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Haematological aspects of antiretroviral naïve HIV patients in a Nigerian tertiary hospital: laboratory and clinical considerations

Caroline E. OMOTI [1*], Waka A. UDEZI [2] and Rhoda E. EDOISE [2]

[1] *Department of Haematology, University of Benin Teaching Hospital, P.M.B. 1111, Benin City, Nigeria.*
[2] *Department of Clinical Pharmacy and Pharmacy Practice, Faculty of Pharmacy, University of Benin, Nigeria.*
[*] *Corresponding author, Tel: +234 8056014028, E mail: ediomoti@yahoo.com*

ABSTRACT

To determine the baseline haematological parameters including CD4+ cell count in naïve HIV patients, which has not been documented in this part of the country, the study group comprised of 191 consecutive antiretroviral (ARV) naïve adults living with HIV and AIDS recruited into the ARV pilot project in University of Benin Teaching Hospital, Nigeria between July and September 2004. They were classified with respect to severity of their disease state in accordance with Center for Diseases Control Clinical Categorization of HIV/AIDS. The patients had CD4+ cell count and haematological indices done to assess disease status and need for ARV therapy. This comprised of 69(36.1%) males and 122 (63.9%) females with a M:F ratio of 1:1.8. The median age at enrollment was 38 years (range, 21 to 75 years). At presentation, there were cytopenias and the males tended to have a slightly higher (195 cells/µl) CD4+ cell count than the females (180 cells/µl) with an overall median CD4+ cell count of 146 cells/µl. The difference was not statistically significant ($p = 0.5407$). There was a no significant correlation between the lymphocyte count and the CD4+ cell count. This study establishes local standard values for haematological indices including CD4+ cell count in naïve HIV infected Nigerians.

Keywords: Features; CD4 cell count, HIV, AIDS, antiretroviral.

INTRODUCTION

Despite best of efforts, the HIV epidemic continues to outpace the global response. In 2004 more than 5 million people became infected with HIV and more than 40 million adults and children around the world are now HIV-positive (Asamoah-Odei et al., 2004). It has been reported that 50% of the total population infected with HIV have severe impact on the sexually active and economically reproductive years (15-45years) of age (Harry et al., 1993). The importance of early recognition, subsequent clinical and haematological assessment of the disease is greatly facilitated by familiarity with patients' clinical state. A recent draft on clinical staging correlating with laboratory markers (eg CD4+ cell count) known to reflect disease progression has been proposed and used as indicators of immune deficiency or to monitor progress of HIV therapy (Roman et al., 2002).

Haematologic manifestations are among the most common presentation of advanced HIV/AIDS including morphologic abnormalities of peripheral blood and bone marrow changes (Aboulafia and Mitsuyasu, 1991). These haematologic abnormalities are most likely the consequence of persistent viral infection in an immunocompromised host. The most important of these manifestations are cytopenias (Coyle, 1997). The haematologic baseline data and CD4+ T

lymphocyte count for naïve HIV patients at presentation have not been documented in this part of the country. There is therefore a problem in monitoring patients' therapeutic outcome: predicting progression to AIDS, monitoring response to HAART (highly active antiretroviral therapy), guide to therapeutic decisions and survival period. Though access to HAART is expanding in Nigeria, there is paucity of published data on such studies. The aim of the study therefore is to establish the baseline haematological parameters and CD4+ T lymphocyte count of naïve HIV patients against which subsequent data can be compared.

MATERIALS AND METHODS

The study group comprised 191 antiretroviral (ARV) naïve adult HIV/AIDS patients attending the consultant outpatient clinic and recruited into the ARV pilot project in University of Benin Teaching Hospital (UBTH), Nigeria between July and September 2004. The UBTH, Benin is a major referral and treatment center for the South-South geopolitical zone of Nigeria where two major, HIV/AIDS treatment units exist: the Federal Government Sponsored Project and PEPFAR (President Emergency Plan for AIDS Relief, USA). Patients' demographic data were documented. They were classified with respect to severity of their disease state in accordance with the WHO CDC Clinical Categorization Staging System of HIV/AIDS for Africa (World Health Organization, 2005). The CD4+ cell count and haematological indices were done at their first visit to the unit as part of the routine workup to assess the disease status and need for ARV therapy. The haematological counts were determined by automation and the CD4+ T lymphocytes were counted by flow cytometre. Antibody to HIV was carried out by ELISA technique and confirmed by Western blot. Data was analyzed using the Mann Whitney and student t-test where appropriate using the GraphPad instat version 2.05a.

RESULTS

A total of 191 consecutively diagnosed HIV patients (between July and September 2004) recruited into the Federal Government and PEPFAR project were seen. This comprised of 69(36.1%) males and 122 (63.9%) females with a M:F ratio of 1:1.8. The median age was 38 years (range, 21 to 75years) with majority in the age bracket 31-40years. The demographic and baseline characteristics of the HIV naïve patients are captioned in Table 1. The WHO CDC Clinical Staging System showed that 151(79.1%) symptomatic patients presented in advanced stage disease (3 and 4) while 40(20.9%) asymptomatic patients were in stages 1 and 2 compared to 84 age and sex matched control. The majority of the study group was diagnosed because they presented AIDS-related illness.

The blood findings obtained from the patients compared with controls are shown in Table 2. There was a significant difference in most of the haematological parameters tested ($P<0.0001$) except for the red cell indices (MCV, MCH, MCHC). The mean haematocrit (Hct) for males and females was 0.36 and 0.30 respectively while the overall mean Hct was 0.32 (range, 0.15-0.50l/l). This was significantly lower than controls (0.38±4.66) ($P<0.0001$) with severe anaemia occurring in 65 patients (34%) while 126 patients (66%) had haemoglobin greater than 10g/dl. The mean total leucocyte count of $5.3\pm2.1 \times 10^9$/l was significantly lower than control ($P<0.0001$) but the lymphocyte count was statistically higher than controls ($P<0.0001$). The mean platelet count was 233×10^9/l with thrombocytopenia occurring in 20 patients (10.5%). The red cell indices were within normal range and there was no statistically significant difference when compared with controls ($P>0.05$). The mean erythrocyte sedimentation rate (ESR) was higher than in controls with a median value of 85mm/hr (range, 6-164mm/hr) by the Westergren method. At presentation, the males tended to have a slightly higher (195 cells/µl) mean CD4+ cell count than the females (180 cells/µl) with an overall median CD4+ cell count of 146 cells/µl. For both sexes combined, the mean CD4+ cell count at enrollment was 185 cells/µl compared to 600 cells/µl in controls and the difference was statistically significant ($P<0.0001$). A total of 125 patients (65.4%) had a CD4+ cell count of <200 cells/µl. There was no significant correlation between lymphocyte count and CD4+ cell count. ($r = -0.7170$, $p = 0.283$).

Table 1: Demographic and Baseline characteristics of naïve HIV patients at presentation.

Variables	Number	%
Gender		
Male	69	36.1
Female	122	63.9
Age (years)		
21-30	47	24.6
31-40	73	38.2
41-50	47	24.6
>50	24	12.6
Marital status		
Single	44	23.0
Married	113	59.2
Widowed	34	17.8
Clinical staging		
1-2	40	20.9
3-4	151	79.1
CD4+ cell count		
<200	125	65.4
201-300	42	22.0
>300	24	12.6

DISCUSSION

Nigeria is one of the countries that are highly burdened by HIV/AIDS, which is the most common cause of death apart from malaria in tropical and subtropical countries. Haematological abnormalities of pancytopenia/cytopenias have been reported to be frequently seen in HIV-infected patients (Coyle, 1997; Wolf et al., 2001). Aetiologies of cytopenias are diverse affecting haemopoietic activity, causing considerable life-threatening clinical problems and impairing the quality of life of these patients. As expected, there was a preponderance of females (63.9%) in this study. In contrast, a study on distribution of AIDS cases by sex carried out in another part of the country reported a male dominance (Rukujei, 1998). No explanation was given for the male dominance. A review of the age and sex distribution showed that 45 of the females seen were above 40 years of age.

The fact that the disease affects mainly young people in their productive years has serious economic implication to the individual and, by extension to the nation. This is similar to the study in Ibadan, Nigeria where people aged between 20-40 years were mostly affected (Oyo State Ministry of Health, Nigeria, 1996).

Pancytopenia was found in increasing incidence and correlates with the severity of the clinical disease similar to another study (Zon et al., 1987). The disease was usually disseminated at presentation and therefore the majority of patients were symptomatic with low CD4 cell count requiring ARV therapy. A total of 151(79.1%) patients presented in advanced stages 3-4 while 40(20.9%) patients were in stages 1-2 according to the WHO CDC Clinical Categorization Staging System of HIV/AIDS for Africa (World Health Organization, 2005). They are based on the clear clinical markers and do not require any of the diagnostic technology which is likely to be lacking in resource poor countries. However, Gilks and Muller have criticized this as being insensitive and too non-specific. The marked differences in environment result in a completely different clinical picture and the absence of high laboratory technology means that some infectious diseases e.g. cytomegalovirus virus and mycobacterium avium intracellular would be difficult to diagnose.

The haematocrit values are similar to previous studies (Erhabor et al., 2005) with the most affected productive group having an overall mean of 0.33. This was significantly lower than in the apparently healthy individuals ($P<0.0001$). Anaemia has been known to be associated with HIV/AIDS and the causes are multifactorial (Claster, 2002). This is due to a number of factors: bone marrow failure as a result of the disease process through abnormal cytokine expression and alteration of the bone marrow microenvironment; progressive damage to the immune complex but rarely due to haemolysis secondary to high fever or associated positive direct antiglobulin test (Coyle, 1997; Claster, 2002; Costello, 1999). Other factors include reduced red blood cell (RBC) production, nutritional deficiencies, increased RBC destruction, or a combination of these problems (Claster, 2002). The anaemia is further worsened as a result of the poor economic condition and also genetically inclined as Europeans have been known to have higher values than apparent healthy Africans (Araba, 1976; Bain, 1996).

Table 2: The haematological and CD4+ cell count findings of HIV naïve patients at the time of diagnosis.

Laboratory Features	Naïve patient	Control	P value
Haematocrit (l/l)	0.32 ± 6.53	0.38 ± 4.66	<0.0001
White cell count (x10^9l/l)	5.3 ± 2.1	5.71± 0.97	<0.0001
Lymphocytes (x10^9l/l)	4.8 ± 14.3	2.90 ± 0.69	<0.0001
Neutrophils (x10^9l/l)	4.7 ± 13.7	2.30 ± 0.51	0.027
Monocytes (x10^9l/l)	0.8 ± 5.7	0.40 ± 0.17	<0.0001
Platelet count (x10^9l/l)	242 ± 12.9	304 ± 61.5	<0.0001
ESR (mm/hr)	84.4 ± 46.3	14.98 ± 7.31	<0.0001
Red cell indices			
MCV (fl)	81.4 ± 14.01	84.5 ± 5.3	ns
MCH (pg)	27.6 ± 14.0	30.2 ± 2.99	ns
MCHC (g/dl)	34.8 ± 18.8	26.2 ± 1.04	ns
CD4+ cell count (µl)	185.4 ± 152	600 ± 0.17	<0.0001

ESR: erythrocyte sedimentation rate; MCV: mean cell volume (femtoliter); MCH: mean cell haemoglobin (pictogram); MCHC: mean cell haemoglobin concentration; ns: not significant.

The total leucocyte count recorded for the naïve HIV patients was slightly higher than that reported in another part of the country (Erhabor et al., 2005). As expected, the total leucocyte count was significantly lower than in the controls (P<0.0001) but the neutrophil count was significantly higher than in the controls (P=0.027). This is in contrast to other studies where neutropenia was associated with HIV patients already on HAART regimen combined with cotrimoxazole or due to autoimmune destruction (Coyle, 1997; Zon et al., 1987; Moh et al., 2005). The high ESR value is an indication of acute and chronic infection, inflammatory process amongst others and was statistically significant when compared to controls (P<0.0001).

HIV/AIDS patients have been known to have reduced CD4 cell count when compared to control as further confirmed in this study. This is as a result of the direct destruction of the CD4 cells by the HIV virus itself. One hundred and twenty five (65.4%) patients had an absolute CD4+ cell count less than 0.20x10^9/l and an overall mean of 1.85x10^9/l. This was lower than 2.33x10^9/l recorded in Lagos, a large urban center in the South-Western rain forest area of Nigeria (Akanmu et al., 2001). The low CD4+ count was also similar to the findings in a previous study in Barbados (Kilaru et al., 2004). There was no significant correlation between the CD4+ cell count and lymphocyte count in contrast to previous studies (Erhabor et al., 2006; Blatt et al., 1993). A study carried out in Kampala, Uganda also showed a correlation between total lymphocyte count and CD4 cell count (Kamya et al., 2004).

In conclusion, this study establishes local standard values of haematological indices including CD4+ cell count in naïve HIV Nigerians. This will serve as reliable values for monitoring treatment outcome/effectiveness of ARV therapy.

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