Original Article

Hematological Changes in Patients Presenting with Pulmonary Tuberculosis

Hematology in pulmonary TB

Shah Taj Khan[1], Muhammad Abbas[2], Subhan Uddin[3], Awal Mir[4], Babar Rehman[1] and Hamid Ullah[2]

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 ± 867 gm/dl. In 15% Patients had leucopenia with TLC was 2.5±1.567×103/µl and 12% patients had leukocytosis, TLC was 18±1.565×103/µl. 10% patients had thrombocytosis, Platelet count was 480±20.545×103/µl and 8% patients had thrombocytopenia with platelet count was 120±118.3 ×103/µl. 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 cytosis 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.

Citation of article:Khan ST, Abbas M, Uddin S, Mir A, Rehman B, Ullah H. Hematological Changes in Patients Presenting with Pulmonary Tuberculosis.Med Forum 2017;28(5):166-169.

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 disease[2] 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] Hemapioetic system is another organ seriously affected by Tuberculosis which cause variety of changes in Hemopoitic cell lines and plasma components . These hematological changes provide useful information to the clinician in the diagnosis of Tuberculosis[5] 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

[1.] Department of Heamatology, Hayatabad Medical Complex, Peshawar.
[2.] Department of Medicine, Bacha Khan Medical College, Mardan.
[3.] Department of Hematology, Gajju Khan Medical College, Swabi.
[4.] Department of Pathology, Khyber Girls Medical, Peshawar.

Correspondence:Shah Taj Khan, Associate Professor of Hematology, Hayatabad Medical Complex, Peshawar.
Contact No: 0301-8929801
Email: drshahtajkh@gmail.com

Received: March 01, 2017; Accepted: April 02, 2017

patient with milliary Tuberculosis present with pancytopenia with hypocellular bone marrow and other hematological alteration include anemia and thrombocytopenia[8] 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 ant T-test level of significance was set at P<.005.

RESULTS

In out of 100 patients 35 % had anemia, hemoglobin level was 10 gm±0.867 gm/dl which was significantly lower than the control group (P<0.0034). 15 % had leucopenia WBC counts was $2.5\pm0.5567\times10^3$/µl which was significantly lower than the control group and 12 % leukocytosis total WBC count was $18\pm1.565\times10^3$/µl 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 $480\pm20.545\times10^3$/µl and 8 % patients showed thrombocytopania mean platelet counts was $120\pm18.365\times10^3$/µl (P<0.0045). ESR for all the patients were raised 100±10 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		%age
Anemia	35		
Leukopenia	15	Control group	20
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 ±0.867 g/dl	13.789±0.678 g/dl
Leukoopenia	$2.5\pm0.567\times10^3$/µl	$7.654\pm1.567\times10^3$/µl
Leukocytosis	$18\pm2.576\times10^3$/µl	$7.654\pm1.567\times10^3$/µl
Thrombocytosis	$480\pm20.576\times10^3$/µl	$350\pm20.545\times10^3$/µl
Thrombocytopenia	$120\pm18.567\times10^3$/µl	$350\pm20.545\times10^3$/µl
ESR	100±10 mm/1st hour	20±6.78 mm/1st 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±.867 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 patients[10] 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 disease[14] various cytokines are released due to activation of T-lymphocytes and macrophages like interferon gamma. (INF.gamma), Tumor necrosis factors (TNF-alpha) interlukine (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 interleckine-6.[19]

Thrombocytopenia has also been reported in various studies of pulmonary Tuberculosis. In our study 8% patients showed Thrombocytopenia. Rudrajilpaul 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, hemituria, 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 al[22] 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 rouluex 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.

REFERENCES

1. Shafee M, Abbas F, Ashraf M, Mengal MA, Kakar N, Ahmed 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. Dye C. Global epidemiology of Tuberculosis. Lancet 2006; 367:603-662.
3. SanjavaN, MarkJ. Detection of tuberculosis public health and law. MJ A 2004;11:573-576.
4. David S, Tuberculosis and non Tuberculosis mycobacterial infections 4th Ed Philadelphia pennsyvania, united states of America: WB Saunder's company;1999.
5. Hungund BR,Sangoli SS, Bannur HB, Malur PR, Pili GS, Chavan RY, et al. Blood and bone marrow findings in Tuberculosis in adults. A cross-sectional study. Al Ameen J Med Sci 2012;4:362-366.
6. Avasthi R, Mohanty D, Chaudhary SC, Mishra K. Disseminated Tuberculosis interesting Hemato-logical observation. JAPI 2010;58:243-244.
7. Yaranal JP, Umoshankar T, Harish GS. Hematolo-gical profile in pulmonary Tuberculosis. Int J Health Rehabil Sci 2013;1:50-55
8. Mishra NR, Panda PC, Dass S, Aran An unusual case of Panacytopenia in an adolescent girl. Ind J Child Health 2015;2:34-36
9. Kerkhoff AD, Wood R, Vogt M, Stephen D, Lawn MD. Predictive value of anemia for Tuberculosis in HIV infected patients in sub-Saharan Africa. An indication for routine Microbiology investigation using New Rapid Assay. J Aquire immune Defic Syndr 2014; 66:33-40.
10. Al-muhammadi OM, AL-shammery GH. Studying some hematological changes in patients with pulmonary Tuberculosis Babylon Governorat. Med J Babylon 2011; 8:608-617.
11. Kamete S, Ramesh B, Bhaktavatchalam N. Study of Hemtological profile before, during after completion of Dots Therapy in pulmonary Tuberculosis. J

EBMI 2014; 1:962-968.
12. AkpanA, Josephine O, Akwiwv C. Some Hematological parameters of Tuberculosis infected Africans. The Nigerian perspective. J Nat Sci Res 2012; 1:50-56.
13. Lambord EH, Manvelt EPG; Hematological changes associated with millariy TB of bone marrow. Tubercle lung Dis 1993; 74:131-135.
14. Eyeshi A, Rahmi E, Gharabaghi N. Anemia and peripheral blood changes in pulmonary Tuberculosis. Hamadan university of Med Sci and H Ser 2009;16:87-96.
15. Weiss G. Pathogenesis and Treatment of chronic disease. Blood Rew 2002;16:87-96.
16. Mean RT. Recent development in the anemia of chronic disease. CurrentHematol2003; 2:116-121.
17. Karyadi E, Dolman W, West C, Vancrevel R, Nelwan R, Amin Z. Cytokines related to nutritional status in patients with untreated pulmonary TB in Indonesia. Asia Pacific J Clin 2009; 2:218-226.
18. Kaushanky K. Thrombopoietin. A tool for understanding Thrombopoiesis. J Thromb and Hemeo 2003; 1:1587-1592.
19. Andrew A, Rensha MD, Edwin W. Gould MD. Thrombocytosis is associated with mycobacterium Tuberculosis infection and positive Acid fast stains in granuloma. Am J Clin Pathol 2013;139:584-586.
20. Paul R. State of the globe-immune Thrombo-cytopenia, an uncommon complication in Tuberculosis. J Global Infect Dis 2014; 6:93-94.
21. Daguonkar RS, Udwandia ZF, Dissiminated Tuberculosis with immune Thrombocytopenia purpura. Lung Ind 2012;29:63-65.
22. Olaniyi JA, Akeuova YA. Hematological profile in patients with pulmonary Tuberculosis in adaban Nigeria. Afr Med Sci 2003;32:239-242.
23. Devi U, Mohan RC, Srivastava VK, Rath PK, Das BS. Effect of iron supplementation on mild to moderate anemia on pulmonary Tuberculosis. Br J Nutr 2003; 28:231-277.
24. Al-Omar LA, Al Shaban SA. Hematological Abnormalities in Saudia suffering from pulmonary Tuberculosis and their response to the treatment. Res J Pharmacol 2009;3:78-85.