

## SOME HAEMATOLOGICAL PARAMETERS OF TUBERCULOSIS INFECTED NIGERIANS: A STUDY IN CALABAR - NIGERIA

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### ABSTRACT

Tuberculosis is a major public health problem in Nigeria. Drug resistant tuberculosis is now common place due to poor patient compliance and lack of detection of resistant strains. The occurrence of HIV has been responsible for an increased frequency of tuberculosis. Knowledge of the blood picture in pulmonary tuberculosis, is believed, will be a valuable tool in the management of patients. This study aimed at providing information on haematological changes in pulmonary tuberculosis. A total of 200 subjects were investigated. One hundred of these were pulmonary tuberculosis patients comprising 62 males and 38 females who attended the University of Calabar Teaching Hospital and the Dr. Lawrence Henshaw Memorial Hospital (Infectious Diseases Hospital), Calabar, Cross River State; while the remaining 100 were non-pulmonary tuberculosis subjects comprising 50 males and 50 females who served as control subjects. Standard techniques were used for the assays. Routine haematological analyses were carried out which included Packed Cell Volume, Haemoglobin concentration, Mean Cell Volume, Mean Cell Haemoglobin, Erythrocyte Sedimentation Rate, Platelet and Total White Blood Cell counts. Age and gender were also evaluated in the enrolled subjects. Results showed significantly lower values ( $p < 0.05$ ) for Packed cell volume, haemoglobin concentration and mean cell haemoglobin concentration in pulmonary tuberculosis patients than in control subjects while mean cell volume and erythrocyte sedimentation rate showed significantly higher values in pulmonary tuberculosis patients than in control subjects. Packed cell volume, Haemoglobin concentration, Mean Cell Volume, Mean Cell Haemoglobin, and Erythrocyte Sedimentation Rate of pulmonary tuberculosis patients co-infected with HIV were significantly affected ( $p < 0.05$ ). The highest prevalence rate of infection (60%) occurred in the age group (10 – 30) years. In conclusion, the study showed that tuberculosis had significant effects on the haematological parameters analysed which were in turn aggravated in co-infection with HIV.

**KEYWORDS:** Pulmonary, Tuberculosis, haematological variables, HIV co-infection.

### INTRODUCTION

Tuberculosis (TB) is one of the most important infectious diseases in the world because of its high global prevalence, chronic debilitating characteristic and heavy attack rate on the wage earning community (Nwankwo *et al.*, 2005). It is a chronic disease caused by a group of five closely related species which form the *Mycobacterium tuberculosis* complex. They include *M. tuberculosis*, *M. bovis*, *M. africanum*, *M. microfti* and *M. canetti* (Iseman, 2000). *Mycobacterium tuberculosis* is the etiologic agent of a vast majority of tuberculosis. Pulmonary tuberculosis (PTB) is a lower respiratory tract infection initiated by the deposition of *Mycobacterium tuberculosis* (MTB), contained in aerosol droplets, onto lung alveolar surfaces within 4 - 12 weeks of settling

(Snider *et al.*, 1994). Tuberculosis can remain in an inactive (dormant) state for years without causing symptoms or spreading to other people. When the immune system of a patient with dormant TB is weakened, the TB can become active (reactivate) and cause infection in the lungs or other parts of the body (Iseman, 2008). The active disease is characterized by a protracted cough lasting up to 2 weeks or more, fatigue, loss of weight and appetite, fever, night sweats, chest pain and shortness of breath. (Kabir *et al.*, 2010). Haemoptysis, secondary infection by fungi and permanent lung damage are few of the complications of PTB (Fraser, 1993). Tuberculosis is transmitted from person to person through the air by infected droplet nuclei, 1 – 5µm in diameter that contain the *Mycobacterium tuberculosis* complex (Edward and Kirk-

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Patrick, 1986). The risk factors for acquiring TB include close-contact situations (overcrowding), malnutrition and certain diseases (example diabetes, cancer and HIV) which lower immunity and occupations (example health care workers) (CDC, 2010). According to the World Health Organization (WHO) worldwide prevalence of TB, nearly 2 billion, one third of the world's population (about 32%) have TB (WHO, 2010). The body had estimated that between 2000 and 2020 nearly one billion people would be infected, 200 million people would become sick and another 35 million people would die from the disease (WHO, 2005). Tuberculosis is a major public health problem in Nigeria with an estimated prevalence of 616 cases per 100,000 (WHO, 2008). Nigeria ranks first in Africa and fourth among the 22 high TB burden countries in the world (WHO, 2008). No fewer than 460,000 cases of tuberculosis are reported annually in Nigeria (WHO, 2008). The co-infection of pulmonary tuberculosis with human immune deficiency virus and acquired immune deficiency syndrome (HIV/AIDS) has in the recent past compounded the epidemiology, clinical outcome, diagnosis and treatment of the disease worldwide (CDC, 1995). Previous study has shown that anaemia, raised erythrocyte sedimentation rate (ESR), high peripheral leucocyte count and neutrophilia are the most common haematological manifestations associated with PTB (Devi *et al*, 2003). Another study carried out in Kano, Northern Nigeria, reported mild anaemia, and raised ESR, leucocytosis, neutrophilia with toxic granulation, thrombocytosis, occasional stickiness of platelets and monocytosis (Nwankwo *et al.*, 2005). In Benin, Southern Nigeria, a study showed significant increase in plasma viscosity and fibrinogen levels and a decrease in platelet count, total white cell count and packed cell volume when compared with values for apparently healthy subjects (Awodu *et al.*, 2007). It is our aim to study the pattern of some haematological parameters in PTB infected subjects in Calabar, Nigeria. It is believed that the findings of this study will be useful as indicators of disease progression, cardiovascular risk factors and response to therapy in pulmonary tuberculosis.

## SUBJECTS, MATERIALS AND METHODOLOGY

### Study area and population

A total of one hundred (100) male and female pulmonary tuberculosis patients aged between ten to seventy-one (10-71) years, attending the Endemic Diseases Clinic, Department of Community Medicine, University of Calabar Teaching Hospital and Dr Lawrence Henshaw Memorial Specialist Hospital, Calabar, Nigeria were selected for the study. Ethical approval was obtained from the Research Ethics Committee of Cross River State Ministry of Health which covered both hospitals. The bio-data and medical history of these patients were obtained through questionnaire, while permission was sought to obtain information from the case notes of those who could not fill questionnaire. Subjects who were diagnosed as PTB patients based on the presence of the acid fast bacilli (AFB) in their sputum smear were

recruited into the study. The HIV status of the patients was determined using two rapid HIV test methods. One hundred (100) age and gender-matched apparently healthy individuals who tested negative for AFB in their sputum smear and HIV sero-negative were used as control subjects in this study. They were selected from staff of Dr Lawrence Henshaw Memorial Hospital who were also residents of Calabar South Local Government Area. Informed consent was sought and obtained from all participants.

### Sample collection and processing

Five millilitres (5 ml) of blood was collected under aseptic conditions with minimal stasis from each subject, 2 ml was in a plain sample bottle while 3 ml was added to ethylene diamine tetra acetic acid (EDTA) anticoagulant with a concentration of 1.5 mg/ml in a sample bottle for determination of packed cell volume (PCV), haemoglobin (Hb) concentration, mean cell volume (MCV), mean cell haemoglobin (MCH), mean cell haemoglobin concentration (MCHC), white blood cell (WBC) and platelet counts, using PCE 210 version 5.10 (ERMA INC. Tokyo) automatic blood cell counter, and erythrocyte sedimentation rate (ESR) by Westergren technique (William *et al.*, 1993). The remaining blood sample (2 ml) was separated by centrifugation and the serum used for HIV screening using two rapid HIV test methods, Determine™ HIV 1/2 (Alere Medical Co. Ltd., Japan) and VIKIA® HIV 1/2 (bioMérieux SA, France). The data generated from this work was subjected to student t-test analysis and one-way analysis of variance. A two tailed P-value of < 0.05 was considered statistically significant.

### Principle of Determine™ HIV 1/2 Test

Alere Determine™ HIV-1/2 is an immunochromatographic test for qualitative detection of antibodies to HIV-1 and HIV-2. Sample is added to the sample pad. As the sample migrates through the conjugate pad, it reconstitutes and mixes with the selenium colloid-antigen conjugate. This mixture continues to migrate through the solid phase to the immobilized recombinant antigens and synthetic peptides at the patient window site.

If antibodies to HIV-1 and/or HIV-2 are present in the sample, the antibodies bind to the antigen-selenium colloid and to the antigen at the patient window, forming a red line at the patient window site. If antibodies to HIV-1 and/or HIV-2 are absent, the antigen-selenium colloid flows past the patient window, and no red line is formed at the patient window site. To insure assay validity, a procedural control bar is incorporated in the assay device (Weniger *et al.*, 1994).

### Principle of VIKIA® HIV 1/2 Test

VIKIA HIV 1/2 is a visually read rapid test, based on the immunochromatography technique (ICT or lateral flow) for the qualitative detection of serumantibodies to HIV-1 and HIV-2 in human serum, plasma or whole blood. The test consists of a plastic

device containing a chromatography membrane to which are fixed: in the test region ("T"), synthetic peptides specific for HIV-1 (gp41 of group M and Group O), and HIV-2 (gp36); in the control region (C), two colour indicators and a test strip impregnated with a conjugate consisting of a mixture of synthetic peptides specific for HIV-1 and HIV-2, coupled to blue dyed polystyrene microspheres. The sample is added to the sample well and migrates by capillarity along the membrane.

If the sample contains anti-HIV antibodies, they form an antigen-antibody complex with the peptides specific to this virus, present on the blue-dyed polystyrene microspheres. The antigen-antibody complexes migrate along the membrane and bind to the synthetic peptides immobilized on the nitrocellulose membrane. This is revealed by a blue line in the test region "T". The test is validated if the colour of the control line in region "C" changes from blue to pink/red. If this line does not change colour, the test is invalid (Sharp *et al.*, 1994).

## RESULTS

In this study, some haematological parameters of pulmonary tuberculosis patients in Calabar were investigated. The tests performed included measurement of packed cell volume, haemoglobin concentration, mean cell haemoglobin, mean cell haemoglobin concentration, mean cell volume, erythrocyte sedimentation rate, white blood cell and platelet counts. The results obtained were compared with apparently healthy subjects (controls).

Table 1 shows the mean values of the various parameters that were analysed. The mean values obtained for HB, PCV, MCH and Platelets of PTB patients were significantly lower ( $p < 0.05$ ) than values obtained for control subjects. While the MCV and erythrocyte sedimentation rate of PTB patients were significantly higher ( $p < 0.05$ ) than those of control subjects. The WBC counts for both groups of subjects did not show any significant difference.

**TABLE 1: MEAN  $\pm$  SD VALUE OF HEMATOLOGICAL PARAMETERS IN BOTH TEST SUBJECTS AND CONTROLS OF THE STUDY**

Parameters	TB Patient	Control	P-value
PCV (L/L)	0.25 $\pm$ 0.05	0.39 $\pm$ 0.04	0.05
ESR (mm/hr)	104.2 $\pm$ 32.4	34 $\pm$ 1.7	0.05
Platelet count ( $\times 10^9/L$ )	111.9 $\pm$ 31.8	218.2 $\pm$ 53.3	0.05
WBC ( $\times 10^9/L$ )	5.9 $\pm$ 2.6	6.3 $\pm$ 1.7	0.05
MCH (pg)	26.6 $\pm$ 3.1	27.8 $\pm$ 2.3	0.05
MCV (fl)	79.8 $\pm$ 7.84	77.06 $\pm$ 4.8	0.05
Hb(g/dl)	8.5 $\pm$ 3.4	14.3 $\pm$ 2.0	0.05

The haematological parameters of PTB patients based on age distribution is shown in Table 2. The age group 10 – 30 years had the highest prevalence rate of infection (60%). The mean values of PCV, ESR obtained were significantly higher in age group 31-50 years while

age group 51-71 years had WBC value that was significantly lower than those of other age groups. The differences in platelets, MCV and MCH values were not statistically significant.

**TABLE 2: HEMATOLOGICAL PARAMETERS OF TB PATIENTS BASED ON AGE DISTRIBUTION**

Age (yrs)	Pop. Affected(%)	PCV (L/L)	ESR (mm/hr)	Platelet count ( $\times 10^9/L$ )	WBC count ( $\times 10^9/L$ )	MCH (pg)	MCV (fl)
10 – 30	60	0.25 $\pm$ 0.15	105 $\pm$ 66.7	109 $\pm$ 68.7	6.18 $\pm$ 3.9	27.9 $\pm$ 2.2	80.1 $\pm$ 1.4
31 – 50	30	0.31 $\pm$ 0.08	133 $\pm$ 34.6	143 $\pm$ 37.2	7.5 $\pm$ 1.9	26.8 $\pm$ 3.6	78 $\pm$ 2.5
51 – 70	10	0.24 $\pm$ 0.02	112 $\pm$ 0.7	115 $\pm$ 7.4	4.1 $\pm$ 12.3	28.7 $\pm$ 1.5	78 $\pm$ 15
P-value	0.05	0.05	0.05	0.05	0.05	0.05	0.05

Table 3 shows haematological parameters of PTB patients based on gender. It was shown that males were more affected than females. The mean values of

PCV, ESR, MCV, MCH, WBC and Platelets counts obtained in both males and females were not significantly different.

**TABLE 3: HEMATOLOGICAL PARAMETERS OF TB PATIENTS BASED ON GENDER**

Gender	Pop. Affected(%)	PCV (L/L)	ESR (mm/hr)	Platelet count ( $\times 10^9/L$ )	WBC count ( $\times 10^9/L$ )	MCH (pg)	MCV (fl)
Males	62	0.25 $\pm$ 0.15	104 $\pm$ 63.8	109 $\pm$ 66.4	5.8 $\pm$ 3.5	27.9 $\pm$ 3.2	80.2 $\pm$ 2.0
Females	38	0.25 $\pm$ 0.09	107 $\pm$ 39.2	118 $\pm$ 43.1	6.3 $\pm$ 2.3	28.7 $\pm$ 3.1	79.3 $\pm$ 3.5
P-value	0.05	0.05	0.05	0.05	0.05	0.05	0.05

The haematological variables of 31 HIV sero-positive pulmonary tuberculosis patients compared with 69 counterparts who were sero-negative for HIV infection is shown in Table 4. Apart from the WBC and Platelets counts which did not change significantly, the

PCV, Hb concentration (decreased), MCV, MCH, and ESR (increased) of the sero-positive patients changed significantly ( $p < 0.05$ ) when compared with values for sero-negative patients.

**TABLE 4: SOME HAEMATOLOGICAL PARAMETERS OF PULMONARY TUBERCULOSIS PATIENTS CO-INFECTED WITH HIV**

Parameters	Sero-positive (n = 31)	Sero-negative (n = 69)	P-value
PCV (L/L)	0.26 $\pm$ 0.14	0.33 $\pm$ 0.08	0.05
ESR (mm/hr)	89.2 $\pm$ 32.4	34.0 $\pm$ 31.7	0.05
Platelets ( $\times 10^9/L$ )	181.9 $\pm$ 31.8	158.2 $\pm$ 53.3	0.05
WBC ( $\times 10^9/L$ )	5.3 $\pm$ 2.6	5.6 $\pm$ 1.7	0.05
MCH (pg)	29.6 $\pm$ 3.1	27.8 $\pm$ 2.3	0.05
MCV (fl)	79.8 $\pm$ 7.84	77.06 $\pm$ 4.8	0.05
Hb (g/dl)	9.0 $\pm$ 1.4	11.1 $\pm$ 1.2	0.05

## DISCUSSION

Pulmonary tuberculosis (PTB) is a major infectious disease with very high incidence in developing countries and this is expected to rise with the incidence of HIV infection. Based on the results obtained from this study, the mean values of haemoglobin concentration, packed cell volume, mean cell haemoglobin and platelets counts of pulmonary tuberculosis patients (8.5  $\pm$  3.4g/dl, 0.25  $\pm$  0.05L/L, 26.6  $\pm$  3.1pg and 111.9 $\pm$ 31.8  $\times 10^9/L$ ) were significantly lower ( $p < 0.05$ ) than those of control subjects (14.3  $\pm$  2.0g/dl, 0.39  $\pm$  0.04L/L, 27.8  $\pm$  2.3pg and 218.2  $\pm$  53.3 $\times 10^9/L$ ), the mean cell volume was (79.8  $\pm$  7.84fl) significantly higher than that of control subjects (77.06  $\pm$  4.8fl). This was a reverse trend but could not be investigated further as it was beyond the scope of the study. Some studies (Erster *et al.*, 1980; Morris *et al.*, 1989; Ebrahim *et al.*, 1995; Ajayi *et al.*, 2005; Lee *et al.*, 2006; Miah *et al.*, 2007) reported significant decreases in these haematological parameters of PTB patients and this agrees with the results of our study. Anaemia, defined as a reduction in haemoglobin concentration and by implication PCV,

alongside the absolute values (MCV, MCH and MCHC), has been reported in some studies (Robson, 1996; Turken *et al.*, 2002). This has been classified as normocytic normochromic with all the characteristics of anaemia of chronic disorders (Nwankwo *et al.*, 2005). Pulmonary tuberculosis being a chronic ailment, has a long term effect on the haemopoietic system through bone marrow depression leading to a decrease in erythropoiesis and resulting in the lower values in the test subjects.

The mean Erythrocyte Sedimentation Rate (ESR) of the TB subjects (104.2  $\pm$  32.4 mm/hr) in this study was significantly higher when compared with that of control subjects (34.0  $\pm$  1.7mm/hr). This could be as a result of inflammation and degenerative changes (these are general features of PTB) due to increase in production of acute phase protein, reduced albumin, often observed in chronic infections and release of proteins by the causative organism (*M.tuberculosis*) into the circulation (Willey *et al.*, 2008). These findings are supported by different studies specifying higher ESR values for PTB patients (Stenius-Aarniala and Tukianinen, 1979; Chia and Machin, 1979; Morris *et al.*,

1989; Akintunde *et al.*, 1995; Olaniyi and Aken'ova, 2003; Ajayi *et al.*, 2005; Awodu *et al.*, 2007; Ibeneme *et al.*, 2009).

Furthermore, mean platelet count of test subjects ( $111.9 \pm 31.8 \times 10^9/L$ ) in the study showed significantly lower value when compared with that of control subjects

( $218.2 \pm 53.3 \times 10^9/L$ ) (thrombocytopenia – platelet  $< 150 \times 10^9/L$ ) and this could be as a result of the effect of the anti-tuberculosis treatment in the test subjects. This is in agreement with previous work done by (Martens *et al.*, 1995; Al-Majed *et al.*, 1995).

In this study, the mean white blood cell count of PTB patients was  $5.9 \pm 2.6 \times 10^9/L$  and this showed no significant difference with control value ( $6.3 \pm 1.7 \times 10^9/L$ ). This result agrees with the mean white blood cell count ( $5.6 \pm 0.4 \times 10^9/L$ ) obtained in the same locality (Olaniyi and Aken'ova, 2003; Ibeneme *et al.*, 2009) but disagrees with leucocytosis that has been reported previously (Robson *et al.*, 1996). It is also at variance with another report of decreased white cell count in PTB patients (Awodu *et al.*, 2007). Although the authors did not state whether their subjects were on treatment or not, this could have affected their results. However, most of the PTB patients enrolled in this study were undergoing anti-tuberculosis treatment and this may account for the disparity in result.

Of the 100 pulmonary tuberculosis patients enrolled in the study, 31 were HIV sero-positive giving a 31 per cent prevalence rate while 69 were HIV sero-negative. The 31 per cent prevalence rate of HIV co-infection observed in this study is similar to that reported by the National Tuberculosis and Leprosy Control Programme of Nigeria (NTBLCP, 2008). The mean Hb, and PCV values of the sero-positive patients were significantly lower ( $p < 0.05$ ) than those obtained for the sero-negative patients while the mean ESR of the sero-positive patients was significantly higher ( $p < 0.05$ ) than that of the sero-negative patients. These differences may be due to the impact of HIV infection on the alveolar macrophages thereby enhancing the pathogenesis of pulmonary tuberculosis and aggravating anaemia. The mean values obtained for white cell and platelet counts, mean cell volume, and mean cell haemoglobin of the sero-positive patients were similar ( $p > 0.05$ ) to those of the sero-negative patients. KpDifferential white cell count was not performed in this study.

## CONCLUSION

This study has established significant changes in the haematological variables studied in pulmonary tuberculosis patients in Calabar. They had low PCV, MCH, Hb and Platelets count, high ESR and MCV values. A higher frequency of pulmonary tuberculosis was revealed within the age group 10 – 30, followed by 31 – 50 and 51 – 71 as the least group. The study also pointed out that males were more infected than females while HIV co-infection affected the Hb, PCV and ESR values significantly. Knowledge of this haematological picture will enhance the overall management of pulmonary tuberculosis patients with regard to monitoring disease progression and response to

antimicrobial chemotherapy as they will serve as useful indicators for treatment success or failure.

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