



Reactive thrombocytosis and erythrocyte sedimentation rate in patients with pulmonary tuberculosis

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ABSTRACT

Background: The bacterium *Mycobacterium tuberculosis* causes TB, a contagious, airborne infection that destroys body tissue, as it is very common disease this article is based on reactive changes of it which help in disease monitoring and screening.

Objective: To evaluate the platelet count and erythrocyte sedimentation rate (ESR) in pulmonary tuberculosis patients who are positive for *Mycobacterium tuberculosis* bacilli in sputum.

Materials and Methods: Seventy patients of pulmonary tuberculosis with sputum positive for acid fast bacilli (AFB) were included. Platelet count was done by cell counter which is verified by examination of peripheral smear. ESR was measured by Westergren method.

Results: Thrombocytosis was observed in 43 patients while thrombocytopenia was observed in 4 patients. 95.5% patients had increased erythrocyte sedimentation rate (ESR).

Conclusion: Thrombocytosis was seen in 61%. Majority of the findings are consistent with reported literature and reinforce the fact that they can be valuable tools in monitoring such as increased ESR.

KEYWORDS

Mycobacterium tuberculosis, Pulmonary tuberculosis, Thrombocytosis, Erythrocyte sedimentation rate.

Aims of this study is to evaluate the reactive thrombocytosis and erythrocyte sedimentation rate in patients with pulmonary tuberculosis. Study period is from August 2014 up to August 2015 at Kalidas Multispecialist hospital Vyara, Surat. 70 patients of tuberculosis is included in this study in which 53 male and 17 female and all are Ziehl-Neelsen stain positive. 40 apparently healthy adult males (25) and females (15) were also randomly selected to be the control group of the study. The ages of the patients ranged from 14 to 70 years old. Thrombocytosis was found in 61% of the patients. The erythrocyte sedimentation rate (ESR) was increased in 95% of the patients. All these changes in parameters are due to inflammatory reaction and these changes raise the suspicion of pulmonary tuberculosis.

INTRODUCTION

Tuberculosis (TB) is a major public health problem and one of the most widely spread infectious diseases. Changes in hematological parameters like increased ESR and reactive thrombocytosis which are part of our study raise the suspicion of other infective conditions. Moreover, hematological parameters are useful indicators of severity in TB infection. Reactive thrombocytosis is defined as an increased number of platelets above $450 \times 10^9/L$ due to a reaction to a stimulus e.g. an inflammatory condition. In reactive thrombocytosis, the increase in platelet count is usually temporary, less than $1000 \times 10^9/L$, and is not normally associated with any serious clinical problems. Thrombocytosis occurs in many chronic inflammatory diseases, including tuberculosis.

Thrombocytosis is typically either a reactive process (secondary thrombocytosis) or is caused by a clonal bone marrow (myeloproliferative) disorder; the latter category includes essential thrombocythemia. Any inflammatory process such as bacterial infection, neoplasia, sepsis, multiple trauma, burns, or pancreatitis that elevates serum IL levels (especially IL-6), may increase the circulating platelet count. Elevated serum IL-6 levels correlate with thrombocytosis in various conditions such as tuberculosis, complicated urinary tract infections, and trauma, for instance. Additionally, C-reactive protein may serve as a correlate to IL-6 since hepatic synthesis increases in response to acute inflammation.

ESR is not a specific test for tuberculosis, as it is raised in many other inflammatory conditions, infective diseases and malignancy. Many cytokines, such as interleukin (IL)-6, IL-1, and tumor necrosis factor (TNF), have been shown to promote *in vivo* and *in vitro* megakaryocytopoiesis, or production of platelets. However, the principal regulator of megakaryocytopoiesis is thrombopoietin (TPO), also called megakaryocyte growth and development factor. Monocytes are the main source of IL-6; but lymphocytes, endothelial cells, and fibroblasts are also able to manufacture it. In inflammatory disorders and malignancies and after surgery and trauma, serum IL-6 levels are increased, and IL-6 is suggested to play a role in inflammation and the immune response. Infusions of IL-6 in humans have led to increased platelet production and numbers. *In vitro* studies have shown that megakaryocyte counts and megakaryocyte size increase with addition of recombinant IL-6. Although the exact mechanism is unknown, more than 80% of patients with reactive thrombocytosis have elevated serum levels of IL-6. However, the concentration of IL-6 in the serum does not predict the observed platelet counts.

Moderately raised sedimentation rates can also be found in healthy people, particularly those living in tropical countries but a "normal" ESR cannot exclude disease.

MATERIALS AND METHODS

Kalidas multispecialist hospital Vyara, Surat, in the period from August 2014 up to August 2015, included the population of this study. Hematological tests were done in 70 pulmonary TB patients which have *Tubercle bacilli* in sputum (Zn stain). The inclusion criteria were: not to be suffering from any other chronic disease. The exclusion criteria included: currently on drugs which affect the ESR and platelet counts. Fifty apparently healthy normal individuals with no clinical signs for pulmonary TB were selected randomly as a control group.

Blood samples were collected in the laboratory of Kalidas hospital. About 5 ml of venous blood was collected from each patient where 2.5 ml of blood was transferred to a dipotassium ethylene diamine tetra acetic acid (EDTA) tube for measuring the platelet count. For measuring ESR, the remaining 2.5 ml of the blood was treated with citrate solution. Platelet count was done

using a cell counter which was verified by peripheral smear examination and ESR was measured by Westergren method.

TABLE NO 1- HEMATOLOGICAL PARAMETERS OF TUBERCULOSIS PATIENT

Sr. no	Parameter	No of Cases	Percentage
1	Platelets:		
	Normal	23	32.9
	Thrombocytosis	43	61.5
	Thrombocytopenia	04	5.8
2	Erythrocyte Sedimentation rate		
	Normal	03	4.2
	Increased:	67	95.8
	20 - 40 mm/1hour	20	13.5
	40 - 60 mm/1hour	27	18.1
	60 - 80 mm /1hour	17	25.4
>100mm/1hour	03	4.2	

RESULTS

70 patients who were sputum positive for AFB were included in the study. There were 53 males and 17 females with mean age of 40 years. 61% of patients were in age group of 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. The control individuals aged between 19 and 63 years (mean age 27 years). In the control group, 25(62.5%) were males and 15 (37.5%) were females.

Thrombocytosis was observed in 43 patients while thrombocytopenia was observed in 4 patients. Other 23 patients had a normal platelet count.

In this study 95.8% of patient had increased ESR. Only three patients had a normal ESR. 20 patients had ESR ranging from 20 to 40 mm in first hour, 27 patients had ESR in the range of 40 – 60 mm in first hour, 17 patients had from 60 to 80 mm in first hr and 3 patients had ESR value more than 100 mm in first hr.

In the patient with pulmonary tuberculosis, thrombocytosis was noted in 20% of patients. The differences between the patient group and the control group in platelets count were found to be significantly higher in the patient group ($P < 0.001$). 67(95.5%) patients had an elevated ESR ranging from 20 to 140 mm/h. The differences between the patient group and the control group in ESR were found to be significantly higher in the patient group (P -value < 0.001).

DISCUSSION

Tuberculosis (TB) is one of the top 10 causes of death worldwide. In 2015, 10.4 million people fell ill with TB and 1.8 million died from the disease (including 0.4 million among people with HIV). Over 95% of TB deaths occur in low- and middle-income countries. Six countries account for 60% of the total, with India leading the count, followed by Indonesia, China, Nigeria, Pakistan and South Africa. In 2015, an estimated 1 million children became ill with TB and 170 000 children died of TB (excluding children with HIV). TB is a leading killer of HIV-positive people: in 2015, 35% of HIV deaths were due to TB. Globally in 2015, an estimated 480 000 people developed multidrug-resistant TB (MDR-TB). TB incidence has fallen by an average of 1.5% per year since 2000. This needs to accelerate to a 4–5% annual decline to reach the 2020 milestones of the "End TB Strategy". An estimated 49 million lives were saved through TB diagnosis and treatment between 2000 and 2015. Ending the TB epidemic by 2030 is among the health targets of the newly adopted Sustainable Development Goals.

Various hematological manifestations have been described in association with tuberculosis. In the present study an attempt has been made to study a reactive thrombocytosis and erythrocyte sedimentation rate in patients with pulmonary tuberculosis.

Thrombocytosis has been reported in patients with miliary or disseminated tuberculosis. It was a striking feature in pulmonary tuberculosis patients in a study done by Morris et al, as they had

more than 50% patient with thrombocytosis. In the present study, 26% had thrombocytosis close to the findings of Singh KJ et al who found in 32% patients with thrombocytosis. 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.

The ESR is very important clue for disease in asymptomatic person but not use as screening test. When the ESR is increased a careful history and physical examination can disclose the cause.

Studies reported on the value of the ESR as a test of activity in pulmonary tuberculosis have concluded that the ESR is useful practical method of obtaining accurate and dependable information about the actual progress or retrogression of tuberculous lesion, before these can be demonstrated by other clinical and laboratory procedures. Changes in the sedimentation rate exactly parallel alteration in the tuberculous focus. Previous studies have documented an elevated ESR level in majority of patients which decreased significantly in those who sputum becomes negative. 95.8% of patients with increased ESR in the present study are in concordance with the reported literature.

CONCLUSION

Thrombocytosis was seen in 61%. Majority of the findings are consistent with reported literature and reinforce the fact that they can be valuable tools in monitoring such as increased ESR.

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