

# A study of total and differential leucocyte count with severity of lung disease in pulmonary tuberculosis

Laxmikant Chavan<sup>1\*</sup>, Saket Kumar Mandal<sup>2</sup>, Raju M Jotkar<sup>3</sup>

<sup>1</sup>Medical Superintendent, Sub District Hospital, Karjat, Raigad, Maharashtra, INDIA.

<sup>2</sup>Resident Physician, Jurong Heath, SINGAPORE.

<sup>3</sup>Deputy Director Health Services, Public Health Department, Aarogya Bhavan, Mumbai, Maharashtra, INDIA.

Email: [laxmikantchavan@gmail.com](mailto:laxmikantchavan@gmail.com)

## Abstract

**Background:** Hematological investigation and basic biochemical tests are routinely, or rather invariably, carried out during the work up of a case of tuberculosis. Studies have shown that hematological and biochemical abnormalities in tuberculosis are common. This cross sectional study was carried out to identify the presenting laboratory features that may help differentiate a freshly diagnosed and uncomplicated case of tuberculosis from other diseases and to correlate it with the severity of pulmonary tuberculosis. **Material and Methods:** The study subjects included 100 patients above 12 years of age without HIV co-infection of newly diagnosed cases of pulmonary and extrapulmonary tuberculosis diagnosed. The DLC and platelet counts were further confirmed with Feild or Leishman's stains using EDTA anticoagulated blood. Initially, a slide was made by spreading a drop of blood on the slide to make a film of at least 3 cm in length. Thickness such that there was some overlap of red cells throughout much of the film's length. **Results:** Out of the 100 cases of tuberculosis collected from our hospital, 55 patients were PTB, and 45 were of extra-pulmonary tuberculosis. The incidence of leucocytosis increased from 1 in 11 cases in mild, 9 in 23 with moderate and 11 in 21 with severe lung involvement. However, in all only 21 out of 55 cases of pulmonary TB showed mild leucocytosis. Lymphocytosis was seen in 2 cases of mild and 3 cases of moderate lung involvement. Increasing lymphopenia was seen with increasing severity of lung parenchymal involvement. 2 cases of eosinophilia were seen. **Discussion:** these parameters can be used as indicators in the assessment of response to chemotherapy. In view of the varied haematological abnormalities observed in patients with tuberculosis in patients of this geographical location. We suggest the differential diagnosis of tuberculosis should be entertained in patients with varied haematological disorders


**Keywords:** Tuberculosis, haematological abnormalities, leucocytosis, lung involvement.

## \*Address for Correspondence:

Dr. Laxmikant Chavan, Medical Superintendent, Sub District Hospital, Karjat, Raigad, Maharashtra, INDIA.

Email: [laxmikantchavan@gmail.com](mailto:laxmikantchavan@gmail.com)

Received Date: 04/06/2016 Revised Date: 19/07/2016 Accepted Date: 12/08/2016

Access this article online	
Quick Response Code:	Website: <a href="http://www.medpulse.in">www.medpulse.in</a>
	DOI: 14 August 2016

## INTRODUCTION

Despite the advances and the fact that nearly all cases can be cured, tuberculosis remains one of the world's biggest threats. In 2014, TB killed 1.5 million people (1.1 million HIV-negative and 0.4 million HIV-positive). The toll comprised 890000 men, 480000 women and 140,000

children<sup>1</sup>. Tuberculosis (TB) is highly prevalent chronic devastating disease caused by *Mycobacterium tuberculosis* present globally especially in the developing countries including India. Reversible peripheral blood abnormalities are commonly associated with pulmonary tuberculosis and these hematological changes act as marker for the diagnosis, prognosis and response to therapy. Hematological investigation and basic biochemical tests are routinely, or rather invariably, carried out during the work up of a case of tuberculosis. Studies have shown that hematological and biochemical abnormalities in tuberculosis are common and varied with a study concluding that the differential diagnosis of tuberculosis should be entertained in patients with those varied hematological disorders<sup>2,3</sup>. Some hematological markers may also reflect response to treatment. The WBC exhibited varying degree of alteration with neutropenia and lymphopenia. Some haematological abnormalities are

quite common in patients with pulmonary TB and physicians must maintain a high index of suspicion for diagnosis of pulmonary TB in patients with these abnormalities. The comprehensive investigations on hematological changes and abnormalities associated with tuberculosis have been incompletely investigated. This cross sectional study was carried out to identify the presenting laboratory features that may help differentiate a freshly diagnosed and uncomplicated case of tuberculosis from other diseases and to correlate it with the severity of pulmonary tuberculosis (PTB).

### MATERIAL AND METHODS

The study subjects included 100 patients of newly diagnosed active cases (defined as up to two weeks after the start of antituberculous treatment) of pulmonary and extra-pulmonary tuberculosis diagnosed between October 2006 to October 2008 in the Medicine and Chest TB department of Mahatma Gandhi Mission's Medical College, New Mumbai. The inclusion criteria were patients first time diagnosis, no current or previous anti-tuberculous drug treatment, and not to be suffering from any other chronic disease. The exclusion criteria included past history of pulmonary TB, currently on antituberculous drug or any other drugs which affected bone marrow or peripheral blood, and known at the time of study to have a chronic disease which will adversely affect the body systems including the bone marrow and the peripheral blood. Depending on the site/s involved, TB was classified as pulmonary or extra-pulmonary as per WHO guidelines<sup>4</sup> and disseminated if the patient had miliary TB or involvement of two or more organ systems. Detailed clinical history and physical examination was done of all the enrolled patients. Pulmonary TB patients were diagnosed on the basis of positive sputum smears for acid fast bacilli (AFB), and /or radiographic reports, skin tests and positive culture reports. For extra pulmonary TB, detection of AFB in the samples, radio-imaging reports, skin tests and positive culture reports were taken into account. Data was collected pertaining to demographics and past history of contact with, or treatment for TB, Skin test results, bacteriologic studies, radiographic reports, and symptoms upon presentation were also assessed for each subject. Blood for estimation of hemoglobin, leucocyte count and differential leucocyte count were collected in EDTA bulb. These investigations were done through SYSMEX (KX-21) 3 cell counter. The KX-21 employs 3 detector blocks and 2 kinds of reagent for blood analysis<sup>20</sup>. The hemoglobin detector block used non-cyanide hemoglobin method. WBC detector block gave DLC as neutrophils, lymphocytes and mixed. The DLC and platelet counts were further confirmed with Feild or Leishman's stains<sup>5</sup> using EDTA

anticoagulated blood. Initially, a slide was made by spreading a drop of blood on the slide to make a film of at least 3 cm in length. Thickness such that there was some overlap of red cells throughout much of the film's length. **Field's stain:** It is a quicker method. The film was fixed on methanol, later poured off. 12 drops of diluted (1:4) stain B (eosin), immediately followed by 12 drops of stain A. After mixing the slides were rinsed in water for a minute. Finally, subjected to phase buffer 6.6 for 5 seconds. **Leishman's stain:** Dry the film in air and flood the slide with stain. After 2 minutes add double the volume of water and stain the film for 5–7 minutes, then wash it in a stream of buffered water till it acquires a pinkish tinge (upto 2 minutes). Then dry and examine.

### RESULTS

A total of 100 patients newly diagnosed as pulmonary and extra pulmonary TB were enrolled in this present study. Of the 100 patients, 63 (63%) were under 40 years of age (range 12 to 39), whereas, 37 (37%) were more or equal to 40 years of age (range 40 to 78). Mean age of young adults (below 40 years) was  $32.71 \pm 3.7$  years and elderly (more than or of 40 years) was  $67.57 \pm 1.03$  respectively. The incidence of leucocytosis increased from 1 in 11 cases in mild, 9 in 23 with moderate and 11 in 21 with severe involvement. However, in all only 21 out of 55 cases of pulmonary TB showed leucocytosis, usually mild (Graph 1,2). Neutrophilia was seen in 3 out of 11 cases of mild lung involvement, 16 of 23 cases of moderate and further increasing to 16 out of 21 cases of severe involvement. No cases of leucopenia or neutropenia were observed. Lymphocyte counts were normal in 33 out of 55 cases. Lymphocytosis was seen in 2 cases of mild and 3 cases of moderate lung involvement. Increasing lymphopenia was seen with increasing severity of lung parenchymal involvement. 2 cases of eosinophilia were seen.

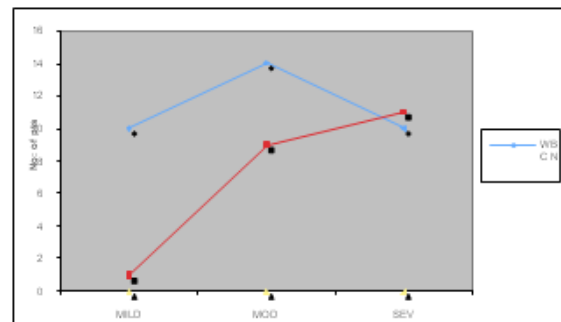


Figure 1: Relation of WBC with Severity of Lung Disease

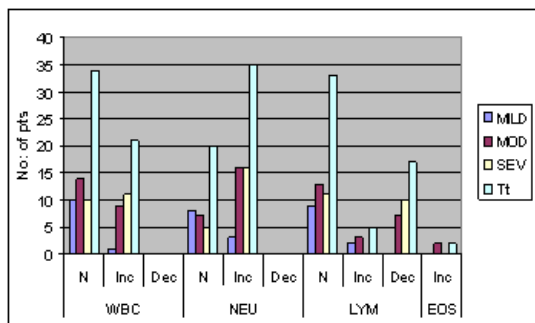


Figure 2: Relation of WBC and Differential count with Severity of Lung Disease

Patients with effusion and lung involvement 2 out of 9 cases had leucocytosis and 7 cases; had neutrophilia. With isolated pleural involvement 2 out of 20 cases showed leucocytosis and 10 showed neutrophilia. Looking at it in another way, WBC was normal in 25 out of 29 cases of pleural effusion (Graph 2). Neutrophilia was seen more commonly (Graph 3). Increased lymphocytes were seen in 3 cases of pleural effusion. Decreased lymphocytes were seen in 6 cases of pleural effusion. Eosinophilia was seen in 1 case. With disseminated diseases, leucocytosis was seen in relatively more cases, i.e. in 6 out of 11 cases and neutrophilia was seen in 7 out of 11 cases. 1 and only case of leucopenia was seen here with miliary lung disease. Both the cases of lymph node TB and all 3 cases of abdominal TB had normal WBC count.

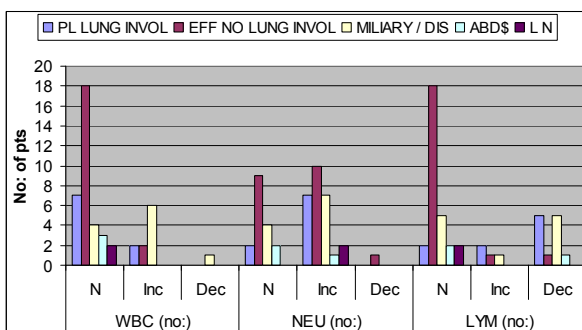


Figure 3: Determination of WBC and Differential count in Extrapulmonary TB

Graph 4 evaluates the neutrophilia and leucopenia along with leucocytosis. As seen leucocytosis was associated with neutrophilia in almost all except 3 cases of PTB. Lymphocytopenia was seen in 12 out 20 cases of PTB with leucocytosis, all 4 effusion cases and in 2 cases of disseminated cases with leucocytosis. Five cases of pulmonary TB, 2 cases of pleural and 3 cases of miliary/disseminated TB was associated lymphocytopenia with normal WBC (however, it may be noted that even these cases of lymphopenia were invariably associated with increased neutrophil percentage).

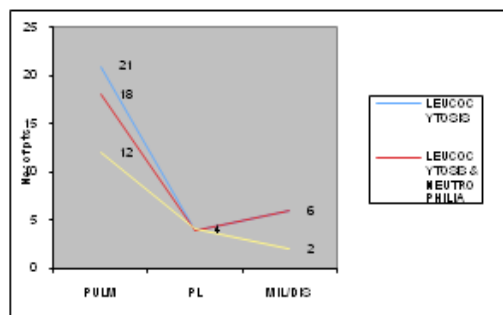


Figure 4: Determination of Leucocytosis and Neutrophilia in TB Patients

## DISCUSSION

Haematological and biochemical abnormalities in pulmonary tuberculosis are common and may be valuable aids in diagnosis. Most commonly the WBC and DC were found to be normal, followed by leucocytosis with neutrophilia and associated lymphopenia. Leucocytosis was seen in only 21 out of 55 or 38% of cases of PTB. Neutrophilia was seen in 63% of cases. Lymphocytopenia was much more common, seen in 32% as compared to 10% of cases with lymphocytosis. Raised eosinophil count was seen in 2 cases of PTB. The number of patient with leucocytosis and neutrophilia increased with increasing severity of lung lesions. Leucocytosis was seen in only 9% of patients with mild affection as compared with 52% of patients with severe lung involvement. Leucocytosis if seen was usually mild. In only 2 cases did it increase more than 15,000/cmm, 1 of the cases showing leukemoid reaction. Thus with very high values of WBC, other differential may be thought of. No cases with monocytosis were seen. These findings were in accordance with earlier studies<sup>6</sup>. A total of 17 cases of neutrophilia in PTB, 13 in pleural and 1 case of miliary TB was probably associated normal WBC. Hence, there were 18 cases of PTB having leucocytosis with neutrophilia, 12 of them had associated lymphopenia. While 4 cases of effusion had leucocytosis with neutrophilia with relative lymphopenia and 6 cases of disseminated TB had leucocytosis with neutrophilia. 2 of them showed decreased lymphocytes. The lymphopenia seen in some of these were invariably secondary to increased percentage of neutrophils. Still, the most common abnormality seen with TB was normal WBC with normal DC seen in 11 cases of pleural, 20 cases of pulmonary, and 2 cases of abdominal TB accounting for 1/3rd of all cases. With miliary/disseminated TB, only 3/11 cases showed normal WBC and DC. Olaniyi *et al*<sup>7</sup>, found that in pre-treatment sputum smear-positive cases leucocytosis was seen in 22.3%, neutrophilia in 45.2% and lymphocytopenia in 4.8% of the patients. Kourbatova<sup>8</sup> found leucocytosis in 25% of cases.

Akitunde EO *et al*<sup>9</sup>, found neutrophilic leucocytosis in 40% of the patients with untreated PTB. Lymphopenia was seen in 46% as compared to 6% cases with lymphocytosis. They observed that in suspected cases of PTB, lymphocytopenia rather than lymphocytosis should be considered. Singh *et al*<sup>3</sup>, also found lymphocytopenia, monocytopenia, leucocytosis, neutrophilia, lymphocytosis and monocytosis among other findings. Morris *et al*<sup>2</sup>, noticed leucocytosis with neutrophilia in 40% of patients with severe PTB, lymphopenia in 17% and monocytopenia in 50%. Wessels G *et al*<sup>10</sup>, found neutrophilia, and monocytosis most commonly in pediatric age group, however, they found these changes with equal frequency in control patients also. Among EPTB, abnormalities in WBC was seen more commonly with miliary/disseminated TB. Leucopenia was seen in 1 case, but the most common was leucocytosis with neutrophilia, WBC being normal in only 4 out of 11 cases. LN and abdominal TB had normal WBC with only 2/5 patients having neutrophilia. 4 of 29 cases of effusion had leucocytosis and neutrophilia with lymphopenia. In effusion with lung lesions, leucocytosis and neutrophilia were seen in 22% and 78% of patients as compared to 11% and 50% in fusion without detectable lung lesion. These figures are higher if compared with study of EPTB by Hee Jung Yoon *et al*<sup>11</sup>. They noticed leucocytosis in only 12.8% of EPTB patients. Here the pleural cases had leucocytosis in only 8.1% cases and miliary TB patients had leucocytosis in 11.1% of patients. Maartens G *et al*<sup>12</sup>, have found leucopenia in 15% as compared to 9% of cases with miliary TB in this study and lymphopenia in 87% as compared to 45% in this study. Also, Singh *et al*<sup>2</sup>, found leucopenia with neutropenia in almost 25% of cases. However, the sample size for miliary TB in our study was much smaller. Patients with tuberculosis had significant lymphopenia associated with anaemia, neutrophilia and monocytosis. None of these derangements correlated with radiological extent of lung disease or cutaneous tuberculin reactivity. Lymphocyte counts returned to normal within 2 weeks of initiating chemotherapy in all lymphopenic patients and normal ranges for all blood counts were restored by 6 months in all the patients studied. In a smear-negative patient, a clinical diagnosis of tuberculosis would be supported by the finding of lymphopenia, not lymphocytosis. This finding is in accordance with former study in which

increased numbers of neutrophils and lymphocytes in TB patients were reported in Ibadan, Nigeria<sup>7</sup>. However, these parameters can be used as indicators in the assessment of response to chemotherapy. In view of the varied haematological abnormalities observed in patients with tuberculosis in patients of this geographical location. We suggest the differential diagnosis of tuberculosis should be entertained in patients with varied haematological disorders and effective awareness programmes should be launched in rural areas to minimize the chances of spread of the disease.

## REFERENCES

1. WHO, Global tuberculosis report. 2015:2.
2. Charles DW Morris, Arthur R Bird and Haylene Nell. The Hematological and Biochemical Changes in Severe Pulmonary Tuberculosis. Q J Med. 1989; 73: 1151–1159.
3. Singh KJ, Ahluwalia G. Significance of hematological manifestations in patients with tuberculosis. J Assoc Physicians India. 2001; 49: 788, 790–794.
4. World Health Organization (2006 a). Global tuberculosis control: Surveillance, planning and financing. Geneva, Switzerland: WHO; 2006. Publication WHO/ HTM/ TB/2006.362.
5. Practical hematology. 9<sup>th</sup> edition. Dacie and Lewis.
6. 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 Mar; 36(3): 280–287.
7. Olaniyi JA, Aken'Ova YA. Haematological profile of patients with pulmonary tuberculosis in Ibadan, Nigeria. Afr J Med Med Sci. 2003; 32: 239–342.
8. Kourbatova EV. Risk factors for mortality among adult patients with newly diagnosed tuberculosis in Samara, Russia. Int J Tuber L Dis. 2006; 10(11) : 1224–1230.
9. Akitunde EO, Shokunbi WA, Adekunle CO. Leucocyte, platelet count and ESR in pulmonary TB. Afr J Med Med Sci. 1995 Jun; 24(2): 131–134.
10. Wessels G, Schaaf HS, Beyers N, Gie RP, Nel E, Donald PR. Haematological abnormalities in children with tuberculosis. J Trop Pediatr. 1999 Oct; 45(5): 307–310.
11. Hee Jung Yoon, Young Goo Song, Woo Il Park, Jay Pil Choi, Kyung Hi Chang and June Myung Kim. Clinical manifestations and diagnosis of extra pulmonary tuberculosis. Yonsei Med J. 2004; 45(3): 453–461.
12. Maartens G, Willcox PA, Benatar SR. Miliary tuberculosis: rapid diagnosis, hematologic abnormalities, and outcome in 109 treated adults. Am J Med. 1990 Sep; 89(3): 291–296.

Source of Support: None Declared  
Conflict of Interest: None Declared