

Hematological Changes in Patients Presenting with Pulmonary Tuberculosis

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ABSTRACT

Objective: To evaluate hematological changes in Pulmonary Tuberculosis (TB).

Study Design: Observational / descriptive / cross sectional study.

Place and Duration of Study: This study was conducted in Pathology Department, Hayatabad Medical Complex Peshawar from Nov 2015 to Oct 2016.

Materials and Methods: In the present study a total of 150 subjects were enrolled, out of them 100 patients diagnosed as pulmonary TB and 50 as control healthy individuals. Pulmonary tuberculosis was diagnosed by direct sputum smear microscopic examination after Ziel Nelson stain. Blood counts were performed on all these patients by hematology analyzer (CD Rubby, Abbott, USA) and ESR was also performed for all these patients by Westergren method.

Results: In the present study 35% had anemia with hemoglobin level was 10 ± 8.67 gm/dl. In 15% Patients had leucopenia with TLC was $2.5 \pm 1.567 \times 10^3/\mu\text{l}$ and 12% patients had leukocytosis TLC was $18 \pm 1.565 \times 10^3/\mu\text{l}$. 10% patients had thrombocytosis, Platelet count was $480 \pm 20.545 \times 10^3/\mu\text{l}$ and 8% patients had thrombocytopenia with platelet count was $120 \pm 118.3 \times 10^3/\mu\text{l}$. ESR were 100 ± 10 mm/1st hour for all the patients. These values were significantly changed as compared to control values.

Conclusion: The study concludes that pulmonary Tuberculosis is significantly associated with hematological abnormalities. The patients presenting with cytopenia or cytosia the physician must have suspicious of the disease and he should immediately screen the patient for pulmonary tuberculosis. This will reduce unnecessary procedure of bone marrow aspiration and will provide prompt treatment to the patient and reduced complication and spread to the community.

Key Words: Pulmonary TB, Anemia, Leukopenia, Leukocytosis, Thrombocytosis, Thrombocytopenia.

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INTRODUCTION

Tuberculosis is a major problem in the developing countries including Pakistan and it is associated with a variety of hematological presentation, so any patient presenting with anemia, thrombocytopenia or leucopenia or pancytopenia should be properly screened for Tuberculosis by rapid diagnostic assay or sputum examination in order for prompt diagnosis of the disease and to avoid unnecessary indication for bone marrow aspiration to provide prompt treatment and reduce its further complication and to prevent its further spread to the community.

Tuberculosis is a chronic bacterial infection caused by Mycobacterium Tuberculosis, present globally in the

developing countries,¹ more than two million people are infected by this disease and 48% of them occur in heavily populated area like Pakistan, China, India, Bangladesh and Indonesia. Pulmonary tuberculosis is highly infectious disease² in which single patient may infect large number of people.³ Its elimination is extremely difficult as long as poverty, overcrowding, dense population and other co-infection exists in large portion of the earth.⁴ Tuberculosis can affect lungs, lymph nodes, pleura, gastrointestinal tract, bones, joints, meninges and peritoneum.⁵ Hemopoietic system is another organ seriously affected by Tuberculosis which cause variety of changes in Hemopoietic cell lines and plasma components. These hematological changes provide useful information to the clinician in the diagnosis of Tuberculosis⁵ Hematological manifestations can vary from anemia of different types to pancytopenia, leukoerythroblastic picture; leukemoid reaction rarely disseminated intravascular coagulation (DIC) and even myelofibrosis.⁶

Pulmonary Tuberculosis is associated with a variety of hematological abnormalities. These include anemia, prolonged ESR, thrombocytosis, thrombocytopenia, leucopenia, leukocytosis and pancytopenia.⁷ Sometimes

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patient with millitary Tuberculosis present with pancytopenia with hypocellular bone marrow and other hematological alteration include anemia and thrombocytopenia⁸ pulmonary Tuberculosis is associated with high prevalence of anemia and other hematological abnormalities.⁹ Patient with pulmonary Tuberculosis has a typical presentation of thrombocytopenia as well.⁸

MATERIALS AND METHODS

The present study was carried out in the Pathology department and Medical department of Hayatabad Medical Complex Peshawar from November 2015 to October 2016.

A total 100 patients of Pulmonary Tuberculosis were studied; both adults' males and females diagnosed by direct sputum smear microscopic examination of slides. All these patients had history of prolong cough more than three weeks. Sputum samples from all the suspected TB patients taken, positive for Acid fast bacilli by direct sputum smear microscopic examination of Zeil Nelson stain slides were included in the study and those negative for acid fast bacilli were excluded from the study.

Complete blood count was performed on all these patients by hematology analyzer (Ruby cell dyne, Abbott, USA) for which 3 ml blood was collected in an EDTA tube (Purple top). All the samples were processed by the hematology analyzer for determination of hemoglobin level, platelet count and TLC. For determination of ESR, 2 ml of anti-coagulated blood was drawn into a Westergren tube up to the mark the tube was placed in a stand vertically for one hour and the reading was noted. All the data were subjected to statistical analysis using chi square test and t test level of significance was set at $P < 0.005$.

RESULTS

In out of 100 patients 35 % had anemia, hemoglobin level was $10 \text{ gm} \pm 0.867 \text{ gm/dl}$ which was significantly lower than the control group ($P < 0.0034$). 15 % had leucopenia WBC counts was $2.5 \pm 0.5567 \times 10^3 / \mu\text{l}$ which was significantly lower than the control group and 12 % leukocytosis total WBC count was $18 \pm 1.565 \times 10^3 / \mu\text{l}$ which was significantly higher than the control group while rest of patients had normal value as compared to control group.

10 % patients showed thrombocytosis mean platelet counts was $480 \pm 20.545 \times 10^3 / \mu\text{l}$ and 8 % patients showed thrombocytopenia mean platelet counts was $120 \pm 18.365 \times 10^3 / \mu\text{l}$ ($P < 0.0045$). ESR for all the patients were raised $100 \pm 10 \text{ mm/hour}$ which were significantly raised as compared to healthy individuals ($P < 0.005$) Tuberculosis is associated with significant Hematological changes so any patient presenting with hematological abnormalities, the physician should

concentrate on the diagnosis of pulmonary Tuberculosis.

Table No.1: Frequency of Hematological changes in Pulmonary Tuberculosis.

Pulmonary Tuberculosis patients	%age	Control group	%age
Anemia	35		
Leukopenia	15		
Leukocytosis	12		
Thrombocytosis	10		
Thrombocytopenia	8		
ESR	100		

Table No.2: Mean value of Hematological parameters in pulmonary Tuberculosis.

Hematological Parameters	Mean values of pulmonary Tuberculosis	Mean value of control group
Hemoglobin level	$10 \pm 0.867 \text{ g/dl}$	$13.789 \pm 0.678 \text{ g/dl}$
Leukoopenia	$2.5 \pm 0.5567 \times 10^3 / \mu\text{l}$	$7.654 \pm 1.567 \times 10^3 / \mu\text{l}$
Leukocytosis	$18 \pm 1.565 \times 10^3 / \mu\text{l}$	$7.654 \pm 1.567 \times 10^3 / \mu\text{l}$
Thrombocytosis	$480 \pm 20.576 \times 10^3 / \mu\text{l}$	$350 \pm 20.545 \times 10^3 / \mu\text{l}$
Thrombocytopenia	$120 \pm 18.567 \times 10^3 / \mu\text{l}$	$350 \pm 20.545 \times 10^3 / \mu\text{l}$
ESR	$100 \pm 10 \text{ mm/1}^{\text{st}} \text{ hour}$	$20 \pm 6.78 \text{ mm/1}^{\text{st}} \text{ hour}$

DISCUSSION

Tuberculosis is a major chronic bacterial infection and in a major public health problem in the developing countries it is associated with hematological abnormalities include anemia raised ESR, leukocytosis, leukopenia, thrombocytosis, thrombocytopenia and rarely DIC and bone marrow necrosis.

In the present study 100 patients of pulmonary Tuberculosis were included in the study out of which 35% patients showed anemia 12% patients leucocytosis and 15% leucopenia and 8% patients Thrombocytopenia and 10% had thrombocytosis and 100 % patients had raised ESR.

In the present study 35 % patients had anemia, mean Hb level was $10 \pm 0.867 \text{ gm/dl}$ which was significantly lower than the control group. A similar study had been concluded by Al-Muhammad et al. on 90 patients of pulmonary Tuberculosis who reported significant anemia in TB patients¹⁰ Another study was conducted by Kamal et al on 100 patients, in which 99 % had anemia, 49 % had lymphopenia and 100 % had elevated ESR which shows similar correlation to our study that hematological changes are significantly associated with pulmonary Tuberculosis.¹¹

Others studies in this regard reported by Akpan et al. that pulmonary Tuberculosis is associated with

significant Hematological changes and include anemia, leukocytosis, leucopenia and Thrombocytosis and raised ESR and DVT as a result of hyper coagulable state.¹² Various studies are available on this subject that hematological abnormalities are common in Pulmonary Tuberculosis most common hematological changes occurring in pulmonary Tuberculosis is Anemia, decreased Hb level reported by various authors. The exact etiology is unknown but may be due to cytokines secreted by macrophages in response to tuberculosis bacilli resulting in decrease erythropoietin percolation and blockage in the reticulo-endothelial transfer of iron in the developing RBC.¹³ It may also due to anemia of chronic disease¹⁴ various cytokines are released due to activation of T-lymphocytes and macrophages like interferon gamma. (INF.gamma), Tumor necrosis factors (TNF-alpha) interleukine (IL-1) and interkine-6 (IL-6) concentrate iron in reticulo-endothelial system, limiting its availability for RBC and decrease Hemoglobin synthesis. These cytokines also inhibit erythroid progenitor cell proliferation and decrease erythropoietin production; these cytokines impair the responsiveness of progenitor cells to erythropoietin. Cytokines directly damage erythrocyte and reduce their life span.¹⁵ Thrombocytosis has also been observed in pulmonary TB which may be attribute to reactive changes occurring in chronic infection and may be due to increase level of cytokines IL-6 induce hepatic Thrombopoietin production and cause reactive thrombocytosis.¹⁸ Andreo et al also reported that mycobacterium Tuberculosis infection is associated with thrombocytosis and this effect might be due to increase level of interleukine-6.¹⁹ Thrombocytopenia has also been reported in various studies of pulmonary Tuberculosis. In our study 8% patients showed Thrombocytopenia. Kudrajpaul also reported immune Thrombocytopenia in his study. The exact cause is unknown, but it is thought that the sensitized plasma cells secrete antibodies against Tuberculosis antigen which cross react with platelet and cause their destruction. It might also be due to bone marrow infiltration by Tuberculosis and TB related intravascular coagulation.²⁰ Thrombocytopenia in TB can be very severe and may present with dissiminated purpura, epistaxis, hematuria, mucosal bleeding and hemoptesis.²¹ Varied mechanisms like drugs, immune mechanisms, bone marrow fibrosis, granulomatous involvement of bone marrow and Hypersplenism have been responsible for thrombocytopenia.⁵ Leucocytosis and leucopenia has also been observed in our study, similar to other studies leukocytosis are thought to be result from immune responses to tuberculosis reported by ohaniyi et al²² while leucopenia has been observed by Hungund et al.⁵ Raised ESR has also been observed in our study which has reported by different authors in pulmonary

Tuberculosis, Elevated ESR result from production of high profile of fibrinogen and other acute phase proteins that cause stickiness of RBC to form rouleux formation which will settle and sediment faster but this raised ESR becomes corrected after using different combination of antituberculus drugs.^{23, 24}

CONCLUSION

The study concluded that hematological abnormalities are common manifestations in pulmonary Tuberculosis, so any patient presenting with cytopenia or leukocytosis or thrombocytosis or thrombocytopenia. The physicians must maintain a high index of suspicious for diagnosis of pulmonary tuberculosis and this will reduce unnecessary procedure for bone marrow aspiration and provide immediate treatment to the patient and reduce its further spread and complications.

Conflict of Interest: The study has no conflict of interest to declare by any author.

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