Available Online at http://www.recentscientific.com

ISSN: 0976-3031

International Journal of Recent Scientific Research
Vol. 6, Issue, 5, pp.4128-4131, May, 2015

International Journal of Recent Scientific Research

RESEARCH ARTICLE

ANEMIA AMONG PATIENTS WITH PULMONARY TUBERCULOSIS IN PORT SUDAN, EASTERN SUDAN

Bashir A. Bashir, Sharif A. Abdallah and Ahmed A. Mohamedani

Department Medical Laboratory Sciences Division, Port Sudan Ahlia College, Port Sudan, Sudan

ARTICLE INFO

Article History:

Received 14th, April, 2015
Received in revised form 23th, April, 2015
Accepted 13th, May, 2015
Published online 28th, May, 2015

Key words:

Anemia, Iron deficiency, TIBC, Tuberculosis, Port Sudan

ABSTRACT

Background: Pulmonary tuberculosis (PTB) and anemia are both prevalent in Red Sea State. There is limited and inconsistent literature on the association between anemia and pulmonary tuberculosis in the studied area. **Aim:** This study aimed at assessing the anemia among patients with pulmonary tuberculosis living in Port Sudan city, Red Sea state, Sudan. **Method:** A prospective study was conducted from June 2006 to December 2008 at Port Sudan Tuberculosis Diagnostic Center. Hundred newly discovered Ziehl Neelsen stain positive randomly selected along with fifty apparently healthy adult also randomly selected were enrolled. Hemoglobin concentration (Hb), serum iron, total iron binding capacity (TIBC) and transferrin saturation were measured. **Results:** Anemia was observed in 44(44%) of pulmonary tuberculosis patients of which 15 (34%) of cases were anemia of chronic disease, 12 (27%) of cases were iron deficiency, 7 (16%) of cases were iron deficiency anemia, 2 (5%) of cases were macrocytic anemia and 8 (18%) of cases were normocytic normochromic anemia. **Conclusion:** Anemia of chronic disease is the most condition associated with pulmonary TB, iron deficiency with or without anemia may contribute to advancing the disease.

INTRODUCTION

Pulmonary tuberculosis (PTB) is still a common disease in developing countries [1, 2]. The diagnosis of tuberculosis mainly relies on acid fast bacilli smear and culture result [3]. However, nucleic acid amplification test and polymerase chain reaction (PCR) test were also found reliable [4, 5]. A variety of haematological changes have been described in patients with PTB such as anaemia, sideroblastic anaemia, and folate deficiency [6]. Anaemia is considered to be present if the hemoglobin concentration (Hb) of the red cells is below the lower limit of the 95% reference interval for the individual ;age, sex, and geographic location [7]. Anaemia can develop as a secondary effect of a disease process that does not physically invade the bone marrow or markedly accelerated the destruction of erythrocyte. One of the most common infections causing anaemia is tuberculosis; the extent of anaemia associated with tuberculosis depends on the extension of the disease. When tuberculosis is localized mainly in one organ e.g. the lung, the haemoglobin level is usually normal until the disease has made considerable progress leading to a mild to moderate normochromic normocytic, or a slightly hypochromic anaemia. The anaemia takes several weeks to develop after the onset of infection, and then progresses slowly over several months until the haemoglobin level eventually stabilizes [8]. Anaemia is a common complication of pulmonary tuberculosis. The precise mechanism of anaemia in pulmonary tuberculosis is not clearly known but anaemia due to inflammation as well as of iron deficiency has been implicated, both are common in developing countries [9, 10]. The possible cause of observed anaemia in PTB patients might be due to cytokines production and eventually many biochemical changes detected [11]. Nutritional deficiency and malabsorption syndrome can deepen the severity of anaemia. However, the observation that patients with tuberculosis-associated anemia display an absence of bone marrow iron, suggests iron deficiency is a possible cause of anaemia in patients with tuberculosis [12]. The prevalence of anemia among TB patients ranges between 30 – 94% [12 – 16]. The increasing prevalence of anemia with age has been explained by increased chronic disease, poor nutritional status, decrease marrow cellularity, and low serum B_{12} level. Therefore, old age could be considered as a risk factor for tuberculosis associated anemia. On the other hand, a disturbance of iron homeostasis develops with increased uptake and retention of iron within the reticuloendothelial system in chronic infections such as tuberculosis because iron is an important growth factor of mycobacterium tuberculosis. The iron retention in reticuloendothelial system is considered as one of the host defense mechanisms and many therapeutic trials are performed. The effect of iron –retention might be exaggerated in women with tuberculosis because women are more likely than men to be iron deficient. This can explained female sex is a risk factor of anemia [12]. Anemia with similar haematological features occurred in a number of chronic disorders other than tuberculosis [8]. The antituberculous (Isoniazid, cycloserine, and pyrazinamide) reportedly may

Corresponding author:* **Bashir A. Bashir
Department Medical Laboratory Sciences Division, Port Sudan Ahlia College, Port Sudan, Sudan

cause a form of sideroblastic anemia by inhibit and interfere with the conversion of vitamin B_6 to its active coenzyme form. This in turn, reduces δ-aminolevulinic acid synthase activity and could produce secondary acquired sideroblastic anemia with characteristics similar to those in the hereditary form. The laboratory diagnosis is made according to the cause [17]. Many of the TB patients show haematological evidence of folate deficiency, and the cause of this deficiency in tuberculous patients is not obvious. The deficiency is equally common among treated and untreated patients, and it is not related to the length or type of antituberculous. Malabsorption of folate is not excluded. It is possible that increased utilization of folate occurs in tuberculosis owing to chronic inflammation, and this increased demand cannot be met by an ordinary diet. Alternatively, folate deficiency might predispose to tuberculosis, and this could be a factor responsible for the known high incidence of tuberculosis in malnourished subjects. Although several studies have shown significantly lower levels of serum folate in patients with active tuberculosis when compared with controls the incidence of significant megaloblastic anaemia is low [18]. Tuberculosis can cause different types of alterations of normal marrow including fibrosis. The characteristic findings are leuco-erythroblastic peripheral blood smear, extramedullary haemopoiesis, and bone marrow fibrosis. Tuberculosis is a rare cause of myelofibrosis in developed countries; however, it is still frequent in some regions due to the high prevalence in the general population [19]. Rare cases of myelofibrosis have been described and thought to be due to disseminated tuberculosis [8].The diagnosis is established with certainty only if the marrow biopsy specimen includes a tuberculous focus [20]. The present study was designed to assess the anemia and find out the variations in hemoglobin, serum iron, total iron binding capacity and transferrin saturation.

MATERIALS AND METHODS

This study was conducted prospectively for a period from June 2006 to December 2008 in Port Sudan tuberculosis diagnostic center in Red Sea State. This study consisted of hundred newly discovered pulmonary TB patients positive with *Tubercle bacilli* in sputum (Zn stain) were randomly selected. The inclusion criteria were patients first time diagnosis, no current or previous anti-tuberculous drug treatment, and not to be suffering from any other chronic disease.

The exclusion criteria included past history of pulmonary TB, currently on antituberculous drug or any other drugs which affected bone marrow or peripheral blood, and known at the time of study to have a chronic disease which will adversely affect the body systems including the bone marrow and the peripheral blood. Fifty, apparently healthy normal individuals with no clinical signs for pulmonary TB were selected randomly to be the control group. Blood samples were collected from all of the studied population.

About 3 ml blood was placed in potassium ethylene diamine tetra acetic acid (EDTA) and 3 ml in plain container. The samples under standard laboratory temperature were processed to obtain serum by using a centrifuge. The analysis was performed in Port Sudan Tuberculosis Diagnostic Center by expert technologists.

Patient's indicators

Patients characteristics of interest included: 1) Demographic: sex, age, residence, tribe, and occupation; 2) Hematological: Hemoglobin concentration (Hb) was measured by cyanmethaemoglobin method using (WP21B Tough biochemistry analyzer, mindary (Genius Electronic Co, Ltd, China); 3) Chemical tests: Serum iron and total iron binding capacity (TIBC) were examined within 2 hours of collection using biochemistry analyzer. Percentage saturation obtained by calculation. Chemical tests were determined by (linear chemicals 1135005, 11402AB, Barcelona (Spain).

Statistical analysis

Measurements of laboratory data hemoglobin, serum iron, TIBC, and transferrin saturation with pulmonary TB were statistically tested by compare mean and chi-square test which ever was appropriate. A *P.value* less than 0.05 were considered statistically significant. The Statistical Package for Social Sciences (SPSS 16.0 version, IBN. Chicago, USA) was used for data analysis.

Ethical consideration

This study was approved from the regional Ethical Review Committee (ERC) and written informed consent was obtained from all the patients.

RESULTS

This is a case control-analytical study conducted in Port Sudan Tuberculosis Diagnostic center, Red Sea State. The total number of the confirmed diagnosed pulmonary TB patients was 100. The age of the patients in this study was between 14 and 70 years (mean age 33 years). The control individuals aged between 19 and 63 years (mean age 27 years). Of the 100 pulmonary TB patients, 77% were males and 23% were females.

Table 1 Characteristics of patients and control in the study

Characteristics	patients (n=100)	Control (n=50)	P. value
Age (mean ± SD)	33 ± 12	27 ± 9	0.004
(Range)	14 – 70 y	19 – 63 y	
Sex			
Male	77 (77%)	38 (76%)	0.892
Female	23 (23%)	12 (24%)	
Demographic data			
Residence	32 (32%)	24 (48%)	
Eastern area	52 (52%)	18 (36%)	0.073
Southern area	16 (16%)	8 (16%)	
Downtown			
Tribe			
Hadandwa	24 (24%)	6 (12%)	0.000
Bani amer	33 (33%)	7 (14%)	
Northern Sudan	8 (8%)	29 (58%)	
Western Sudan	35 (35%)	8 (16%)	
Occupation			
Students	11 (11%)	25 (50%)	
Workers	42 (42%)	12 (24%)	0.000
House wife	13 (13%)	—	
Other jobs	20 (20%)	—	
Employees	14 (14%)	13 (26%)	

Table 2 The difference between test and control in studied parameters

Parameters	Test group Mean ± SD	Control group Mean ± SD	Median test	Median control	Range test	Range control	P.value
Hb gm/dl	10.3± 1.9	13.4 ± 1.5	10.4	13.4	6 – 13.8	10.3- 15.9	0.000
S. Iron µg/dl	60 ± 19	91 ± 22	60	86	33 – 133	60 – 171	0.000
TIBC µg/dl	301 ± 137	313 ± 84	250	300	100 – 600	171 – 500	0.000
T. saturation%	25 ± 13	32 ± 12	25	30	5 – 67	16 – 60	0.000

Table 3 Laboratory findings and types of anemia among the pulmonary TB patients

Parameters	ACD n=29	Fe deficiency n=16	IDA n=7	Macro. anemia n=6	N. Normoch. n=42	Total n=100
Low Hb	15 (34%)	12 (27%)	7 (16%)	2 (5%)	8 (18%)	44 (44%)
Normal Hb	14 (25%)	4 (7%)	0	4 (7%)	34 (61%)	56 (56%)
Low Iron	18 (37%)	15 (31%)	7 (14%)	2 (4%)	7 (14%)	49 (49%)
Normal Iron	11 (22%)	1 (2%)	0	4 (8%)	35 (69%)	51 (51%)
High TIBC	0	16 (70%)	7 (30%)	0	0	23 (23%)
Low TIBC	27 (66%)	0	0	5 (12%)	9 (22%)	41 (41%)
Normal TIBC	2 (6%)	0	0	1 (3%)	33 (91%)	36 (36%)
Low T. saturation	1 (4.5%)	14 (64%)	6 (27%)	0	1 (4.5%)	22 (22%)
High T. saturation	3 (60%)	0	0	0	2 (40%)	5.0 (5%)
Norm T. saturation	25 (34.2%)	2 (2.8%)	1 (1.4%)	6 (8.2%)	39 (53.4%)	73 (73%)

In the control group, 38 (76%) were males and 12 (24%) were females. Table 1 shows the comparison of different characteristics between patients and controls. It shows that the southern part of the study area (Darussalam) represented the highest incidence (52%) region affected by tuberculosis infection and the workers were the most common segment of occupation affected (42%). Also table 1 illustrates that the overwhelming majority of pulmonary TB is among the western tribe (35%), followed by Bani amer (33%), Hadandwa tribe (24%), and northern tribe (8%). The differences between the patient group and the control group were found to be significant in haemoglobin concentration, iron, total iron binding capacity, transferrin saturation (Table 2). Hemoglobin concentration, serum iron, TIBC, and transferrin saturation were lower in the patient group than in the control group (P< 0.000). Anemia was present in 44(44%) pulmonary TB cases. Accordingly, most of cases in the current study are anemia of chronic disease (ACD) 15 (34%); followed by iron (Fe) deficiency 12 (27%), severe iron deficiency anemia (IDA) 7 (16%), macrocytic anemia 2 (5%), and normocytic normochromic anemia 8 (18%) (Table 3). The low Hb concentration found in 15(34%) of anemia of chronic disease was correlated positively with low serum iron in 18(37%) and the decreased TIBC in 27 (66%) (P< 0.000). The low Hb concentration found in 12(27%) and 7(16%) of the iron deficiency and severe iron deficiency anemia respectively were correlated positive with low serum iron in 15(31%), 7(14%) and the increased TIBC in 16 (70%), 7(30%) and decreased transferrin saturation in 14(64%), 6(27%) respectively (P< 0.000) (Table 3).

DISCUSSION

To our knowledge, this is the first study to assess the anemia in Pulmonary TB patients in Red Sea State, Sudan. In this study we found the majority of patients had anemia of chronic disease anemia (microcytic hypochromic anaemia). These findings are different from those of a study by Muzaffar TM et al, 2008; Morris CW et al, 1989; Dosumu EA, 2001; Singh KJ et al, 2001; Baynes RD et al, 1986; Lombard EH, 1993 and Lee SW et al, 2006 who found normocytic normochromic anaemia in the majority of their patients, the difference may be due to nutritional factors and small sample size [12, 17, 24 – 28]. Anemia with and without iron deficiency were positively associated with increased risk of mortality. Anemia without iron deficiency was associated with an increased risk of TB recurrence. Similar to other studies, we found a high burden of anemia in TB patients supporting the clinical importance of this routinely measured indicator [29, 30]. Previous study data also suggest, in their population the iron deficiency is an important contributor to anemia [12].

We found a strong positive association of anemia of chronic disease (15/44: 34%) and iron deficiency with TB recurrence and mortality, suggesting that iron deficiency (12/44: 27%) also contribute to poor clinical outcomes. The possible explanation for the findings is that the presence of macrocytic anemia (2/44: 5%) and normocytic normochromic anemia (8/44: 18%) in our study due to factors associated with poor health status or advanced disease. The other causes of anemia including inflammation, parasitic infection, hemoglobinpathy, and other nutritional deficiencies are also important in adult with PTB.

Studies to identify these other contributing factors are necessary to reduce the burden of TB-associated anemia [31]. Kaminskaia GO and Abdullaev R studying the iron metabolism in patients with different degrees of severity of pulmonary tuberculosis stated that in patients with acutely progressive pulmonary tuberculosis , serum iron and serum total iron binding capacity were drastically decreased, while serum unsaturated iron binding capacity was reduced [32, 33]. These findings are considerably in agreement with our present study. This study has a limitation, we did not have information on several factors that may be associated with both iron imbalance and TB infection, including smoking, alcohol history, and diabetes; therefore we cannot exclude the possibility that such factors may contribute to the associations observed.

CONCLUSION

Anemia of chronic disease is the most condition associated with pulmonary TB, iron deficiency with or without anemia may contribute to advancing the disease.

Reference

1. Andre J, Schwartz R, Dameshek W. Tuberculosis and Myelosclerosis with Myeloid Metaplasia. *JAMA*, 1961; 178:1169-74.
2. Baynes RD et al. Haematological and iron-related measurements in active pulmonary tuberculosis. *Scand. J. Haematol*., 1986; 36(3): 280-287.
3. Ben-Kahla I *et al*. Evaluation of a simplified IS6110 PCR for rapid diagnosis of *Mycobacterium tuberculosis* I an area with high tuberculosis incidence. *Pathol. Biol. (Paris)*. 2009; 22: 121-108.
4. Cameron SJ, Horne NW. The effect of tuberculosis and its treatment on erythropoiesis and folate activity. *Tubercle*, 1971; 52:37-48.
5. Das BS *et al*. Effect of iron supplementation on mild to moderate anaemia in pulmonary tuberculosis. *Brit J Nutr*. 2003; 90:541-50.
6. Dosumu EA. Pattern of some haematological indices in newly diagnosed pulmonary tuberculosis case in Iwo,Nigeria: diagnostic and therapeutic implications. *Niger J Med*, 2001; 10:18-20.
7. Douglas SW, Adamson JW. The anaemia of chronic disorders: Studies of marrow regulation and iron metabolism. *Blood*, 1975; 45(1): 55-65.
8. Eakins D, Nelson MG. Disseminated with associated Haematological disorder. *I J Med Sc*. 1969; vol 2, No 2.
9. Ebrahim O, Folb PI, Robson JP. Blunted erythropoietin response to anaemia in tuberculosis. *Eur. J.Hematol*., 1995; 55: 251-254.
10. Espinal MA *et al*. Global trends in resistance to antituberculosis drugs: WHO.Inernational Union against tuberculosis and lung disease working group on Antituberculosis Drug Resistance Surveillance. *N. Engl. J. Med*. 2001; 344: 1294-1303.
11. Firkin F *et al*. de Grouchy's Clinical Haematology in Medical Practice. 5th ed. India: Blackwell Science. 1996; P 96-119.
12. Gladwion M, Trattler B. Clinical Microbiology. 3th ed. United state America. Miami, *Med Master. Inc*. 2007; pp 102-111.
13. Hoffbrand AV, Pettit JE. Essential Haematology. 3th ed. United Kingdom: Blackwell Science, 1993; P. 209-377.
14. Hoffbrand VA, Lewis SM, Tuddenham EGD. Postgraduate Haematology. 14th ed. England (London): Butterwarth Heinemann, 1999; p.40.
15. Hussain SF, Irfan M, Abbasi M, Anwer SS, Davidson S et al. Clinical characteristics of 110 miliary tuberculosis patients from a low HIV prevalence country. *Int J Tuberc Lung Dis*. 2004; 8(4):493–99.
16. Isanaka S, Mugusi FM, Urassa W, Willet WC, Bosch RJ et al. Iron deficiency and anemia predict mortality in patients with tuberculosis. *J Nutr*. 2012; 142(2): 350 – 57.
17. Kaminskaia GO, Abdullaev RIu. Iron metabolism in patients with different variants of pulmonary tuberculosis. *Probl Tuberk*, 2002; 49-51.
18. Karyadi E,Schultink Nelwan RH, Gross R, Amin Z, Dolmans WM et al. Poor micronutrient status of active pulmonary tuberculosis patients in Indonesia. *J Nutr*. 2000; 130: 2953 – 8.
19. Kochan I. The role of iron in bacterial infection, with special consideration of host-tubercle bacillus interaction. Curr Top Microbiol Immunol. 1973; 60: 1 – 30.
20. Laraque F *et al*. Performance of nucleic acid amplification test for diagnosis of tuberculosis in a large urban setting. *Clin. Infect. Dis*. 2009; 49(1): 46-54.
21. Lee GR. The anaemia of chronic disease. *Semin Hematol.*, 1983; 20(2): 61-80.
22. Lee SW *et al*. The prevalence and Evolution of anemia Associated with tuberculosis. *J Korean Med Sci*. 2006; 21:1028-32.
23. Lombard EH, Mansvett EP. Haematological changes associated with miliary tuberculosis of the bone marrow. *Tuber Lung Dis*, 1993; 74:131-5.
24. Morris CW, Bird AR, Nell H. The haematological and biochemical changes in severe pulmonary tuberculosis.*Q J Med*, 1989; 73:115-9.
25. Muzaffar TM *et al*. Hematological changes in tuberculous spondilities patients at the Hospital Unversiti sains Malaysia. *Southeast Asian J Med Trop Public Health*, 2008; 39:686-9.
26. Olaniyi JA, Aken'Ova YA. Haematological profile of patients with pulmonary tuberculosis in Ibadan, Nigeria. *Afr J Med Med Sci*. 2003, 32(3): 239–42.
27. Roberts PD, Hoff brand AV, Mollin DL. Iron and folate metabolism in tuberculosis. *Bri med J*, 1966; 2: 198-202.
28. Saathoff E, Villamor E, Mugusi F, Bosch RJ, Urassa W et al. Anemia in adults with tuberculosis is associated with HIV and anthropometric status in Dares Salaam, Tanzania. *Int J Tuberc Lung Dis*.2011; 15(7): 925–32.
29. Singh KJ *et al*. Significance of haematological manifestations in patients with tuberculosis. *J Assoc Physician India*, 2001; 49:788,790-4.
30. Turgeon ML. Clinical Haematology theory and Procedures. 3th ed. United States of America: Lippincott Williams & Wilkins. 1999; P. 96-119.
31. Unsal C *et al*. Tuberculosis leading to reversible myelofibrosis: a case report. *Haema*, 2004; 7(4): 505-508.
32. van Lettow M, West CE, van der Meer JW, Wiering FT, Semba RD. Low plasma selenium concentrations, high plasma human immunodeficiency virus load and high interleukin-6 concentrations are risk factors associated with anemia in adults presenting with pulmonary tuberculosis in Zomba district, Malawi. *Eur J Clin Nutr*. 2005; 59: 526 – 32.
33. WHO (World Health Organization). Anti-tuberculosis drug resistance in the world: report 2; Prevalence and trends Global Project on antituberculosis Drug Resistance Surveillance. Geneva, Switzerland. 2000; pp 1-253.

How to cite this article:
Bashir A. Bashir *et al*., Anemia Among Patients With Pulmonary Tuberculosis In Port Sudan, Eastern Sudan. *International Journal of Recent Scientific Research Vol. 6, Issue, 5, pp.4128-4131, May, 2015*