**Evaluation of hematological parameters in pulmonary tuberculosis patients**

Amar R. Shah¹, Killol N. Desai², Alpeshkumar M. Maru¹

¹Department of Pathology, Dr N. D. Desai Faculty of Medical Science and Research, Nadiad, Gujarat, ²Department of Pathology, Nootan Medical College and Research, Visnagar, Gujarat, India

**ABSTRACT**

Introduction: Tuberculosis (TB) is the most common infectious disease caused by mycobacterium tuberculosis. Apart from the lungs, tuberculosis also affects the bone marrow. There are significant hematological abnormalities that occur in association with tuberculosis. So we can use these hematological parameters as a marker for the diagnosis, prognosis, and response to therapy.

Aims: To evaluate the hematological parameters in pulmonary tuberculosis patients. Methods and Materials: A total of 70 diagnosed tuberculosis patients and 70 healthy controls were selected by purposive sampling in this study. About 4 ml of venous blood was collected with proper aseptic precaution. 2 ml ethylenediamine tetra acetic acid (EDTA) tube blood was used for hematological analysis by using Siemens Advia 2120i 5-part hematology analyzer. Rest 2 ml blood was used for measurement of erythrocyte sedimentation rate (ESR) by Wintrobe’s method. Results: The hemoglobin, packed cell volume (PCV), and blood indices values were significantly lower compared to healthy controls in both sexes. White blood cell (WBC) count, absolute neutrophil count, platelet count, and ESR values were significantly increased in tuberculosis patients as compared to healthy controls and were found to be statistically significant (P-value < 0.05). Conclusions: To measure hematological parameters in tuberculosis is a simple and cost-effective method to predict the course of the disease and monitor complications in developing countries like India.

**Keywords:** Anemia, leucocytosis, pulmonary tuberculosis, thrombocytosis

**Introduction**

Tuberculosis (TB) is the most common infectious disease caused by mycobacterium tuberculosis. Although novel diagnostic modalities and treatments have developed, it remains one of the world’s important public health problems. It causes ill-health for approximately 10 million people each year and it is one of the most common causes of death across the world. In the last five years, it has been the leading cause of death from a single etiological agent, ranking above HIV/AIDS. Pathogenesis of the disease is explained by cell-mediated immune response. About 40% of the Indian population is infected with TB bacilli. Patients with cavitary lesions are the prime source of infection. Most of such patients are usually sputum smear-positive. Coughing produces very small droplets which are infective in nature and approximately 3000 droplet nuclei, and these remain in the air for a prolonged period of time. There is a crucial role of T-cells in immunity to mycobacteria, evidenced by the dramatically increased susceptibility of an individual with human immunodeficiency virus (HIV) infection. To prevent and control this infection, early diagnosis and treatment should be done. However, monitoring TB patients during treatment is important for better outcomes.

Apart from the lungs, tuberculosis also affects the bone marrow. There are significant hematological abnormalities that occur in association with tuberculosis. So we can use these hematological...
parameters as a marker for the diagnosis, prognosis, and response to therapy.\textsuperscript{51}

Hematological parameters like hemoglobin, Packed Cell Volume (PCV), red blood cell (RBC) count, blood indices, platelet count, white blood cell (WBC) count, erythrocyte sedimentation rate (ESR) can be used for diagnosis, prognosis, and follow-up of patients.\textsuperscript{51} There are few studies done that show that ESR and (C-reactive protein) CRP can serve as sensitive markers for tuberculosis.\textsuperscript{51}

This study was carried out to analyze early changes in hematological parameters in sputum smear-positive tuberculosis patients and to evaluate its diagnostic and prognostic importance in the course of the disease. Hematological parameters have a vital role in treatment strategies and monitoring of treatment. It can influence a patient’s outcome. This study has shown marked variations in hematological parameters of test groups when compared to healthy groups. Evaluation and management of infectious diseases like tuberculosis pertaining to hematological markers are of importance to improve treatment outcomes, patients’ survival, and quality of life.

Thus, such hematological findings are cost-effective and can help to get quick attention from physicians and primary health care support teams to diagnose early changes in TB patients in a very cost-effective way.

**Materials and Methods**

This study was carried out in the department of pathology at the tertiary care Center from June 2019 to May 2021. This study includes 70 patients diagnosed with pulmonary tuberculosis (PTB). The diagnosis was confirmed by the Ziehl-Neelsen staining method on sputum as well as chest radiogram. There are 70 healthy controls that were included for comparison of study results. Sampling was done by simple random method. The acquisition of patients was based on their positive status while consulting the chest department, and with prior consent, we collected blood samples. All the data was recorded in case record form.

Ethical approval was granted by the Institutional Ethics Committee. (Ref: NDDFMSR/IEC/04/21),

**Inclusion criteria**

All sputum smears positive TB patients (Age beyond 18 years)

**Exclusion criteria**

Pregnant women, pediatric patients, patients with extrapulmonary TB and old TB with multi-drug resistance (MDR), chronic renal or liver disease, leukemia, HIV.

About 4 ml of venous blood was collected with proper aseptic precaution. 2 ml EDTA tube blood was used for hematological analysis by using Siemens Advia 2120i 5-part hematology analyzer. Rest 2 ml blood was used for measurement of ESR by the Wintrobe method. Written informed consent was obtained from all the patients. Hematological parameters, including hemoglobin (Hb), total leukocyte count (TLC), differential leukocyte count (DLC), hematocrit (HCT), platelet counts, blood indices like mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), and mean corpuscular hemoglobin concentration (MCHC).

Data were collected and analyzed by using Statistical Package for the Social Sciences (SPSS) 2.0 software. The association between the course of disease and hematological parameters was analyzed by the Chi-square test. In the present study, P value < 0.05 was considered statistically significant.

**Results**

A total of 70 newly diagnosed mycobacterium tuberculosis cases and 70 healthy controls were included in the present study.

Table 1 shows the age group distribution among tuberculosis cases. The majority belonged to the 4th and 5th decade of age group. Out of 100 cases, 45 (64%) cases were male, and 25 (36%) cases were female. While among the control group, an equal proportion of males and females were included in the study.

Tables 2a and 2b show hematological parameters among sputum-positive patients. We have assessed parameters like hemoglobin, WBC, platelet count, ESR, and other indices among cases as well as among the control group.

As per Table 2a, we have assessed anemia parameters among 70 cases. Out of which 50% cases were found to be having a mild degree of anemia (Hb: 10–13 g/dl), 37% cases had a moderate degree of anemia (Hb: 8.1–9.9 g/dl), followed by 13% cases showing a severe degree of anemia (Hb < 8 g/dl).

Morphological typing of anemia was based on MCV, MCH, and peripheral blood picture findings. The commonest type is microcytic hypochromic anemia (52%), followed by 40% cases having normocytic normochromic anemia. There were 8% cases showing macrocytic hypochromic patterns.

Regarding WBC count, in spite of chronic inflammation, 43% of cases showed normal total leukocyte count. Leukocytosis was observed in 53% of the cases. Most of the cases with

| Table 1: Showing age distribution of TB cases |
|---------------------------------------------|
| **Age group** | **Number of cases (n=70)** | **Percentage (%)** |
|=============|=================|-------------------|
| 20-30 years  | 08               | 11.42%            |
| 31-40 years  | 12               | 17.14%            |
| 41-50 years  | 26               | 37.14%            |
| 51-60 years  | 20               | 28.57%            |
| > 60 years   | 04               | 5.71%             |
Discussion

Tuberculosis continues to remain one of the most important communicable diseases in the world and is a leading health problem in India. Symptoms of tuberculosis range from productive cough for more than three weeks, to chest pain and systemic symptoms. That includes evening rise fever, chills, night sweats, loss of appetite, weight loss, pallor, and fatigue. In some active cases, the infection may spread to other organs, known as extrapulmonary TB.

The approach to the diagnosis of TB is led by blood or sputum culture along with an X-ray of the chest. Some other modalities like skin tests, Interferon Gamma Release Assays (IGRAs), in vitro blood tests, and polymerase chain reaction (PCR) tests are also available. However, in developing countries, a rapid and cost-effective diagnostic test would be valuable. Assessment of hematological parameters is one such cost-effective approach in such a scenario.

Our study showed that 46 cases (65%) belong to the age group 20–50 years. This finding was correlated with other studies like Rohini K et al, Yasin A et al, and Rajesh H et al. The lowest prevalence was reported in extreme age (> 60 years).

We have reported 64% cases of tuberculosis in men as compared to 36% cases in women. Findings were correlated well with other studies like Thatoi PK and Banerjee M. This result differs from a study done by Yasin A et al, where cases were reported more among women than men.

Anemia is the most common complication observed in hematological parameters among tuberculosis patients, and it is one of the risk factors for mortality. Increased release of cytokines like tumor necrosis factor-α (TNF-α), Interferon γ (IFN-γ), and Interleukin-6 (IL-6) leads to reduction of erythropoietin formation, resulting in bone marrow depression along with altered iron metabolism leads to anemia. Some studies postulated that the anemia was due to an absence of bone marrow iron, resulting in iron deficiency anemia. TNF-α and IL-1 released by activated monocytes reduce erythropoietin production leading to anemia. TNF-α and IL-1 also increase iron uptake and ferritin synthesis. In the present study, the severity of anemia was accessed by hemoglobin level. We have reported 50% cases with mild anemia, 37% cases with moderate anemia, and only 13% of the patients had severe anemia. Morphologically, a microcytic hypochromic pattern was observed in 52% of the cases, followed by normocytic normochromic anemia in 40% of the cases, while only 8% of the cases showed a macrocytic hypochromic picture. Apart from these, all tuberculosis-positive patients showed low PCV, MCV, MCH, and MCHC. These findings are comparable with other studies like Bashir et al and Yasin et al.

Leukocytosis is an elemental feature of tuberculosis. Our study showed leukocytosis in 53% of the cases, while 43% of the
cases showed normal leukocyte count, with 4% cases having leukopenia. Such findings attributed to the traditional conclusion that in patients of tuberculosis, WBC count increases during infection along with macrophages as a part of the body’s defense mechanism.

Although absolute lymphocyte count remained within the normal range in 80% of the cases, it was found to be having higher lymphocytes as compared to the control group. In addition to that, we have reported neutrophilia in 56% of the cases which is thought to be an immune-mediated response to tuberculosis. Similar findings were reported in previous studies.[10,11,13]

On the contrary, a study by Thatoi PK.[13] reported neutropenia as a predominant finding, which may be due to hypersplenism, excessive margination of neutrophils, or granulopoiesis inhibitor activity by T-lymphocytes.

Thrombocytosis has been reported in 70% of the cases in this study which was correlated with the findings of Yasin et al.[10] and Banerjee M.[13] Various cytokines like IL-6 involved in granuloma formation promote platelet production and could be the reason for thrombocytosis. Various morphological features of platelets like high platelet distribution width (PDW) and mean platelet volume (MPV) values in patients with TB is nothing but a reflection of activated platelet, just like other cells of the immune system.

A constant finding observed in the present study is that Erythrocyte sedimentation rate (ESR) value gets significantly higher in tuberculosis patients than that of normal controls. In our study, ESR was elevated in 98% of the patients. Similar findings were observed in other studies like Rohini K et al.,[1] Yasin A et al.,[10] and Thatoi Pk et al.[13] ESR is a sensitive marker for inflammatory response. It is used to obtain information regarding disease progression and retrogression.

The findings of the current study can be used to decrease the rate of morbidity and mortality and also to prevent complications of the disease. It can be useful as an indicator of disease progression.

Conclusion

Tuberculosis remains one of the world’s important public health problems. Many markers are available to assess and monitor the disease in the market, but these are expensive and cannot be done routinely. Complete blood count (CBC) is a simple test along with ESR, readily measured by a simple and cost-effective method to predict the course of the disease and monitor complications in developing countries like India. Among hematological parameters, anemia was frequently encountered in patients with pulmonary TB, with a microcytic hypochromic pattern predominant. Other findings like PCV, MCV, MCH, and MCHC decreased, while WBC count, absolute neutrophil count, platelet count, and ESR values were significantly increased in tuberculosis patients as compared to healthy controls. So the take-home message is that awareness regarding clinical features, laboratory findings (hematological parameters), and demographical data of TB patients may facilitate early diagnosis. The unexplained presence of any such abnormal hematological findings should definitely raise a strong suspicion of tuberculosis.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published, and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

Acknowledgements

I acknowledge this research and express enough thanks to my mentor and guide, Respected Dean sir, for their continued support and encouragement. I offer my sincere appreciation for the learning opportunities provided by the research committee of the institute.

Authors contribution

All authors have contributed equally.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

References

1. Shafee M, Abbas F, Ashraf M, Alammengal M, Kakar N, Ahmad Z, et al. Hematological profile and risk factors associated with pulmonary tuberculosis patients in Quetta, Pakistan. Pak J Med Sci 2014;30:36-40.
2. Kahase D, Solomon A, Alemayehu M. Evaluation of peripheral blood parameters of pulmonary tuberculosis patients at St. Paul’s hospital millennium medical college, Addis Ababa, Ethiopia: Comparative study. J Blood Med 2020:11:115-21.
3. Maphasa RE, Meyer M, Dube A. The macrophage response to mycobacterium tuberculosis and opportunities for autophagy inducing nano medicines for tuberculosis therapy. Front Cell Infect Microbiol 2021;10:618414. doi: 10.3389/fcimb.2020.618414.
4. Ottenhoff TH. New pathways of protective and pathological host defence to mycobacteria. Trends Microbial 2012;20:419-28.
5. Abay F, Yalaw A, Shibawaw A, Enawgaw B. Hematological abnormalities of pulmonary tuberculosis patients with and without HIV at the University of Gondar hospital, Northwest Ethiopia: A comparative cross-sectional study. Tuberc Res Treat 2018;2018:5740951. doi: 10.1155/2018/5740951.
6. Kurup R, Fleming K, Dainiram S, Marks-James S, Roberts Martin R. Hematological and biochemistry profile and risk
factors associated with pulmonary tuberculosis patients in Guyana. Tuberc Res Treat 2016;2016:6983747. doi: 10.1155/2016/6983747.

7. Peresi E, Silva SM, Calvi SA, Marcondes-Machado J. Cytokines and acute phase serum proteins as markers of inflammatory regression during the treatment of pulmonary tuberculosis. J Bras Pneumol 2008;34:942-9.

8. Shaikh MK, Samo JA, Devrajani BR, Shah SZA, Shaikh S, Shaikh I. C-reactive protein in patients with pulmonary tuberculosis. World Appl Sci J 2012;17:140-4.

9. Rohini K, Surekha M, Srikumar PS, Kumar AM. Assessment of hematological parameters in pulmonary tuberculosis patients. Indian J Clin Biochem 2016;31:332-5.

10. Yasin A, Hashim, AM, Haithym A. Hematological changes in pulmonary tuberculosis. AAMJ 2015;13:224-9.

11. Rajesh H, Sangeetha B, Indhu S, Manimaran, Nishanth M. Evaluation of hematological profile in pulmonary tuberculosis. Indian J Pathol Oncol 2020;7:39-42.

12. Thatoi PK. Pulmonary tuberculosis and its haematological correlates. Trans World Med J 2013;1:11-3.

13. Banerjee M, Chaudhary BL, Shukla S. Hematological profile among pulmonary tuberculosis patients in tertiary care hospital. Int J Bioassays 2015;4:3900-2.

14. Ciglenecki I, Glynn JR, Mwinga A, Ngwira B, Zumla A, Fine PE, et al. Population differences in death rates in HIV-positive patients with tuberculosis. Int J Tuberc Lung Dis 2007;11:1121-8.

15. Weiss G, Goodnough LT. Anemia of chronic disease. N Engl J Med 2005;352:1011-23.

16. Bashir AB, Ageep Ali K, Abufatima AS, Mohamedani AA. Reactive thrombocytosis and ESR in patients with pulmonary tuberculosis. J Clin Pathol 2014;5:29-34.