Impact of Pulmonary Tuberculosis on Total and Differential Peripheral Blood Leukocytes Count

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Abstract: This study aimed at assessing the impact of pulmonary tuberculosis on leukocytes (count and differential) in patients living in Port Sudan city, Red Sea state, Sudan. This is a case control study covers the period from June 2006 to December 2008 at Port Sudan Tuberculosis Diagnostic Center. Hundred newly discovered, Ziehl Neelsen stain positive, males (77%) and females (23%) were randomly selected to be the study sample and fifty, apparently healthy adults males (76%) and females (24%) were also randomly selected to be the control group of the study. The ages of the patients ranged from 14-70 years old. The ratio of males to females was 3.3:1. Monocytosis was seen in (39%) of patients while (82%) of patients showed features of left shift granulocytes. Therefore, the presences of such haematological peripheral blood changes may predict raise the suspicion of pulmonary tuberculosis.

Key words: Tuberculosis, monocytosis, differential leukocyte, port sudan, blood, male

INTRODUCTION

Pulmonary Tuberculosis (PTB) is a major public health problem in Port Sudan, Sudan (Ageep, 2012). The pulmonary type is the most important form of tuberculosis, continues to be one of most wide spread infectious diseases (WHO, 2001). The differential diagnosis of tuberculosis should be entertained in patients with some abnormal haematological findings (Singh *et al.*, 2001). The blood count in pulmonary tuberculosis is usually unremarkable. Formerly the ratio of monocytes to lymphocytes was regarded significant, especially with respect to evaluation of the activity of the disease, the ratio declining with decreasing activity. This index has fallen into disuse. Occasionally in florid tuberculous infection, the polymorph nuclear neutrophil count may be elevated and there may be a characteristic shift to left picture, more often encountered in other infections. The total leukocyte count may be high but this is rare, such a degree of leukocytosis usually indicates some pyogenic complication or the presence of another disease (Beenson and Mcdermott, 1963).

Leukemoid reaction in patients with pulmonary tuberculosis: The term leukemoid reaction is used to describe the occurrence of a peripheral blood picture resembling that of leukaemia in a subject who does not have leukaemia. The blood picture may suggest the presence of leukaemia because of marked elevation of total white cell count or the presence of immature white cells (blast) or both (Firkin *et al.*, 1996). Leukemoid reaction can occur in association with many infections but most frequently with tuberculosis, the incidence of leukemoid reaction in tuberculosis is not known but usually occurs in miliary tuberculosis (Siddiqui *et al.*, 1977). Disseminated Tuberculosis (DTB) is associated with Leukemoid reactions and patients with involvement of bone marrow may show leuco-erythroblastic changes in the peripheral blood film (Hoffbrand and Pettit, 2006). Leukemoid reaction may be either myeloid or lymphoid. Myeloid leukemoid reactions have been reported in patient with tuberculosis (Stiene *et al.*, 1998). Rare cases of disseminated tuberculosis simulating acute myeloid leukaemia have been described. Rare cases of tuberculosis with either lymphocytic or lymphoblastic blood picture have been reported. Most have occurred with disseminated tuberculosis in which the lymph node, liver and spleen were enlarged.

Monocytosis in pulmonary tuberculosis: A wide variety of acute bacterial infections have been reported to be accompanied by monocytosis, one of the most consistently reported is tuberculosis. Tuberculosis is thought to elicit increased monocyte because of their role in the cellular response to the bacillus (granuloma formation) cell mediated immunity leading to

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mycobacterium tuberculosis containing granuloma is the major component of host defense against tuberculosis and regulated by the balance of cytokines secreted mostly by mononuclear phagocytes and lymphocyte (Pereira *et al.*, 2004). Monocytosis in such cases is believed to reflect active disease. There is little or no storage of monocytes therefore, they are released into the circulation before neutrophils are. Because of this relative monocytosis frequently heralds recovery from agranulocytosis or marrow hypoplasia (Stiene *et al.*, 1998).

Atypical lymphocyte in pulmonary tuberculosis: It may be referred to by several names including variant lymphocyte, downey cells, reactive or transformed lymphocyte, lymphocytoid, plasmacytoid lymphocyte, and virocyte. These terms denotes that the lymphocyte is not normal but does not further classify a lymphocyte. Normal person may have up to 5 or 6% of variant lymphocytes. These represent morphological evidence of normal immune mechanism. Variant lymphocytes can be found in increased number in disorders such as tuberculosis (Stiene *et al.*, 1998).

Leukaemia in patients with tuberculosis: Leukaemias are characterized by an overproduction of various types of immature or mature leukocytes in the bone marrow and/or peripheral blood. These abnormal cells may cause bone marrow failure, a raised circulating leukocytes count and infiltrate organs (Hoffbrand and Pettit, 2006). Tuberculosis has been associated with a variety of haematological abnormalities such as leukemoid reaction which have been reported in association with disseminated tuberculosis. This leukemoid reaction closely simulated leukaemia and in some cases it was impossible to differentiate from true leukaemia especially in patients with disseminated tuberculosis. So, in some cases of disseminated tuberculosis presenting with a blood picture closely simulating acute myeloid leukaemia the diagnosis was evident only at autopsy.

The onset of tuberculous infection might induce a spontaneous remission and hence the lack of tissue evidence of leukaemia at autopsy (Subramanyam *et al.*, 1975). The haematological changes that occasionally accompany acute tuberculosis may resemble acute leukaemia in that primitive white blood cells appear in the blood and marrow but at post mortem examination no conclusive evidence of leukaemia can be found there been no leukaemic infiltration of the tissue. Sometimes when the blast cells are particularly numerous an underling acute leukaemia is presumed and indeed would probably be diagnosed as such were it not for tuberculosis. At other times the abnormal white cells are less primitive and

the so-called leukemoid reaction is suspected (Oswald, 1963). In recent years, ultrastructural studies, cytogenetic, immunologic technique and chromosomal studies have been developed to help and classify leukaemic types (Stiene *et al.*, 1998).

MATERIALS AND METHODS

All newly discovered Pulmonary Tuberculosis (PTB) patients attending the tuberculosis center of Port Sudan town in the period from June 2006 to December 2008, constituted the population of this study. Hundred newly discovered pulmonary TB patient's positive with *Tubercle bacilli* in sputum (Zn stain) were subjected to the haematological tests. The inclusion criteria were: first time diagnosis, no current or previous antituberculous 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 affect 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 any clinical signs for pulmonary TB were selected randomly to be the control group.

Ethical clearance of this study was approved from the regional Ethical Review Committee (ERC). Data regarding the age and sex was recorded in predesigned forms.

Blood samples were collected from all the studied population. About 3 mL of venous blood was collected from each patient where 3 mL of blood was transferred to tri potassium Ethylene Diamine Tetra Acetic acid (EDTA) tube. However, a thin blood film was prepared for each specimen immediately after blood withdrawal before the adding to anticoagulant containers. The thin blood film was stained using standard laboratory method and processed to obtain differential count on the usual way. Leukocytes count was done using a Manual Counting Method. The analysis was performed in Port Sudan Tuberculosis Diagnostic Center by expert technologists. Statistical analysis: Data were analyzed by using a computer Statistical Package for Social Sciences (SPSS 16.0 Version, IBN. Chicago, USA). χ^2-test was performed to compare categorical variables. All reported p-values are two-tailed and value <0.05 were considered statistically significant.

RESULTS

This is a case control-analytical study conducted in Port Sudan Tuberculosis Diagnostic center. The total number of the confirmed TB patients was 100. The age of
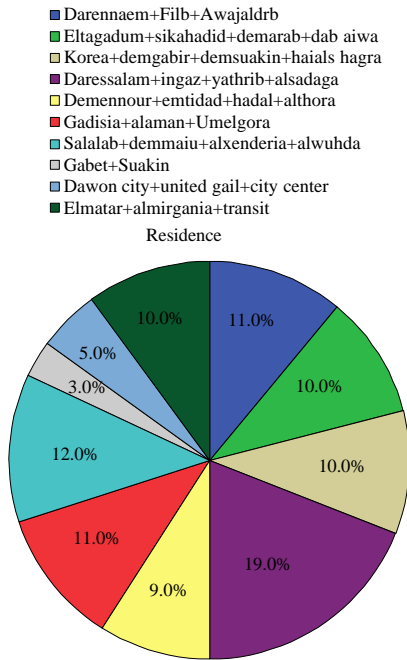
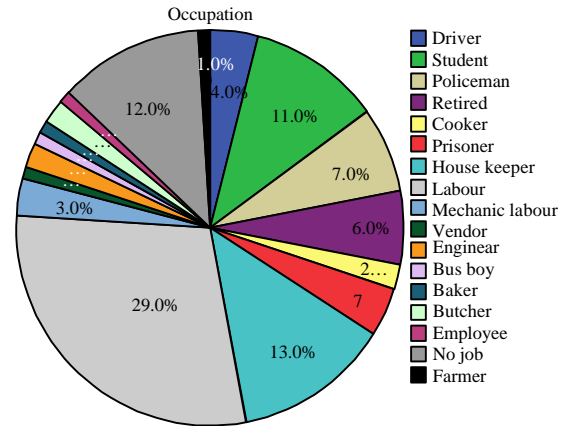Fig. 1: Residence distributions among the test group of the study

Fig. 2: Frequency of the occupational status for the individuals included in the test group of the study

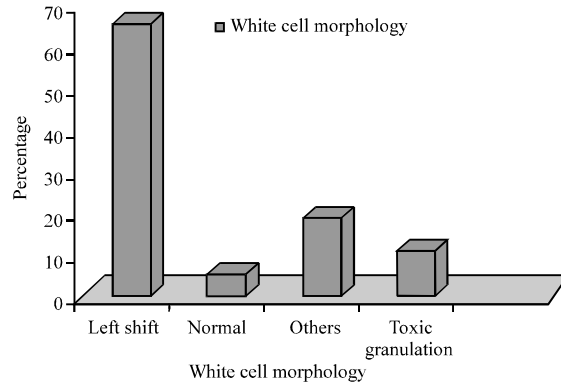Fig. 3: Frequency of white cell morphology among the test group of the study

Table 1: Frequency of pulmonary TB in different (red sea state) tribes

Tribes	Number	Frequency (%)
Western Sudan	31	31.33
Bani amer	27	26.67
Shemalien	25	24.67
Hadandwa	17	17.33
Total	100	100.00

Table 2: The difference between case and control groups in hematological parameters

Parameters	Test group (mean)	Control group (mean)	p-values
Total white blood cell (µL)	6468.50	4486.00	0.000
Neutrophil (%)	54.26	51.48	0.119
Lymphocyte (%)	12.35	29.70	0.000
Monocyte (%)	9.84	7.58	0.002
Eosinophil (%)	1.77	4.32	0.000
Basophil (%)	0.29	0.26	0.762
Stab form (%)	15.73	0.76	0.000
Atypical lymphocyte (%)	5.43	5.92	0.633
Myelocyte (%)	0.06	0.00	0.256
Metamyelocyte (%)	0.25	0.00	0.067

the patients in this study was between 14 and 70 years (mean age 33 years). 50 individuals, age and sex matched were selected as control group. The control individuals age between19 and 63 years (mean age 27 years). Of the 100 PTB patients, 77% were males and 23% were females. In the control group, 38 (76%) were males and 12 (24%) were females. Demographics were obtained from patients had pulmonary TB include residence, tribe and occupation. The 19% was noted as high incidence of pulmonary TB in the Southern neighborhood (Daressalam) (Fig. 1). Table 1 illustrates that the overwhelming majority of pulmonary TB is among the Western Sudan tribe 31.33%, followed by the Bani Amer tribe 26.67%, Shimalein tribe 24.67% and the Hadandwa tribe 17.33%. The labour was the most segment of occupation affected 29%, followed by House keeper 13%, and the individuals with no job 12% (Fig. 2). The differences between the patient group and the control group were found to be significant in lymphocyte count and eosinophil count these values were lower in the patient group than in the control group (Table 2). While

leukocyte count, presence of stab form and monocytosis were found to be significantly higher in the patient group than in the control group reflecting leukocytosis, high stab form frequency and monocytosis respectively (Table 2) (Fig. 3). On the other hand, the differences were found to be insignificant in the frequencies of neutrophil, basophil, atypical lymphocytes, myelocytes and metamyelocytes (p = 0.119, 0.762, 0.633, 0.256 and

0.067, respectively) (Table 2). Among the patients included in this study, relative monocytosis was seen in (35%) of those with normal leukocytes count and in (4%) of those with leukocytosis which is true with the tuberculosis disease. Left shift granulocytes-indicating the presence of an inflammatory condition-was seen in (65%) of patients with normal total leukocytes count and in (17%) of those with leukocytosis (Fig. 3).

DISCUSSION

Nwankwo *et al.* (2007) studying the haematological changes in tuberculosis in Kano. Nigeria reported significant leukocytosis (neutrophilia with toxic granulation) and monocytosis (p<0.05). Morris *et al.* (1989) studying the haematological and biochemical changes in severe pulmonary tuberculosis found the occurrence of leukocytosis with neutrophilia in 40% of cases. Awodu *et al.* (2007) studying the hematological variable in Nigeria pulmonary tuberculosis patients undergoing therapy reported significant leukocytosis. Monocytosis, neutrophilia and lymphocytosis were reported by Singh *et al.* (2001), Olaniyi and AkenOva (2003), Akintunde *et al.* (1995), Bozoky *et al.* (1997), Wessels *et al.* (1999), Eakins and Nelson (1969), Lombard and Mansvett (1993) and Araujo *et al.* (2002). Moreover, monocytosis was reported by McKenzie and Laudicina (1997). These results are generally quite similar to our findings regarding the presence of monocytosis in pulmonary tuberculosis patients but differ strongly in the presence of neutrophilia and lymphocytosis which are not observed in our study most probably due to the small sample size or confounding other diseases.

In contrast, lymphopenia in pulmonary tuberculosis was reported by Morris (1989), Olaniyi and AkenOva (2003), Onwubalili (1990) and Onwubalili *et al.* (1987). Result quite similar to those of the present study.

CONCLUSION

The presence of haematological peripheral leukocytes blood changes in endemic areas like Red Sea State may predict and raise the suspicion of pulmonary tuberculosis.

REFERENCES

Ageep, A.K., 2012. Diagnosis of tuberculous lymphadenitis in Red Sea state, Sudan. Int. J. Trop. Med., 7: 53-56.

Akintunde, E.O., W.A. Shokunbi and C.O. Adekunle, 1995. Leucocyte count, platelet count and erythrocyte sedimentation rate in pulmonary tuberculosis. Afr. J. Med. Med. Sci., 24: 131-134.

Araujo, Z., D.L.C. Fernandez, D. Lopez, C. Fandino and M. Chirinos *et al.*, 2002. Hematologic values among Warao indians with tuberculosis from the Orinoco delta of Venezuela. Acta Cientifica Venezolana, 54: 247-253.

Awodu, O.A., I.O. Ajavi and A.A. Famodu, 2007. Hemorheological variables in Nigeria pulmonary tuberculosis patients undergoing therapy. Clin. Hemorheol. Microcircula, 36: 267-275.

Beenson, P.B. and W. Mcdermott, 1963. Cecil-Loeb Textbook of Medicine. 11th Edn., W.B. Saunders Co., Philadelphia, London, pp: 289-290.

Bozoky, G., E. Ruby, I. Goher, J. Toth and A. Mohos, 1997. [Hematologic abnormalities in pulmonary tuberculosiss]. Orvosi Hetilap, 138: 1053-1056.

Eakins, D. and M.G. Nelson, 1969. Disseminated tuberculosis with associated haematological disorders. Irish J. Med. Sci., 2: 79-90.

Firkin, F., C. Chesterman, D. Penington and B. Rush, 1996. Clinical Haematology in Medical Practice. 5th Edn., Blackwell Science, India, pp: 96-119.

Hoffbrand, A.V. and J.E. Pettit, 2006. Essential Haematology. 5th Edn., Blackwell Science, UK., pp: 209-377.

Lombard, E.H. and E.P.G. Mansvelt, 1993. Haematological changes associated with miliary tuberculosis of the bone marrow. Tubercle Lung Dis., 74: 131-135.

McKenzie, S.B. and R.J. Laudicina, 1997. Hematologic changes associated with infection. Clin. Lab. Sci.: J. Am. Soc. Med. Technol., 11: 239-251.

Morris, C.W., A.R. Bird and H. Nell, 1989. The haematological and biochemical changes in severe pulmonary tuberculosis. Q. J. Med., 73: 1151-1159.

Nwankwo, E.K., A. Kwaru, A. Ofulu and M. Babashani, 2007. Haematological changes in tuberculosis in Kano, Nigeria. J. Med. Lab. Sci., 14: 35-39.

Olaniyi, J.A. and Y.A. AkenOva, 2003. Bone marrow findings in patients with pulmonary tuberculosis. Afr. J. Med. Sci., 32: 155-157.

Onwubalili, J.K., 1990. Untreated tuberculosis may be associated with lymphopoenia, not lymphocytosis. Afr. J. Med. Sci., 19: 181-183.

Onwubalili, J.K., J. Andrew, A.J. Edwards and L. Palmer, 1987. T4 lymphopenia in human tuberculosis. Tubercle, 68: 195-200.

Oswald, N.C., 1963. Acute tuberculosis and granulocytic disorders. Br. Med. J., 2: 1489-1496.

Pereira, C.B., M. Palaci, O.H. Leite, A.J. Duarte and G. Benard, 2004. Monocyte cytokine secretion in patients with pulmonary tuberculosis differs from that of healthy infected subjects and correlates with clinical manifestations. Microbes Infect., 6: 25-33.

Siddiqui, M.A., A.K. Abdullah, M.U. Quraishy and M. Tajuddin, 1977. Pulmonary tuberculosis and leukaemia. Ind. J. Tub., 24: 34-36.

Singh, K.J., G. Ahulwalia, S.K. Sharma, R. Saxena, V.P. Chaudhary and M. Anant, 2001. Significance of haematological manifestations in patients with tuberculosis. J. Assoc. Physicians India, 49: 790-794.

Stiene, A.E., A. Cheryl and J.A. Koepke, 1998. Clinical Hematology Principles, Procedures, Correlations. 2th Edn., Lippincott, USA., pp: 355-360, 725-726.

Subramanyam, C.S.V., J.M. Ahuja and M.L. Sapra, 1975. Miliary tuberculosis simulating acute myeloid leukaemia-review of literature and report of a case. Indian J. Tuberculosis, 22: 136-141.

WHO, 2001. World health reports the global tuberculosis epidemic. World health Organization (WHO), Report No. 233, Geneva, pp: 1-3.

Wessels, G., H.S. Schaaf, N. Beyers, R.P. Gie, E. Nel and P.R. Donald, 1999. Brief report. Haematological abnormalities in children with tuberculosis. J. Trop. Pediatrics, 45: 307-310.