P; Lewis D; Haematological and iron-related measurements in active pulmonary tuberculosis. Scand J Haematol 1986; 36: 280-7.
- Morris CD; Bird AR; Nell H; The haematological and biochemical changes in severe pulmonary tuberculosis. Q J Med 1989; 73: 1151-9.
- Cartwright, G.E; 1966. The anemia of infection. Hypoferremia, hyper-cupremia and alterations in porphyrin metabolism in patients. J. Clin. Invest. 25: 65-80.
- Ronald H et al; Clin chem.1983; 2916: 1109 – 1113.
- Siedel, J; et al. (1984). Clin Chem. 30:975.
- Tietz NW (ed). Textbook of Clinical Chemistry, ed.3. Philadelphia, PA: WB Saunders; 1701-1703; 1999.
- Iron deficiency anemia. WHO Tech Rep Ser 1959; 182:4
- Al Omar IA; Al Ashban RM and Shah AH; Hematological abnormalities in Saudis suffering from pulmonary tuberculosis and their response to the treatment. Research Journal of pharmacology. 2009; 3 (4):78 – 85.
- Lee SW; Young Ae Kang; Young soon yoon; The prevalence and Evolution of Anemia Associated with Tuberculosis. J Korean Med Sci 2006; 21: 1028 -1032.
- Henderson A; Ferritin levels in patients with microcytic anaemia complicating pulmonary tuberculosis. Tubercle. 1984; 65 (3):185-9.
- Henrik Friss; Nyagosya Range; Camilla Braendgaard Kristensen; Pernille kaestel; Acute phase response and iron status marker study in Mwanza, Tanzania. British journal of Nutrition. 2009; 102: 310- 317.
- Perronne C; Tuberculosis, HIV infection, and malnutrition: an infernal trio in central Africa. Nutrition.Apr 1999; 15(4):321-322.
- De Beer FC; Nel AE; Gie RP; Donald PR; Strachan AF; Serum amyloid A protein and C-reactive protein levels in pulmonary tuberculosis: relationship to amyloidosis. Thorax. 1984; 39(3):196-200.
- G. K. Schleicher; V. Herbert; A. Brink; S. Martin; R. Maraj; J. S. Galpin; and C. Feldman; Procalcitonin and C-reactive protein levels in HIV-positive subjects with tuberculosis and pneumonia. Eur.Respir. J 2005 vol. 25. (4) 688-692.
- Rao, Sukhesh; Bernhardt, Vidya; Serum C - reactive protein in Pulmonary Tuberculosis: Correlation with Bacteriological Load and Extent of Disease. Infectious Diseases in Clinical Practice: 2009; 17 (5):314-316.
- Means RT., Jr Recent developments in the anemia of chronic disease. Curr Hematol Rep.2003; 2:116–121.
- Weiss G; Goodnough LT; Anemia of chronic disease. N Engl J Med. 2005; 352:1011–1023.
- Das Bhabani S; Uma Devi C; Mohan Rao; Vinod K. Srivastava and Pramod K.Rath; Effect of iron supplementation on mild to moderate anemia in pulmonary tuberculosis. British Journal of Nutrition. 2003; 90: 541- 550.
- Fleck A & Myers MA; Diagnostic and prognostic significance of acute phase proteins. In the Acute Phase Response to Injury and Infection. 1985: 249-271 (AH Gordon and A Koj,editors). Amsterdam : Elsevier science publishers.
- Punnonen K; Irjala K; Rajamaki A; Iron-deficiency anemia is associated with high concentrations of transferrin receptor in serum. Clin Chem 1994; 40(5):774-6.
- Elvina Karyadi; Wil MV Dolmans; Clive E West; Reinout Van Crevel; Ronald HH Nelwan; Zulkifli Amin et al; Cytokines related to nutritional status in patients with untreated pulmonary tuberculosis in Indonesia. Asia Pac J Clin Nutr. 2007; 16 (2): 218 – 226.



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