

*Full Length Research Paper*

## Reactive thrombocytosis and erythrocyte sedimentation rate in patients with pulmonary tuberculosis

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This study aimed at assessing the reactive thrombocytosis and erythrocyte sedimentation rate in patients with pulmonary tuberculosis living in Port Sudan City, Red Sea State, Sudan. This study covers the period from June 2006 up 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 adult 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 to 70 years old. Thrombocytosis was detected in 20% of the patients. The erythrocyte sedimentation rate (ESR) was increased in 100% of the patients. The changes in these parameters (platelets count and ESR) may reflect a reaction to the inflammatory condition. Therefore, in endemic areas, the presence of such hematological peripheral blood changes may raise the suspicion of pulmonary tuberculosis.

**Key words:** Tuberculosis, thrombocytosis, erythrocyte sedimentation rate (ESR), Port Sudan.

### INTRODUCTION

Tuberculosis (TB) 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 the most wide spread infectious diseases (World health Organization, 2001). The differential diagnosis of tuberculosis should be entertained in patients with some abnormal hematological findings (Singh et al., 2001). Moreover, hematological parameters are useful indicators of severity in TB infection (Bozoky et al., 1997).

Hematological changes associated with pulmonary TB infection have been the first documented study in Red Sea State (Ageep, 2012).

Reactive thrombocytosis is defined as an increased number of platelets above  $450 \times 10^9 \text{ L}^{-1}$  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  $1000 \times 10^9 \text{ L}^{-1}$ , and is not normally associated with any serious clinical problems (Stiene et

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al.,1998). Thrombocytosis occurs in many chronic inflammatory diseases, including tuberculosis. The precise stimulus for increased platelet production is not clear, but it is associated with increased numbers of small megakaryocytes in the marrow, which shows reduced nuclear ploidy.

The platelets are also small, but it has recently been suggested, that this may simply reflect the thrombocytosis, as there is normally an inverse correlation between the number and volume of platelets (Baynes et al., 1987). Reactive thrombocytosis is associated with an increase in erythrocyte sedimentation rate (ESR) and acute phase reactants (fibrinogen, VIII.C, VWF: Ag, C-reactive protein, and interleukin-6 (IL-6)). The most potent stimulator for hepatic synthesis of C-reactive protein is IL-6, which also has thrombopoietic activity (Hollen et al., 1991). IL-6 is known to promote megakaryocytopoiesis *in vitro* and raise platelet counts *in vivo*. Unfortunately, due to short facilities, IL-6 level was not assessed in this study.

ESR is a non specific test, it is raised in a wide range of infections, inflammatory, degenerative, and malignant conditions associated with changes in plasma protein, particularly increase in fibrinogen, immunoglobulin, and C-reactive protein. The ESR is also affected by many other factors including anemia, pregnancy, hemoglobinopathies, hemoconcentration and treatment with anti-inflammatory drugs (Cheesbrough, 1984). The rate of sedimentation appears to be dependent on the amount of fibrinogen and, to a lesser extent, the amount of globulins present in the plasma. In normal blood, the red cells tend to remain separate from one another because they are negatively charged (zeta potential) and tend to repel one another. In many pathologic conditions, the phenomenon of erythrocyte aggregation is caused by alteration of erythrocyte surface charge by plasma protein (Linne and Ringsrad, 1999).

Moderately raised sedimentation rates can sometimes be found in healthy people, particularly those living in tropical countries and a "normal" ESR cannot exclude disease. In many tropical countries, ESR measurement has been discontinued, because they added little to diagnosing disease, assessing its progress and monitoring response to treatment (Firkin et al., 1996). The ESR may rise in tuberculosis to over 100 mm/1 h as well as blood viscosity due to the increase in immunoglobulins mainly IgG and IgA (Morris et al., 1989). Furthermore, reduction in erythrocyte sedimentation rate was regarded as good indicator for disease control (Kartaloglu et al., 2001).

Although, tuberculosis is endemic in our region, no previous data regarding the hematological changes was reported. So, this work aimed to study the changes in the platelet count and ESR level in patients having pulmonary tuberculosis.

## MATERIALS AND METHODS

All newly discovered pulmonary tuberculosis patients attending the tuberculosis center of Port Sudan town, in the period from June 2006 up 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 hematological tests. The inclusion criteria were: 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 anti-tuberculous 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.

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 of the studied population. About 5 ml of venous blood was collected from each patient where 2.5 ml of blood was transferred to dipotassium ethylene diamine tetra acetic acid (EDTA) tube for measuring the platelets count. For measuring ESR, the remaining 2.5 ml of the blood was treated with citrate solution. Platelet count was done using a manual counting method and ESR was measured by Westergren method.

The analysis was performed in Port Sudan Tuberculosis Diagnostic Center by expert technologists.

### Statistical analysis

Data were analyzed using a Computer Statistical Package for Social Sciences (SPSS) program version 16. Descriptive statistics were used for analysis (e.g, t test, pie chart).

## 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 the patients in this study was between 14 and 70 years (mean age 33 years). Fifty individuals, age and sex matched, were selected as control group. 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. In the control group, 38 (76%) were males and 12 (24%) were females. Demographics were obtained from patients with pulmonary TB include residence, tribe, and occupation. 19% was noted with high incidence of pulmonary TB in the southern neighborhood (Daressalam) (Figure 2). 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%). Labour was the most segment of occupation affected (29%), followed by house keeper (13%), and the individuals with no job (12%) (Figure 3).

**Table 1.** Frequency of pulmonary TB in different (Red Sea State) tribes.

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

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

Parameter	Test group (mean)	Control group (mean)	P-value
Platelet count/ $\mu$ l	344800	248200	0.000
ESR mm/h	115.17	11.08	0.000

In the patient with pulmonary tuberculosis, the platelet count range from  $150 \times 10^9$  to  $900 \times 10^9 \text{ L}^{-1}$ . Thrombocytosis was noted in 20% of patients (Figure 1). The differences between the patient group and the control group in platelets count were found to be significantly higher in the patient group ( $P < 0.000$ ) (Table 2).

All patients had an elevated ESR ranging from 50 to 155 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 0.000). There was a linear correlation between the platelet count and ESR ( $p < 0.000$ ).

## DISCUSSION

TB is a major public health problem in the studied area (Ageep, 2012). To our knowledge, this is the first research that studies the ESR and platelets changes in tuberculous patients in Port Sudan City, Red Sea State, Sudan.

In this study, ESR was elevated in all patients which is similar to results stated by Chakrabarti et al. (1995), Nwankwo et al. (2007), Stenius-Aarniala and Tuhianen (1975), Chia and Machin (1979), Morris (1989), Awodu OA et al. (2007) and Olaniyi et al. (2003a). Invariably (but moderately) elevated ESRs were observed by Akintude et al. (1995) in Ibadan, Nigeria which is in agreement with our findings. The ESR, a sensitive but not a specific measure of the inflammatory response, is elevated in 90% of patients who have a serious problem like orthopaedic infection (Olaniyi et al., 2003b; Akintunde et al., 1995). An ESR value exceeding 100 mm/h has a 90% predictive value for serious underlying disease, such as infection (Schulac et al., 1982). This is almost 100% true to our findings in tuberculous patients of elevated ESR

values (that is, higher than 100 mm/h in our study).

Significant correlation between thrombocytosis and elevated ESR was observed by Baynes et al. (1987) and Muzaffar et al. (2008) results which are strongly in agreement with the findings of this study. Most of the patients in our study with pulmonary tuberculosis had thrombocytosis. Reactive thrombocytosis is found in a number of clinical situations including infectious diseases (Brigden, 1998). The regulation of thrombopoiesis is under the control of an array of haemopoietic growth factor (Muzaffar et al., 2008). Significant elevation of thrombopoietin during the acute phase of infection precedes the development of thrombocytosis, suggesting an important role of thrombopoietin in reactive thrombocytosis. Elevated values of thrombopoietin were found in majority of patients with acute infection and were observed more frequently during the acute phase with fever than after the fever disappeared (Unsal et al., 2005). The exact mechanism of elevated thrombopoietin levels in reactive thrombocytosis is still unknown; however, it has been observed to be correlated with inflammatory processes (Ishiguro et al., 2002). Serum IL-6 concentration is significantly correlated with thrombocyte count and albumin concentration. IL-6 may play a contributory role on reactive thrombocytosis and the acute phase response in pulmonary tuberculosis (Muzaffar TM et al., 2008; Hsu et al., 1999; Turken et al., 2002).

In contrast, Olaniyi et al. (2003a) and Akintude et al. (1995) studying the haematological profile of patients with pulmonary tuberculosis in Ibadan, Nigeria reported that thrombocytosis occurred in 12.9 and 18% of patients, respectively, results which are relatively agreeing.

On the other hand, Singh et al. (2001) studying the significance of haematological manifestations in patients with tuberculosis in Indian Institute of Medical Sciences,

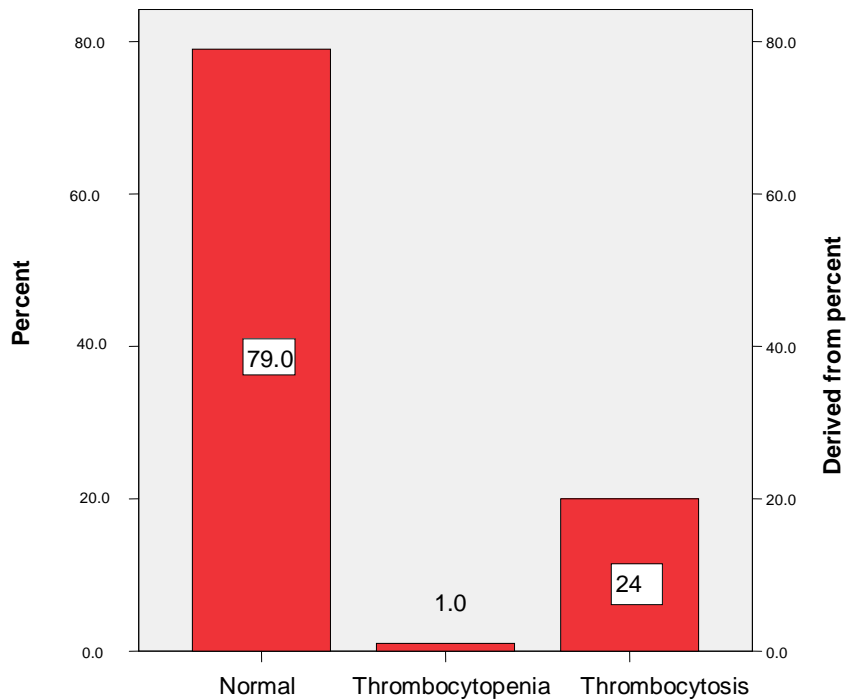


Figure 1. Frequency of thrombocytopenia and thrombocytosis in the study group.

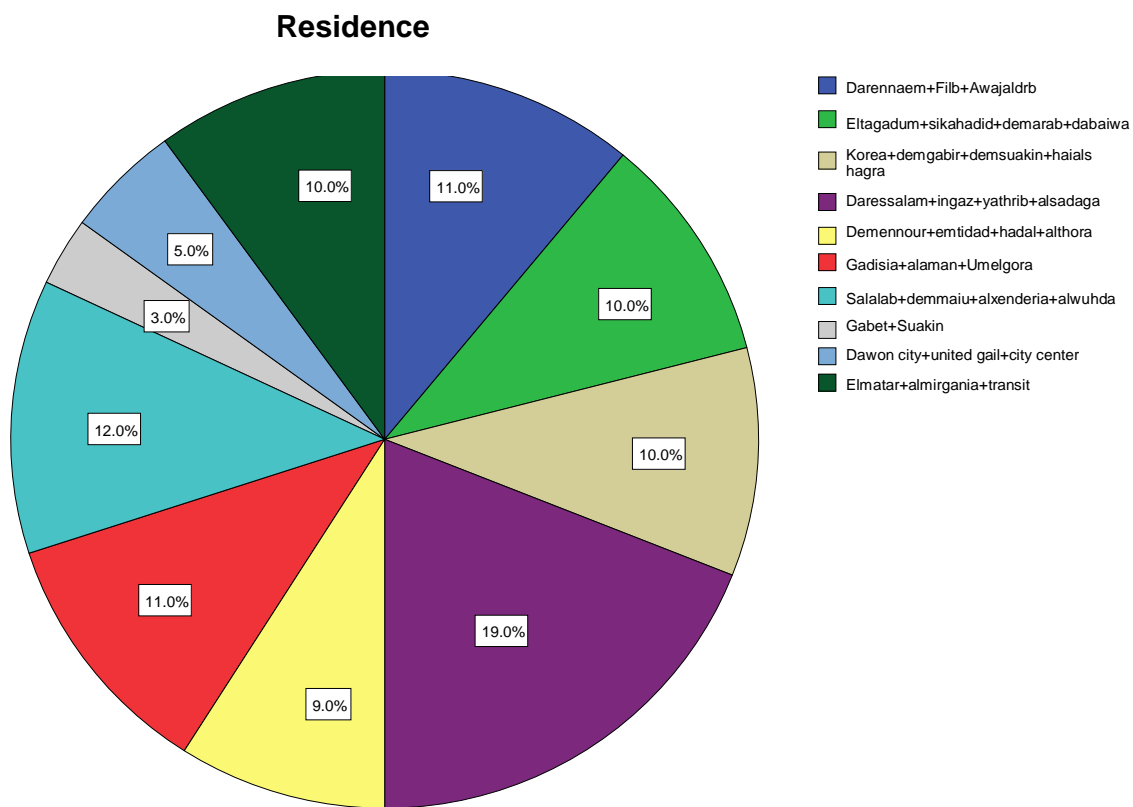
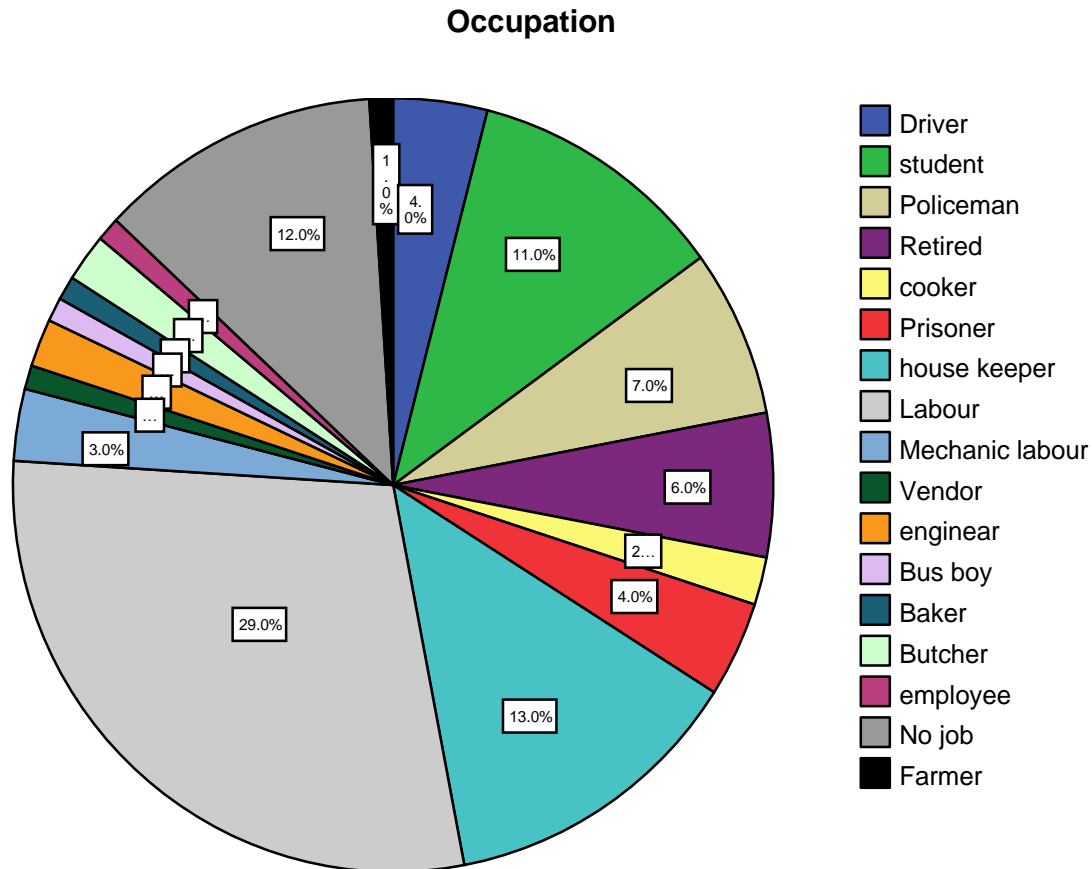


Figure 2. Residence distributions among the test group of the study.



**Figure 3.** Frequency of the occupational status for the individuals included in the test group of the study.

New Delhi, India reported that thrombocytopenia was more common in patients with disseminated tuberculosis ( $p < 0.007$ ) a result which is significantly different from ours perhaps due to environmental and geographical factors (Omer et al., 1983).

**Conclusion**

The presence of reactive thrombocytosis and/or elevated ESR, in endemic areas like Red Sea State, may raise the suspicion of pulmonary tuberculosis.

**Conflict of Interests**

The author(s) have not declared any conflict of interests.

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