Hematological indices in human immunodeficiency virus and pulmonary tuberculosis infections in parts of Delta State, Nigeria

Johnson D. Jemikalajah, MMLS, PhD, Godwin A. Okogun, MSc, PhD.

ABSTRACT

الأهداف: لتعزيز الرعاية والعلاج للمرضى المصابين بفيروس نقص المناعة المكتسبة (HIV) والدرن الرئوي (PTB) كجزء من الجهد الكلي من أجل تخفيض الحالة المرضية والوفيات ذات الصلة بمرض فيروس نقص المناعة المكتسبة (HIV) بنيجيريا.

الطريقة: أجريت الفحوصات الدموية على 205 مريضاً يشتبه إصابتهم بفيروس نقص المناعة المكتسبة (HIV) والدرن الرئوي (PTB) و 100 شخص يبدون أصحاء (مجموعة التحكم) في كويل – أجبور وإيكو في أجزاء من ولاية دلتا بنيجيريا، خلال الفترة ما بين فبراير 2006م وحتى فبراير 2008م. تم استخدام نظامي منظمة الصحة العالمية (WHO) لفيروس نقص المناعة المكتسبة (HIV) وتقنية فحص الأجسام المضادة لفحص حالة فيروس نقص المناعة المكتسبة (HIV)، وتم استخدام تقنية زيهيل نيلسون الصبغية لفحص الدرن الرئوي (PTB) واستعمال تقنية هيماتوكريت وليشمان الصبغية لتحديد تعداد الدم الكامل.

النتائج: أظهرت دراستنا أن حجم الخلية الرئيسي (PCV) والذي تم الحصول عليه من الأشخاص المصابين: ((HIV (TB) – 0.5±27.5، 0.6±25.9 – ، و HIV / TB – 0.9±25.0 كان مختلفاً وملحوظاً من الناحية الإحصائية (p=0.0000074) عند المقارنة مع قيم مجموعة التحكم. كان تعداد عدلة الكريات البيضاء وتعداد أليفة الإيوسين التي تم الحصول عليها للانتشار التشخيصي للمرض المحدد عند المقارنة مع مجموعة التحكم. تمت مقارنة الجنس ذو العلاقة بتوزيع النسب الدموية مع مجموعة التحكم.

خاتمة: تؤكد الدراسة أهمية تعداد الدم الكامل في المراقبة والعلاج لعدوى فيروس نقص المناعة المكتسبة (HIV) والدرن الرئوي (TB)

Objectives: To enhance the care and management of human immunodeficiency virus (HIV) and pulmonary tuberculosis (TB) positive patients, as part of an overall effort to reduce morbidity and mortality of HIV-related death in Nigeria.

Methods: Hematological investigations were carried out on 205 patients suspected of HIV and/or TB, and 100 apparently healthy control subjects in Kwale, Agbor, and Eku in parts of Delta State, Nigeria from February 2006 to February 2008. World Health Organization systems 2 for HIV-1&2 antibodies screening technique was used for the screening of the subject's HIV status, Ziehl Nelson technique for TB, hematocrit, and Leishman staining techniques were used for full blood count determination.

Results: Our results showed that the mean packed cell volume obtained for infected subjects was statistically significant (p=0.0000074) when compared to the control subject's value. The mean neutrophil and eosinophil counts obtained were of specific disease diagnostic relevance when compared to the control group. The gender related distributions of hematological indices were compared with the control group.

Conclusion: The study confirms the importance of full blood count in the monitoring and management of HIV and TB infections.

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From the Medical Laboratory Department (Jemikalajah), Central Hospital, Kwale, and Department of Medical Laboratory Science (Okugon), Ambrose Alli University, Ekpoma, Nigeria.

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Address correspondence and reprint request to: Dr. Godwin A. Okogun, Medical Entomology & Parasitology Laboratories, College of Medicine, Amrose Alli University, Ekpoma, Nigeria. Tel. +234 (805) 8815346. E-mail: graokogun@yahoo.com

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The reduction in the number of circulating cells is a common complication of infection with human immunodeficiency virus (HIV) and tuberculosis (TB), and in the course of the disease, more than 70% of the patients develop anemia that frequently require transfusion.[1] The most commonly employed hematological indices includes; packed cell volume (PCV), thrombocytes, total and differential leucocytes counts.[2] Neutropenia, lymphopenia, and thrombocytopenia are common features, indicating that more than one hematopoietic linage may be impaired. Dysfunction of the bone marrow was suggested as a possible mechanism, and the degree of cytopenia often reflect severity of the disease.[3] Reports also indicate that as HIV disease progresses, the prevalence and severity of anemia increase. Anemia was found to significantly enhance progression to HIV/AIDS, and lead to an increased risk of death in patients with HIV.[4] Many researchers have reported the significance of hematological indices in TB as dependent on the type of disease, and extent of infection.[5] However, TB may occur in some patients with hematological disease by coincidence, or more probably arise as a result of opportunistic infection due to debility, or to impaired immunological response to infection, which characterizes the disease of the reticuloendothelial system. However, due to the dearth of information on hematological indices in HIV and TB in Nigeria, this study was undertaken to enhance the care and management of HIV and TB positive patients, as part of an overall effort to reduce mortality and morbidity of HIV related deaths.

Methods. A prospective study was conducted in 3 foci of Delta State with voluntary testing and counseling facilities namely, Kwale Central Hospital, Agbor Central Hospital, Eku Tuberculosis and Leprosy Referral Center, in Delta State from February 2006 to February 2008. The study areas of Agbor, Eku, and Kwale lie approximately between longitude $5^{0}00'$ and $6^{0}45'$ East, and latitude $5^{0}00'$ and $6^{0}30'$ North. The study area has a population of: 109,204 (Agbor), 113,929 (Eku), and 114,117 (Kwale).[6] After informed consent were obtained, venous blood and sputum samples were collected from 205 patients suspected with HIV and/or tuberculosis into ethylene diamine-tetraacetic acid (EDTA) containers, and from 100 apparently healthy subjects by random sampling into clean universal containers. Subjects less than 10 years were not included during the course of study. All samples were analyzed immediately after collection. Human immunodeficiency virus screening was carried out using 2 enzyme-linked immunosorbent assay (ELISA) rapid screening kits, based on WHO systems-2 for detecting antibodies of HIV-1&2.[7] To determine rapid screening, kits of Abbott Laboratories (Minato-Ku, Tokyo, Japan), and ImmunoComb II Organics (Courbevoie, France) were used in this study. Test was carried out according to the manufacturer's instruction, and sputum were examined for *Mycobacterium tuberculosis* using Ziehl Nelson staining method.[8] Hematocrit method and Leishman staining technique was carried out on all blood samples collected for the estimation of PCV, leukocyte, and differential counts.[8] Ethical approval was obtained from the ethical committee of the Delta State Ministry of Health, and the hospitals located in the 3 foci where the study was carried out.

All the data generated were presented in tables and subjected to statistical analysis using one-way analysis of variance (ANOVA) and Graph Pad Prism version 5.

Results. The results obtained in this study showed the mean PCV of infected subjects with HIV, TB, and HIV/TB were statistically significant (p=0.0000074), when compared with the control values. The mean neutrophil values obtained for HIV, TB, HIV/TB were statistically higher (p=0.0000074), when compared with the control group. The mean lymphocyte count for HIV, TB, HIV/TB were statistically different (p=0.0000074), when compared with the control group. Also, the mean eosinophil value for tuberculosis was statistically elevated (p=0.0000074), when compared with the control group (**Table 1**). **Table 2** shows that the male subjects' mean PCV obtained for HIV, TB, and HIV/TB were significantly different (p=0.0000037), when compared with the control values for male subjects. Similarly, the values obtained for female infected subjects, and HIV/TB mixed infections were significantly different (p=0.0000110), when compared to the control values for females (**Table 3**). The males' total leukocyte count for TB infected subjects was significantly elevated (p=0.0000037), when compared to both control. On the contrary the female infected subjects' HIV and HIV/TB co-infections total leukocytes was significantly reduced (p=0.0000110), when compared to control and TB infection values. The mean lymphocyte count was significantly reduced (p=0.0000110) in HIV and TB infected females when compared to controls, while the mean neutrophil of TB infected females was significantly higher (p=0.4266930) than controls (**Table 3**).

Discussion. Human immunodeficiency virus fuels the TB epidemic in several ways,[9] and promotes progression to active TB, both in people with recently acquired,[10] and with latent TB[11] infections. It was reported that PCV, thrombocytes, and total differential

Table 1 - Hematological indices of HIV, TB, and HIV/TB infected patients and control subjects (Mean ± SEM).

Parameters	Control n=100	HIV positive n=109	TB positive n=101	HIV/TB positive n=33	F test values	*P*-value
PCV	35.9±0.3	25.9±0.6	27.5±0.5	25.0±0.9	87.0	0.0000074
WBC	4648.0±127.0	4164.0±234.1	5480.9±475.9	5080.4±518.7	3.2	0.0000074
Neutrophils	54.9±0.9	62.9±1.6	62.5±1.4	63.7±2.8	7.7	0.0000074
Lymphocyte	44.5±0.9	36.0±1.5	34.7±1.3	34.4±2.7	11.8	0.0000074
Eosinophil	2.0±0.2	3.9±0.4	6.4±1.7	3.3±0.7	3.5	0.0000074

HIV - human immunodeficiency virus, TB - tuberculosis, PCV - packed cell volume, WBC - white blood cells

Table 2 - Hematological indices of HIV, TB, and HIV/TB infected male patients and control subjects (Mean ± SEM).

Parameters	Control n=60	HIV positive n=47	TB positive n=62	HIV/TB positive n=16	F test values	*P*-value
PCV	37.9±0.4	26.2±1.1	28.6±1.0	24.6±1.4	40.1	0.0000037
WBC	4325.0±219.4	4223.4±471.5	7751.4±1364.8	5823.5±1055.5	3.6	0.0000037
Neutrophils	55.2±1.5	62.8±3.2	61.3±3.0	65.1±5.5	1.9	0.4267762
Lymphocyte	44.2±1.5	36.1±3.0	36.4±2.9	34.1±5.3	2.6	0.4267762
Eosinophil	1.6±0.2	4.0±2.0	14.2±10.0	2.0±.00	0.9	0.4267762

HIV - human immunodeficiency virus, TB - tuberculosis, PCV - packed cell volume, WBC - white blood cells

Table 3 - Hematological indices of HIV, TB, and HIV/TB infected female patients and control subjects (Mean ± SEM).

Parameters	Control n=40	HIV positive n=62	TB positive n=39	HIV/TB positive n=17	F test values	*P*-value
PCV	32.9±0.7	25.8±1.0	26.7±1.19	25.8±2.0	9.3	0.0000110
WBC	5132.5±293.9	3627.7±277.6	4216.5±236.1	3353.2±360.9	32.7	0.0000110
Neutrophils	54.5±2.4	62.1±2.4	64.1±2.6	60.9±3.4	2.5	0.4266930
Lymphocytes	45.0±2.4	36.8±2.4	33.7±2.6	34.8±3.2	3.5	0.4266930
Eosinophil	2.4±0.79	4.0±2.0	4.7±1.0	7.0±5.0	0.6	0.4266930

HIV - human immunodeficiency virus, TB - tuberculosis, PCV - packed cell volume, WBC - white blood cells

leucocyte counts are essential hematological indices,[2] and that neutropenia, lymphopenia, and thrombocytopenia are regular features in the prognosis of TB infections.

In this study, **Table 1** showed a statistically significant reduction (p=0.0000074) in the hematological indices among HIV, TB, and HIV/TB subjects when compared with controls, especially the PCV, neutrophil, lymphocyte, and eosinophil. This findings agreed with the report by Jacobson et al,[1] that in HIV and TB infections, there is a reduction in the number of circulating cells, and 70% of the patients develop anemia and requires transfusion. The anemia may be attributed to some factors earlier reported by Odunukwe et al[12] such as chronic diseases, opportunistic infections, and certain nutritional deficiencies. In addition, we confirm that neutropenia and lymphopenia are common features as reported by Acria.[2] It has also been reported by Belperio and Rhew[4] that anemia is a statistically significant predictor of progression to AIDS, and is independently associated with increased risk of death in patient with HIV.[4] These may be attributed to the impairment of more than one hematopoietic linage, in addition to the dysfunction of the bone marrow, which had been suggested as the possible mechanism.[3]

As reported by other researcher's, the significance of hematological indices in TB is dependent on the type of disease, and extent of infection.[5] This may be due to hematological diseases, opportunistic infections, and/or impaired immunological response to infection.

Packed cell volume (for HIV), and total leucocyte count (white blood cells [for TB infections]) were found to be statistically significant indices among males. The marked elevated total leukocytes counts among males with TB infections are thought to be secondary to both

immunological, and cellular response to the debilitating disease. Hence, apoptosis is often the fatal end result of the prognosis of TB in a resource-constrained settings like Nigeria. The differences in total leukocytes response to TB infections according to gender may be hormonal, but the end results are similar. Lymphocytes were statistically reduced in HIV and TB infections. Okogun et al[13] confirms the report that the reduction in circulating lymphocytes is a good approximate index of CD4 co-receptor (CD4+) counts in monitoring HIV prognosis and management. These facts also agreed with the earlier report by Acria[2] that lymphopenia is common in HIV and TB infection, but did not differentiate between males and females. Our hematocrit controls show that females are more prone to blood loss, implying higher strain on their erythropoietic activities, secondary to regulate menstrual blood flow, and when this is considered against the backdrop of a relatively poor nutritional status, the debilitating effect of HIV and TB infections in Africa is better understood.

Resource constraints were a major limitation of this study, in addition to the ability to persuade the patients to accept testing and counseling.

This study therefore, emphasizes the need for routine hematological investigations such as PCV, leucocyte, and lymphocyte counts as a monitoring tool to enable proper care and management of HIV and TB patients. In addition to improving the social conditions, chemotherapeutic effect, case finding, and prophylaxis by Bacille Calmette-Guérin (BCG) vaccination as suggested by Nwankwo et al,[5] are also recommended, since recovery from anemia has been linked to improved survival outcomes.[14] This will however, go a long way to reduce morbidity and mortality associated with HIV and TB infections. Correlation of hematological indices with immunological factors such as CD4, CD8, T-cell ratio and cytokines may provide a more reliable management tool in the prognosis and management of HIV and TB infections.

References

1. Jacobson MA, Peiperl L, Volberding PA, Porteous D, Toy PT, Feigal D. Red cell transfusion therapy for anemia in patients with AIDS and ARC: incidence, associated factors, and outcome. ***Transfusion*** 1990; 30: 133-137.
2. ACRIA Update Newsletter. Understanding your laboratory result. New York (NY): Ortho Biotech Publication; 2004. p. 16.
3. Scadden DT, Zeira M, Woon A, Wang Z, Schieve L, Ikeuchi K, et al. Human immunodeficiency virus infection of human bone marrow stromal fibroblasts. ***Blood*** 1990; 76: 317-22.
4. Belperio PS, Rhew DC. Prevalence and outcomes of anemia in individuals with human immunodeficiency virus: a systematic review of the literature. ***Am J Med*** 2004; 116 (Suppl 7): S27-S43.
5. Nwankwo EK, Kwaru A, Ofulu A, Babashani M. Haematological changes in tuberculosis in Kano. ***Journal of Medical Laboratory Sciences*** 2005; 14: 35-39.
6. World Gazetteer Nigeria: largest cities and towns and statistics of their population. [accessed July 3, 2007] Available at URL: http://world-gazetteer.com.
7. Kassler WJ, Alwano-Edyegu MG, Marum E, Biryahwaho B, Kataaha P, Dillon B. Rapid HIV testing with same-day results: a field trial in Uganda. ***Int J STD AIDS*** 1998; 9: 134-138.
8. Cheesbrough M. District laboratory practice in tropical countries, part 2. Cambridge (UK): Cambridge University Press; 2000. p. 434.
9. Lienhardt C, Rodrigues LC. Estimation of the impact of the human immunodeficiency virus infection on tuberculosis: tuberculosis risks re-visited? ***Int J Tuberc Lung Dis*** 1997; 1: 196-204.
10. DiPerri G, Cruciani M, Danzi MC, Luzzati R, DeChecchi G, Malena M, et al. Nosocomial epidemic of active tuberculosis in HIV related patients. ***Lancet*** 1989; 2: 1502-1504.
11. Raviglione MC, Harries AD, Msiska R, Wilkinson D, Nunn P. Tuberculosis and HIV: current status in Africa. ***AIDS*** 1997; 11 (Suppl B): S115-S123.
12. Odunukwe N, Idigbe O, Kanki P, AdewoleT. Haematological and Biochemical Response to treatment of HIV-1 infection with a combination of Nevirapine + Stavudine+ Lamivudine. ***Nigeria Biomedical Science Journal*** 2006; 2: 12-19.
13. Okogun GR, Oledinma SN, Uwagbae MA. Absolute lymphocyte count, CD4, T cells and haematocrit as index of responses to antiretroviral therapy in party of northern Nigeria. ***International Journal of Natural and Applied Sciences*** 2007; 3: 274-278.
14. Sullivan P. Associations of anemia, treatments for anemia, and survival in patients with human immunodeficiency virus infection. ***J Infect Dis 2002;*** 185 (Suppl 2): S138-S142.

Related topics

Alzahrani AJ. Analysis of HIV subtypes and the phylogenetic tree in HIV-positive samples from Saudi Arabia. ***Saudi Med J*** 2008; 29: 1394-1396.

Sharifi-Mood B, Alavi-Naini R, Salehi M, Hashemi M, Rakhshani F. Spectrum of clinical disease in a series of hospitalized HIV-infected patients from southeast of Iran. ***Saudi Med J*** 2006; 27: 1362-1366.