

# Study of Hematological Profile and Effect of Antitubercular Medications on the Hematological Derangements in Patients Suffering from Tuberculosis

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## Abstract

Tuberculosis (TB) affects large number of people, especially the low socioeconomic status. It continues to intimidate the human race since time immemorial Tuberculosis can cause various haematological abnormalities. The comprehensive study on haematological changes and abnormalities associated with tuberculosis are still lacking. Also there is no systematic documentation about pre-treatment and regular follow up of post-treatment changes in haematological parameters of patients suffering from TB. In this study, an attempt has been made to investigate haematological changes in adult patients suffering from TB and whether deranged haematological parameters in them improves after intensive phase (IP) of antitubercular treatment (ATT). Fifty bacteriologically proven cases of pulmonary and extrapulmonary tuberculosis (EPTB) were studied for various haematological changes at diagnosis and at the end of IP ATT by using automated hematology analyser. At the end of IP ATT, in the RBC series there was statistically significant improvement in the mean haemoglobin, Packed Cell Volume (PCV), Red cell distribution width (RDW), Mean Corpuscular Volume (MCV), Mean corpuscular Hemoglobin (MCH) and Mean Corpuscular Hemoglobin concentration (MCHC) In the WBC series, mean WBC count and mean granulocyte count in males showed a significant decrease. Rest of the WBC series showed no significant difference in both the groups before and after treatment. In the platelet series, mean platelet volume and mean platelet distribution width showed significant improvement after IP ATT. Thus various haematological changes occur in tuberculosis and these parameters improved after IP ATT without any transfusion of blood products.

**Keywords:** Haematological Changes; Post Treatment; Pre-Treatment; Tuberculosis.

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## Introduction

Tuberculosis is a common disease in developing countries like India where each year about 2.7 lakhs die of tuberculosis. Every day in India more than 900 people die of TB (i.e. 2 death every 3 minutes) [1]. PTB is the most common form of TB (more than 85% of all tuberculosis cases) while EPTB can affect almost any organ in the body. Though the bacilli was discovered over a century back (1882, Robert Koch's) and drugs have been available for more than 70 years, nearly a third of world population has been infected with TB bacilli i.e. have a latent infection and of these 10%

have lifetime risk of developing active disease. Poor living condition, debility, malnutrition and immune compromised state predisposes to disease.

The atypical and varied spectrum of clinical presentation of tuberculosis poses a diagnostic and therapeutic challenge to the physician. The comprehensive study on haematological changes and abnormalities associated to tuberculosis are still lacking [2]. Moreover studies on haematological profile in tuberculosis have also not been fully determined in TB patients living in developing countries like India. Various hematological manifestations in tuberculosis are [3].

- Anemia
- Leucocyte changes: leucopenia or leukocytosis
- Lymphocytopenia or Lymphocytosis
- Neutropenia or Neutrophilia
- Monocytopenia or Monocytosis
- Thrombocytopenia or thrombocytosis
- Pancytopenia
- Leukemoid reactions
- Deep Vein Thrombosis
- Disseminated intravascular coagulation

Hematological parameters are useful indicators of severity in TB infection [5]. Early detection and effective treatment are important strategy to control the spread of tuberculosis in the community. Also by testing the underlying cause of abnormal haematological parameters like tuberculosis, we can avoid unnecessary treatment like blood, platelet and blood product transfusion.

In this study, an attempt has been made to investigate hematological changes in adult patients suffering from TB and whether deranged hematological parameter in these patients improves after IP of ATT (8 weeks for CAT – I, 12 weeks for CAT II).

### Materials and Methods

A hospital based prospective study was done for a period of six months in Department of Respiratory Medicine, Sikkim Manipal Institute of Medical Sciences, Gangtok, India

### Inclusion Criteria

All bacteriologically proven cases of pulmonary and extra pulmonary tuberculosis, as per the RNTCP guidelines, were included in the study.

### Exclusion Criteria

1. Patients with any other medical condition that can cause hematologic abnormalities such as chronic renal disease, liver diseases, haemoglobinopathies, malignancy, HIV/AIDS, auto immune disease, drugs.
2. Those that cannot be followed up to end of intensive phase of treatment of TB.
3. Patients who are on hematinic or have received blood transfusion in the past 3 months before ATT.

### Sample Size

A total of fifty patients who were enrolled in department of Respiratory Medicine in the fourth quarter of 2016 and fulfilled the above criteria were taken in the study

### Data Collection

After approval from Institutional Ethics Committee, Sikkim Manipal Institute of Medical Sciences, written informed consent was taken from the participants. A detailed clinical history was taken with emphasis on age, sex, caste, occupation, duration of symptoms and specific complaints like fever, chest pain, shortness of breath, expectoration, loss of appetite, weight loss, back pain, joint pain, pain abdomen and other constitutional symptoms. A clinical diagnosis was made after thorough physical examination and following investigations were done.

1. Sputum for Acid Fast Bacilli (AFB),
2. Chest x-ray.
3. Pus for AFB in selected group of patients
4. FNAC of lymph nodes in selected cases.
5. Hematological profiles which included:
  - Hemoglobin (Hb)
  - Hematocrit (Hct)
  - Total RBC Count (RBC)
  - Red cell distribution width (RDW)
  - Total leucocyte count (TLC)
  - Differential leucocyte Count (DLC)
  - Mean Corpuscular Volume (MCV)
  - Mean Corpuscular Hemoglobin concentration (MCHC)
  - Mean corpuscular Hemoglobin (MCH)
  - Platelet count (PLC)
  - Mean Platelet Volume (MPV)
  - Platelet Distribution Width (PDW)
  - Peripheral smear

The analysis was performed by using automated hematology analyzer Beckman Counter Act Diss 5. The data obtained was collected in a proforma sheet .

### Statistical Analysis

The results were expressed in percentages represented by tables and statistically analyzed by appropriate test of significance (t- test and chi square

test with 95% confidence interval).

**Treatment**

All patients diagnosed to have tuberculosis were given standard Category 1 or category 2 ATT under RNTCP DOTS based on previous history of ATT intake. Isoniazid, Rifampicin, Pyrazinamide, and Ethambutol for CAT-1 and Streptomycin along with above drugs for CAT-2 patients were given.

**Results**

Out of 50 patients in the study population, males were 37(74%) and females were 13(26%). Mean age

for males and females were 37.83 and 35.15years respectively. Majority of males were in the age group 46-60 years (26%) and in females, majority were in the age group 31-45 years (12%). 15(30%) males were labourers and in females, majority 11(22%) were housewives. Majority 34(68%) of patients belonged to low socio economic group followed by middle socio economic status 16(32%). Most of the patients presented with cough and fever 48(96%) & 45(90%) respectively, followed by loss of appetite in 31(62%) and loss of weight in 28(56%). Other less common symptoms were expectoration, hemoptysis, breathlessness and chest pain. 48(96%) had PTB and 2(4%) cases had extra pulmonary TB. In extra pulmonary tuberculosis, tubercular cold abscess and

**Table 1:** Showing Red Cell Indices before and after treatment

RBC Indices	Males n=37				P Value	Females n=13				P Value
	Before Treatment		After Treatment			Before Treatment		After Treatment		
	Mean	SD	Mean	SD		Mean	SD	Mean	SD	
HB(g/dl)	8.96	2.13	10.83	1.69	P=0.00	8.56	2.12	10.60	2.02	P=0.00
PCV (%)	28.48	6.04	39.69	4.61	P=0.00	27.90	6.21	36.74	5.79	P=0.00
RBC(X 10 <sup>12</sup> /l)	4.07	0.92	4.23	0.59	P=0.182	4.07	0.9	4.22	0.92	P=0.287
RDW (%)	15.38	2.28	13.52	0.86	P=0.00	16.92	2.6	13.63	1.03	P=0.00
MCV(fl)	69.46	8.44	78.69	5.1	P=0.00	68.84	6.69	76.39	4.01	P=0.00
MCH(Pg)	22.46	3.74	28.86	2.36	P=0.00	21.14	3.1	28.66	2.21	P=0.00
MCHC(g/dl)	31.77	1.87	32.87	0.99	P=0.00	30.57	2.35	32.14	1.07	P=0.006

tubercular empyema comprised one case each in the study population.

The mean haemoglobin level in males was 8.96± 2.13 g/dl and in females 8.56±2.12 g/dl before treatment and after intensive phase ATT it increased to 10.83± 1.69 g/dl in males and 10.60 ± 2.02 g/dl in females which was statistically significant (P=0.00).

The mean PCV level was 28.48 ± 6.04 % and 27.90 ± 6.21 % in males & females respectively before treatment which increased to 39.69 ± 4.61 % and 36.74 ± 5.79 % respectively which is statistically significant (P=0.00).

**Table 2:** Showing WBC series pre-treatment and post treatment.

WBC Series	Males n=37				P value	Females n=13				P value
	Before Treatment		After Treatment			Before Treatment		After Treatment		
	Mean	SD	Mean	SD		Mean	SD	Mean	SD	
Total Leucocyte Count(X10 <sup>9</sup> /L)	10.72	53.63	8.54	14.30	P=0.014	9.61	36.50	8.55	93.77	P=0.230
Granulocyte (%)	81.42	8.1	77.93	2.85	P=0.006	78.57	11.43	74.47	5.84	P=0.241
Lymphocyte (%)	12.84	5.71	15.48	4.27	P=0.012	17.12	11.91	17.43	3.41	P=0.929
Monocyte (%)	5.79	5.29	6.69	3.63	P=0.225	7.20	4.433	7.88	3.83	P=0.656

The mean RBC count in males and females were similar (4.07 x 10<sup>12</sup>/L) before treatment. After treatment, it increased to 4.23± 0.59 in males and 4.22 ± 0.92 in females which was statistically not significant (P=0.182, male) (P=0.287, female).

The mean RDW in males was 15.38 ± 2.28 % and 16.92± 2.6 % in females before treatment. After IP ATT it was reduced to 13.52 ± 0.86 % in males and 13.63 ± 1.03 % in females. The reduction was statistically significant (P=0.00).

The change in mean MCV, MCH and MCHC from pre-treatment to post treatment, as depicted in Table 1,

**Table 3:** Showing platelet series pre-treatment and post treatment

Platelet Series	Males n=37				P Value	Females n=13				P Value
	Before Treatment		After Treatment			Before Treatment		After Treatment		
	Mean	SD	Mean	SD		Mean	SD	Mean	SD	
TPC( $\times 10^9/l$ )	3.81	1.39	3.56	1.26	P=0.407	3.65	2.02	3.14	0.66	P=0.338
MPV( $\mu m^3$ )	8.16	1.35	9.70	1.38	P=0.00	8.43	1.14	9.69	1.4	P=0.001
PDW (%)	10.77	3.36	11.94	1.37	P=0.010	12.74	3.16	12.24	1.83	P=0.476

was statistically significant. ( $p=0.00,0.00,0.006$  respectively.)

The mean WBC count ( $10^9/L$ ) before treatment for males was  $10.72 \pm 53.63$  which was greater than in females ( $9.61 \pm 36.50$ ). After IP ATT, it was significantly reduced in males ( $P=0.014$ ) but not in females ( $P=0.230$ ). The mean granulocyte count in males showed a significant decrease ( $P=0.006$ ) after treatment with ATT, but no significant decrease in females ( $P=0.241$ ). Rest of the WBC series showed no significant difference in both the groups before and after treatment with anti tubercular medications.

The mean platelet count (TPC) was within normal range in both males and females before and after treatment. The platelet series showed significant difference in MPV and PDW before and after treatment in males and in females, after treatment MPV was increased statistically significantly ( $P=0.001$ ). Rest of the platelet series showed no significant changes before and after treatment in both males and females ( $P>0.05$ ).

In the peripheral smear study, neutrophilia was seen in 22(44%) of cases, leucocytosis in 12(24%) followed by thrombocytosis in 7(14%). Others were having monocytosis 3(6%), thrombocytopenia 3(6%), leucopenia 2(4%) and monocytopenia 1(2%). Following IP ATT most of the patients had normal counts. Peripheral smear revealed hypochromic microcytic picture in 35(70%) patients followed by normochromic normocytic in 15(30%) patients at presentation. After treatment, 38(76%) patients had normochromic normocytic anaemia and 12(24%) patients had hypochromic microcytic anaemia respectively. There were no cases having normochromic microcytic or macrocytic anaemia in the whole population under study.

## Discussion

### Demographic Distribution

In this study males were affected more than females with tuberculosis. This finding is similar to the study

according to Kannan S. et al [4] where 76% males and 24% females were affected. Causes of this predominance in men in relation to women have been cited as biological differences such as immunity, exposure to M. tuberculosis associated with different social miscegenation profiles and social behaviours including smoking [5].

Mean age for males was 37.83 years and females were 35.15 years which shows that the economically productive age group people were most commonly affected with tuberculosis. Present study showed that poor socioeconomic status people were more prone for tuberculosis. This may be due to low body mass index and indoor air pollution, overcrowding, which is common in low socio economic status people. TB is a poverty related disease which is associated with poor living condition, lack of financial support, less access to health care services.

Symptoms of presentation in this study were almost similar to previous studies. Chest symptoms were seen more in this study which may be due to more number of PTB patients than the EPTB.

### Blood Cell Indices and Response to Antitubercular Medications

#### RBC Indices

In this study, at the time of diagnosis of tuberculosis, the mean haemoglobin level were significantly lower than the healthy population (14-16g/dl for male and 13-15g/dl for females). According to Omar AL I.A et al [6], mean haemoglobin level in males was 12.58 g/dl and females 11.54g/dl respectively which was also significantly lower than the healthy population. This low level may be due to nutritional deficiencies, worm infestations and the tubercular disease itself. After treatment with ATT, mean haemoglobin level increased significantly which is due to correction of the inflammatory process in the bone marrow or correction of nutritional deficiency due to improvement of appetite. The hematocrit values increased proportionately.

The mean red cell distribution width in males and females was higher compared to healthy population (normal: 11-15%). After treatment with ATT, RDW normalised in both was statistically significant. The low RDW may be due to nutritional deficiency.

Anaemia was present in majority of the patients. The observations are in agreement with the earlier reports which showed mild anaemia to be a common feature in PTB patients. The precise mechanism for anaemia in tuberculosis is not known, however, anaemia due to inflammation as well as that due to iron deficiency has been implicated. Factors such as decrease in red cell survival and reduced erythropoietin response by the bone marrow erythroid cells are also known to cause anaemia.

Anaemia was predominantly hypochromic microcytic in 35(70%) patients followed by normochromic normocytic in 15(30%) patients at the time of presentation. After treatment 38(76%) had normochromic normocytic anaemia and 12(24%) patients had hypochromic microcytic anaemia respectively. This result was in contrast to the previous studies which showed majority of patients (95%) had normochromic normocytic anaemia in tuberculosis. This may be due to the fact that after treatment with antitubercular drugs, anaemia improved but was not fully corrected, reflecting anaemia of chronic disease.

In the present study, the mean MCV, MCH and MCHC was significantly lower in both males and females as compared to the healthy population (MCV:  $87 \pm 5$  fL, MCH:  $29.5 \pm 2.5$  Pg, MCHC:  $34 \pm 2$  g/dl). After treatment, mean MCV, MCH and MCHC values increased significantly ( $P=0.00$ ). However even after the increase the values were lower as compared to the healthy population.

#### WBC Series

In this study, the mean WBC count before treatment for males was greater than in females and also greater than to previous study done by Omar Ali. A et al (Male- $10.32 \times 10^9/l$  and Female- $8.88 \times 10^9/l$ ). After treatment with ATT, the mean WBC count reduced both in males and females. The increase in mean total leucocyte count at diagnosis favoured the previous studies indicating leucocytosis in patients with tuberculosis. The increase in WBC count in tuberculosis might be due to bone marrow reactive response to infection. WBC count decreased after ATT which is probably due to decrease in infection load leading to decrease in the reactive response.

The mean lymphocyte percentage before treatment which was very low compared to healthy population

(Normal: 20-50%). After IP ATT, the mean lymphocyte percentage had a significant difference in between males before and after treatment ( $P=0.012$ ) but not in females. According to Onwubalili J. K et al [7] both lymphocytosis and lymphopenia has been observed.

#### Platelet Series

The mean platelet count in present study was within normal range of healthy population (1.5-4 lakh/cu.mm). There was no significant difference in mean platelet count before and after treatment with anti tuberculosis medications both in males and females.

Study by Omar Ali A. et al showed mean platelet count of 3.74 lakh/cu.mm in males and 3.85 lakh/cu.mm in females which was almost similar to findings in this study. Earlier reports showed both thrombocytosis [8] and thrombocytopenia [9] in tuberculosis. But in this study, platelet count was not affected in tuberculosis. The cause for thrombocytopenia may be due to an immune phenomenon due to production of antibodies and to reactive myeloid hyperplasia. It was also suggested that thrombocytopenia might be due to active tuberculosis and possible peripheral destruction of platelets by the mycobacterium or hyperactive splenomegaly.

The mean platelet volume in the study group was in females before treatment was less than the healthy population ( $9.7-12.8 \mu m^3$ ). After treatment with antitubercular drugs, it increased and the increase was statistically significant. The mean platelet distribution width in present study was lower than the healthy population (15.5-18.1%). After IP ATT, the improvement was statistically significant in males ( $P=0.010$ ) but not in females ( $P=0.476$ ).

#### Conclusion

Various types of haematological changes occur in tuberculosis and these haematological parameters improved with anti tubercular medications without any transfusion of blood products. Also the differential diagnosis of tuberculosis should be considered in patient with varied haematological abnormalities.

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