Original Research Article

A study on hematological profile in pulmonary tuberculosis in south rural part of Tamil Nadu

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Abstract

Background: Tuberculosis is a major public health problem in India. There is a paucity of literature on the hematological changes associated with tuberculosis, though tuberculosis is a common condition. Advances in the management of patients in terms of the diagnosis and treatment of hematologic malignancies and treatment-related complications, especially infectious complications, have increased survival time. However, more than half of the patients treated for hematologic malignancies will develop a pulmonary complication during their follow-up, with infectious pneumonia remaining the most common diagnosis that should be considered first regarding its potential severity. Otherwise, new complications that may involve different organs, including the lungs, have been increasingly reported. Currently, over a quarter of lung infiltrates occurring in the context of hematological diseases are due to noninfectious causes.

Aim of the study: To evaluate the hematological parameters in patient with Ziehl Nelson smear positive pulmonary tuberculosis.

Materials and methods: The study was conducted in the Department of Thoracic Medicine, Madras Medical College, Chennai from 2018-2019 (12 months). One hundred patients with sputum who were positive for acid-fast bacilli were included in the study. The various hematological manifestations in tuberculosis were studied using a hemogram by automated cell counter and peripheral smear examination.

Results: Anemia was seen in 74% of patients. Despite the infection, 71 patients had a normal leukocyte count. Leukocytosis as a response to infection was observed in 26 patients. Thrombocytosis was observed in 24 patients while thrombocytopenia was observed in 9 patients. 99% of patients had increased ESR. Two patients had pancytopenia.

Conclusions: Broad spectrum of hematological abnormalities has been demonstrated in patients with pulmonary tuberculosis in the present study. While many of them are consistent with reported literature and reinforce the fact that they can be valuable tools in monitoring e.g. anemia and increased ESR, other findings such as thrombocytosis, pancytopenia suggest the need for further studies in this field.

Key words

Mycobacterium tuberculosis, Pulmonary Tuberculosis, Anemia, Leukocytosis, Thrombocytosis, Erythrocyte Sedimentation Rate.

Introduction

Tuberculosis is a highly prevalent chronic infectious disease caused by mycobacterium tuberculosis. Globally mycobacterium tuberculosis infection remains at the epidemic level. One-third of the world population is infected and approximately 3 million people die annually from pulmonary tuberculosis. The condition in India is equally alarming. About one-third of the Indian population is infected with mycobacterium tuberculosis [1]. Every year one million cases are being added to the existing tuberculosis burden. Reversible peripheral blood abnormalities are commonly associated with pulmonary tuberculosis, but whether disseminated tuberculosis or atypical disease can cause profound bone marrow and peripheral blood abnormalities by modulating normal hematopoiesis remains controversial. Insight into the relationship between profound blood abnormalities and mycobacterial infection has come from an understanding of the immunology of mycobacterial infection, the defects seen in immunologic function in patients with acquired immunodeficiency syndrome (AIDS), and hematologic malignancies [2]. These diseases may have substantial effects on hematopoiesis and may increase the susceptibility of the patient to pulmonary and disseminated mycobacterial infections. The atypical and varied spectrum of clinical presentation of tuberculosis poses a diagnostic and therapeutic challenge to physicians [3]. Little is known about the prevalence of these hematological abnormalities and the effect of anti-tuberculosis treatment on the various hematological parameters in the Indian subcontinent. Mycobacterium tuberculosis can survive in the dark for a long period [4]. Of the several factors determining an individual risk of exposure, two factors are important, these include, the concentration of droplet nuclei in contaminated air and the length of time that air is breathed. The risk of transmission of infection from a person with sputum negative pulmonary tuberculosis and miliary tuberculosis is low and with extra-pulmonary tuberculosis is even lower. This study was undertaken to analyze the hematological parameters in pulmonary tuberculosis and to evaluate their diagnostic and prognostic significance [5].

Materials and methods

Patient inclusion criteria: The criteria essential for the diagnosis of pulmonary tuberculosis include: Clinical features were suggestive of pulmonary tuberculosis. Positive sputum smear acid-fast bacilli or sputum culture yielding mycobacterium tuberculosis.

The study was conducted in the Department of Thoracic Medicine, Madras Medical College, Chennai in 2018-2019 (12 months). One hundred patients with sputum who were positive for acid-fast bacilli were included in the study. The various hematological manifestations in tuberculosis were studied using a hemogram by automated cell counter and peripheral smear examination.

Hematological examination: All patients had a detailed hemogram including, Hemoglobin, Total leucocyte count, Differential leucocyte count, Platelet count, Hematocrit, Mean corpuscular volume, mean corpuscular hemoglobin, mean

corpuscular hemoglobin concentration, Erythrocyte sedimentation rate. Peripheral smear was done whenever possible and required to study the RBC and WBC morphology. The analysis was performed by using automated hematology analyzers SysmexXT1800I and SysmexXT2000i, using EDTA anti-coagulated blood fresh venous blood sample.

Statistical analysis

Data entry and statistical analysis was done using the software package IBM SPSS version 20. Based on the normality of distribution, either mean difference were calculated by the independent sample *t*-test.

Results

Mean age of the total population was 41 years, 61% of patients were in the age group 20-50 years. 8% of the total population was below the age of 20 years and 31% of the total population was above 50 years. There were 71 males and 29 females with a mean age of 41 years. Mean age of the males were 42 years and the mean age of the females were 35 age in years (**Graph – 1**).

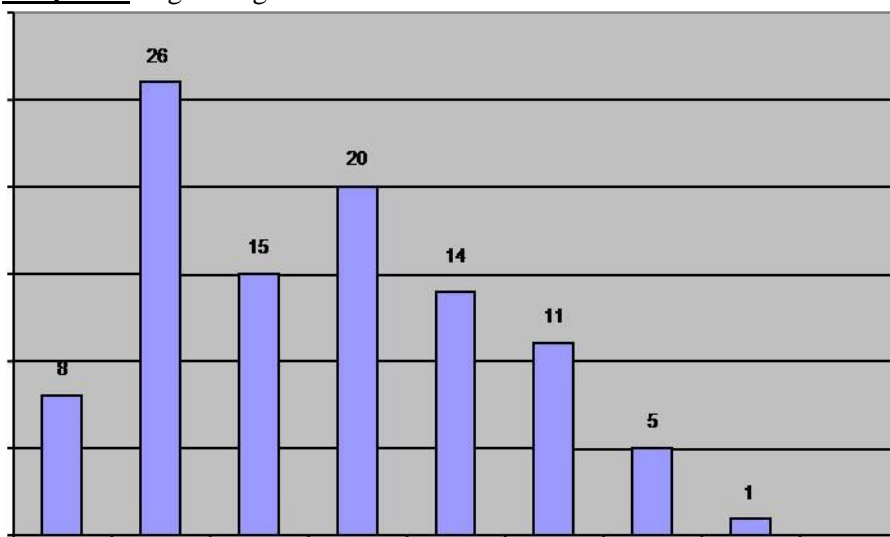**Graph – 1:** Age and gender distribution.

Table – 1: Hemoglobin range.

Hemoglobin gm %	Male		Female		Total	
	No	%	No	%	No	%
<8	2	2.8	7	24	9	9
8-11	30	42.3	9	31	39	39
11-14	28	39.4	12	41.5	40	40
>14	11	15.5	1	3.5	12	12
Total	71	100	29	100	100	100

The mean hemoglobin level was 11.1 g/dl, the mean hemoglobin level in males was 11.5g/dl and the maximum range was 16.3g/dl and the minimum was 6.9g/dl. In females the mean hemoglobin level was 10 g/dl, the maximum was 14.4 g/dl, and the minimum were 7.1 g/dl. 28 % were the hemoglobin below the 10 gm/dl. 39 patients had hemoglobin in the range of 8-11 g/dl (**Table – 1**).
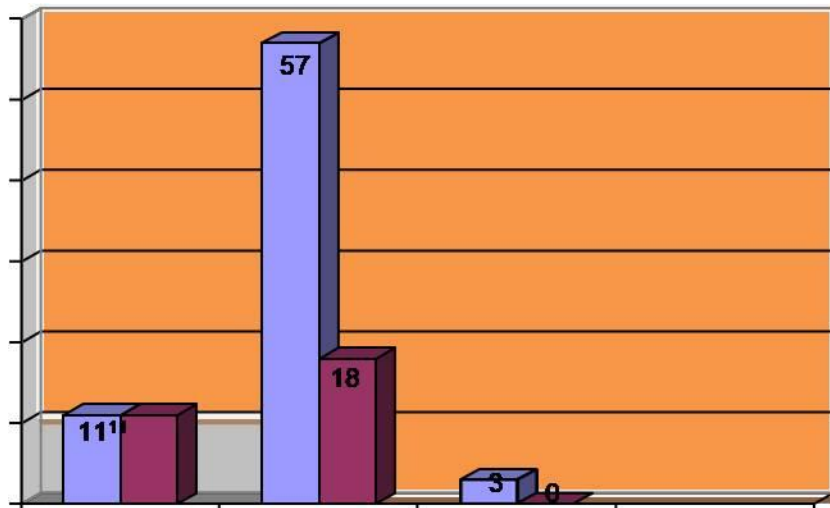
The definition of anemia used in this study was hemoglobin concentration less than13g/dl in men and 12 g/dl in women (WHO Recommendation). Anemia was identified in74 patients at the time of diagnosis of tuberculosis. 51 (71.8%) men and
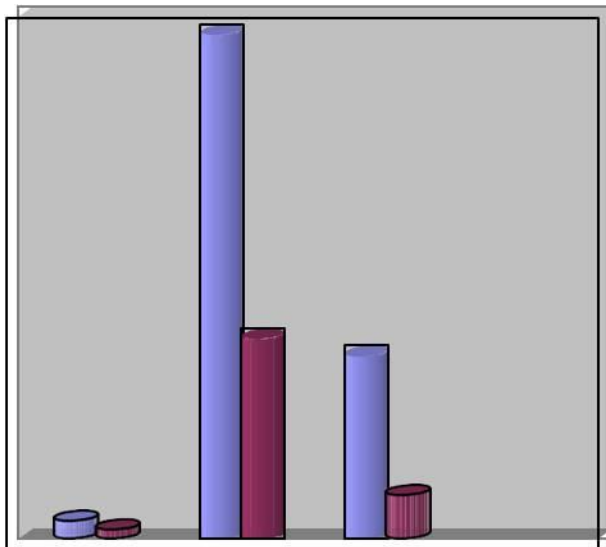
23 (32.3%) women had anemia. Normocytic anemia was the most common, and was identified in 49 (66.2 %) patients Microcytic anemia was next common, 22 patients were identified with microcytic, anemia. Only 3 male patients showed Macrocytic anemia in whom the MCV was above 100 fl. The MCV by cell counter was taken and was correlated with hemoglobin and peripheral smear (**Graph – 2**).

Graph – 2: Prevalence of anemia.

Graph – 3: Total leukocyte count.

Despite the infection, 71 patients had a normal leukocyte count. Leukocytosis as a response to infection was observed in 26 patients (21(80.7%) were males and5 (19.2%) were females) All patients with leukocytosis had neutrophilia. Only 3 patients had leucopenia (**Graph – 3**).

Thrombocytosis occurs in many chronic inflammatory diseases including tuberculosis.

Thrombocytosis was observed in 24 patients while thrombocytopenia was observed in 9 patients. Other 67 patients had a normal platelet count. Interestingly thrombocytosis was observed in patients who had leukocytosis (**Graph – 4**).
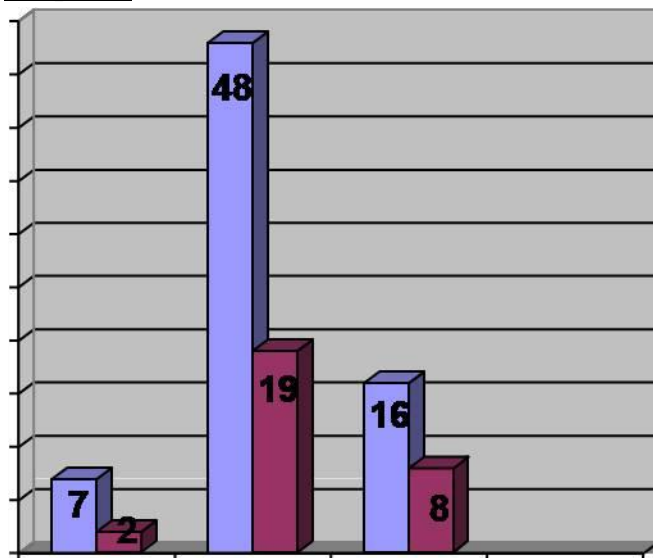
In this study 99% of patients with pulmonary tuberculosis had increased ESR value. Only one patient had a normal ESR value. 13 patients had
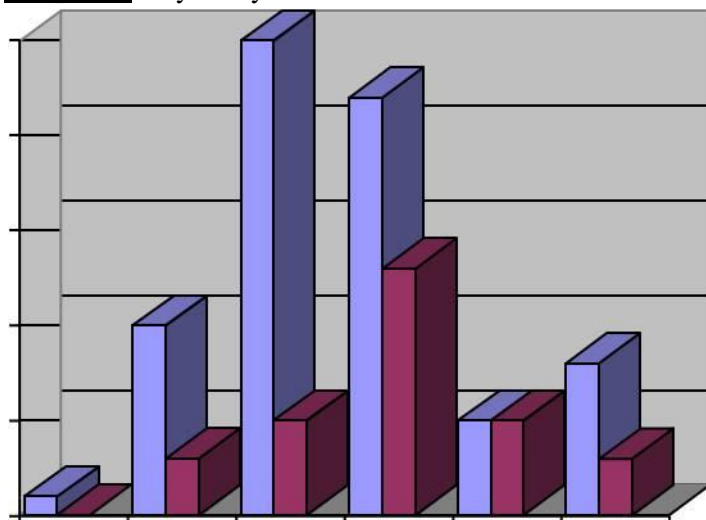
an ESR value of 20-40 mm/hr 30 patients had ESR in the range of 40-60 mm/hr, 35 patients had a value in the range of 60-80 mm/hr and 11 patient had ESR value above 100 mm/hr. The number of males was always more in all ranges (**Graph – 5**).

Graph – 4: Platelet count.

Graph – 5: Erythrocyte sedimentation rate.

Discussion

Tuberculosis continues to be an important communicable disease in the world and is a major public health problem in India. World Health Organization has declared tuberculosis is a global emergency in 1993. Various hematological manifestations have been described in association with tuberculosis. There is a paucity of literature about the hematologic abnormalities in patients from the Indian population. In the present study, an attempt has been made to study a complete hematological profile restricted to pulmonary tuberculosis. The prevalence of anemia in the present study was similar to the other studies. The type of anemia was predominantly normocytic normochromic [6]. The bone marrow study by Danek SJ, et al. found blunted erythropoietic response of bone marrow. Other authors have also reported a blunted erythropoietin response to anemia of untreated tuberculosis. It is postulated that the tumor necrosis factor-α and other cytokines by

tuberculosis-activated monocytes suppress the erythropoietin production leading to anemia [7]. All patients with leukocytosis had neutrophilia. Although changes have been reported in the relative number of lymphocyte and monocyte and polymorphonuclear leucocytes, these had not proved useful either as clinical or prognostic values. The reported prevalence of leucopenia in pulmonary tuberculosis is 1-4%. The results of the present study are in agreement with these studies. Neutropenia was the predominant finding in these patients. The various pathophysiological mechanism implicated in neutropenia is poorly understood [8]. However, it is a consequence of the combined effect of hypersplenism, excessive margination of neutrophil and/ or marrow granulopoietic failure mediated by the expansion of T lymphocyte showing granulopoies is inhibitor activity. Associated malnutrition may also result in neutropenia [9]. Many authors reported lymphocytopenia in a patient with pulmonary tuberculosis. The exact reason for the development of lymphocytopenia has not been elucidated. Nevertheless, the role of cytokine including tumor necrosis factor in the pathogenesis of lymphocytopenia has been suggested. Previous studies have documented pancytopenia in patient with disseminated /military tuberculosis and but it is a rare finding in patients with pulmonary tuberculosis. In the present study, there were two cases reported with mean values of Hb 8.5 g/dl, TC 3500 cells/cmm, and platelet count 60000 cells/cmm [10]. As no bone marrow examination was done, no further evaluation could be done. A case of pancytopenia with tuberculosis has been reported by Paul JS, et al. They observed normocellular and normal maturation of all three cell series in the bone marrow and found a significant improvement in all parameters after anti-tuberculous treatment. Splenomegaly was observed in patients with tuberculosis associated pancytopenia [11]. The various postulated mechanism for pancytopenia include splenic sequestration, immune- mediated bone marrow suppression, and a decreased bone marrow reserve [12]. It has been suggested by Philip CH, et al. that identification of pancytopenia or thrombocytopenia in association with tuberculosis suggests the possibility of drug toxicity or another underlying process and requires further evaluation. Thrombocytosis has been reported in patients with military/ disseminated tuberculosis [13]. The stimulus for increased platelet production in reactive thrombocytosis is not clear Various inflammatory cells, cytokines, and mediators are involved in the formation of granulomatous lesions encountered in tuberculosis. Among them, interleukin-6 (IL-6) has been known to promote platelet production. Since platelets have been proposed as immune cells in recent years, the distinctive morphologic features of platelets with higher PDW and MPV values in tuberculosis may be a reflection of an activated platelet form as observed for most other cells of the immune system. In the present study, only the platelet count was studied and as other parameters were not included such concepts could not be validated [14]. The erythrocyte sedimentation rate is seldom the sole clue to disease in an asymptomatic person and is not a useful screening test. When the rate is increased a careful history and physical examination can disclose the cause [15]. Papers reported on the value of the erythrocyte sedimentation rate as a test of activity in pulmonary tuberculosis have concluded that the ESR is a useful practical method for obtaining accurate and dependable information about the actual progress or retrogression of the tuberculous lesion before these can be demonstrated by other clinical and laboratory procedures [16]. Nevertheless, there was a large range of individual values with considerable overlap, making it difficult to see how individual patient values could be of any utility in either diagnosing or excluding tuberculosis. They concluded that the ESR value is likely to be of little or no diagnostic utility in the diagnosis of childhood tuberculosis [17]. A broad spectrum of hematological abnormalities has been demonstrated in patients with pulmonary tuberculosis in the present study. While many of them are consistent with reported literature and reinforce the fact that they can be valuable tools in monitoring e.g. anemia and increased ESR, other findings such as

thrombocytosis, pancytopenia suggest the need for further studies in this field [18, 19, 20].

Conclusion

In this study, 74% had anemia, indicating the morbidity status in pulmonary tuberculosis. 99% of patients had increased ESR which is consistent with documented literature. Thrombocytosis was observed in 24% of patients and pancytopenia in 2% were the unusual findings, which require further studies. A broad spectrum of hematological abnormalities has been demonstrated in patients with pulmonary tuberculosis in the present study. While many of them are consistent with reported literature and reinforce the fact that they can be valuable tools in monitoring e.g. anemia and increased ESR, other findings such as thrombocytosis, pancytopenia suggest the need for further studies in this field.

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