



Asian Journal of Epidemiology

ISSN 1992-1462

science
alert
<http://www.scialert.net>

ANSI*net*
an open access publisher
<http://ansinet.com>

Hematological Changes in HIV Patients Placed on Anti Retroviral Therapy in Markurdi, Benue State of Nigeria

¹O.F. Amegor, ³D.A. Bigila, ²O.A. Oyesola, ²T.O. Oyesola and ⁴S.T. Buseni

¹Department of Medical Laboratory Sciences,

²Department of Physiology, School of Basic Medical Sciences,

College of Health Sciences, Igbinedion University Okada, Okada, Edo State, Nigeria

³Nigeria Airforce Base Medical Center, Benin City, Edo State, Nigeria

⁴Nigeria Airforce Base Hospital Markurdi, Benue State, Nigeria

Abstract: This present study was conducted to investigate the observed trend in the Hematological parameter in Makurdi; Beune state of Nigeria. Due to the ongoing campaign about HIV/AIDS management, practical knowledge and supportive information becomes necessary about antiretroviral drugs (ARVDs) therapy. This will assist health workers and encourage HIV/AIDS patients in the management of the disease. This study was carried out in Markurdi, Benue state of Nigeria in the Nigerian Air Force Hospital. Two hundred freshly diagnosed HIV patients were used (119 females and 81 males). They were grouped into three categories as follows: group 1, control group were HIV negative subjects, group 2 were HIV positive subjects without ARVDS and group 3 were HIV positive subject on ARVDS. The percentage distribution for both male and female are as follows: group 1 are 37% male and 63% female, group 2 are 40.5% male and 59.5% female, group 3 are 42% and 57.2% female. Blood samples were collected from anti-cubital vein into ethylene diamine tetra-acetic for laboratory study. The report from the laboratory analysis of the blood sample showed that ARVDS therapy increased PCV, Hb, WBC and CD4 cell count of the subjects. Subject on ARVDS therapy showed insignificant increase from $31.56 \pm 65\%$ to $32.26 \pm 0.49\%$ for PCV, from 10.30 ± 1.170 to $10.44 \pm 0.17g\ dL^{-1}$ for hemoglobin concentration, from 412.53 ± 15.23 to $422.93 \pm 25.73\ cell\ mm^{-3}$ and a significant increase in WBC (total) from 4.07 ± 0.25 to 4.76 ± 0.17 . Conclusion from this study was in agreement with other works that ARVDS therapy has the ability to improve on the Hematological parameters (PVC, Hg, WBC and CD4 cell count) and as a result boost the immune system of the body.

Key words: Hematological changes, HIV patients, antiretroviral drugs

INTRODUCTION

The cause of death among young adults worldwide is HIV/AIDS (human immunodeficiency virus /acquired immune deficiency syndrome). It has a devastating impact on people in developing countries (Horowitz *et al.*, 1998). The AIDS is caused by HIV, it can be contracted through sexual contact exposure to blood including sharing of needle and

Corresponding Author: Olusoji Adebusoye Oyesola, Department of Physiology,
School of Basic Medical Sciences, College of Health Sciences,
Igbinedion University Okada, Okada, Edo State, Nigeria

syringe and by certain blood product of body fluid. Clinical presentation include pneumonia, fever, pyrexia, loss of vision, chronic diarrhea, weight loss, lymphadenopathy, cough and itch maculopapular generalized skin rash, blue discoloration anemia and hairy leukoplakia (Lloyd, 1996; James *et al.*, 1997; Kelly, 1998).

Antiretroviral drugs (ARVDS) are medication for the treatment of infection by retro viruses primarily HIV. Different classes ARVDS act at different stages of HIV cycle (World Health Organization, 2003) combination of several (typically three or four) ARVDS are known as Highly Active Anti Retroviral Therapy (HAART) (Kovacs *et al.*, 1989) combination of ARVDS create multiple obstacles to HIV replication to keep the number to offspring low and reduce the possibility of a superior mutation arising which convey resistance to one of the drug being taken, the other drug continue to suppress reproduction of that mutation. With rare exception no individual ARVDS has been demonstrated to suppress HIV infection for long. These ARVDS must be taken in combination in order to have a lasting effect (Graham *et al.*, 1992).

Limitation of Anti-Retroviral Therapy (ART) to HIV infection is evident and restricts such an individual to limited option. A large combination of ARVDS and approach known as mega-haart or salvage therapy often increase the drug side effect and treatment list (Chow and Merrill, 1993). Ho *et al.* (1995) and Wei *et al.* (1995) reported the initial dynamic effect of patient, anti-retroviral therapy on plasma HIV RNA level provided significant insight into retroviral pathogenesis. Within week after administration of highly active anti-retroviral therapy there were steep decline in plasma HIV RNA with coincidental abrupt rise in CD4⁺T circulating in the blood. Interpretation of these finding by Wei *et al.* (1995) and Ho *et al.* (1995) was that therapeutic perturbation of a steady-state relationship reveals a constant and dynamic equilibrium between viruses-mediated cell killing and endogenous production of uninfected CD4⁺T lymphocytes. In tap and drain model of Wei *et al.* (1995), he said decreased viral killing quickly top the balance in favor of lymphocytes production which allow at least a partial immune reconstitution to occur. Opposing view about this, from Mosier *et al.* (1995), Dimitrov and Martin (1995) and Grossman and Herberman (1997) reported that the adult immune system might not have capacity for the rapid CD4⁺T cell regeneration proposed, there is lack of evidence for heightened CD4⁺T cell turnover cell among HIV-infected individual and the observation of increase in lymphoid subset in blood rather than a specific increase in CD4⁺ cell that are target of HIV infection.

Pakker *et al.* (1998) in his own finding reported that a significant proportion of the CD4⁺T cell rise in treated individual may be attributed to redistribution of cell from tissues to blood rather to rapid replacement of the cell eliminated by viral infection.

Mohri *et al.* (1998) compared the generalized immune activation and heightened blood lymphocyte turnover in macaques infected with the simian immunodeficiency virus with uninfected control animals, he reported that rapid regeneration of T cells is a characteristics feature of the host response to retrovirus infection.

Bucy *et al.* (1999) analyzed blood and lymph nodes tissues obtained concurrently from HIV-infected patient before and after initiation of HAART and reported that activated T cells were significantly more frequent in lymph node tissue compared with blood CD4⁺ cell count on HAART which were suggested to be as a result of redistribution which is mediated by resolution of the immune activation that had sequestered T cells within lymphoid tissue.

During the investigation of Imarhiagbe and Kubeyirje (2005) elevation of CD4⁺ cell count were observed in the cases that were considered during the administration of ARVDS among HIV/AIDS patient in University of Benin teaching Hospital in Nigeria. In another independent work conducted by Chukwurah *et al.* (2007) at the University of Nigeria teaching Hospital Enugu Nigeria, they reported that ART and nutrition increase platelet count than ESR and PCV in HIV positive patients on ART.

The present study was conducted to investigate the observed trend in the Hematological parameter in Makurdi; Beune state of Nigeria, since available information on antiretroviral drugs has not mentioned changes observed in hematological parameters in this region. The available report focus on the side effects of ARVDs in the part of Nigeria. This study however will further provide information about the effectiveness of antiretroviral drugs therapy among HIV positive patient in this part of Nigeria despite the reported side effects (Iornon *et al.*, 2008). This will also serve as supporting information for health workers to emphasize the use of ARVDs in their campaign, for HIV management and encourage the HIV patients in making themselves available to be treated especially at the early stage and to ignore the experienced side effects.

MATERIALS AND METHODS

Period of Study, Ethical Clearance and Informed Clearance

The study was conducted between 18th day of April 2008 and 17th day of April 2009 in the Nigerian Air Force Hospital, Markurdi in Benue state. The consent of the patients (subjects) was sought as well as that of the Nigeria Air Force Hospital Research Ethical committee before blood samples were taken for the study.

Study Population

Two hundred freshly diagnosed HIV patients subjects (119 females and 81 males) without ARVDS and one hundred and ten known, HIV subjects (63 females and 47 males) on ARVDS were used for the study. Included were one hundred apparently healthy HIV negative subjects (63 females and 37 males). They all were of the ages ranging from 15 to 55 years of age. Excluded from these categories are subjects' below 15 years and above 55 years, subjects with diabetes, venereal disease or any other disease. Similarly subjects on traditional herbs were also excluded. All subjects used were patients who were attending the hospital.

Blood Sample Collection

Five milliliter syringe was used to draw blood from the anti-cubital vein of each subject. The blood was dispensed into a tube containing ethylenediamine tetra-acetic acid (EDTA) and was used immediately for hematological parameters.

Haematological Study

CD4⁺ Count

This was done using CD4⁺ Dynal bead technique which uses the principle of immune-magnetic cell isolation using Dynal bead at T4-T8 Quant, enables rapid quantification of T4 and T8 lymphocytes directly from samples of EDTA and anti-coagulated blood. This is based on isolation technique of depletion of Monocytes, isolation of CD4⁺T cells and CD4⁺T cells counting.

Packed Cell Volume Determination

Blood sample was drawn into capillary tube and sealed. It is placed in a haematocrit centrifuge. Centrifugation of blood was done at approximately 12000 g for 5 min, PCV determined by a haematocrit-reader.

$$\text{PCV (\%)} = \frac{\text{Height of red cell column}}{\text{Height of total blood column}} \times 100$$

Hemoglobin Estimation

This was done using the method of Van Kampen and Zijlstra (1961).

White Blood Cell Count

This was done using the method of Burkner.

HIV Test

The method of CHEMBIO was used by Essex *et al.* (1983).

Statistical Analysis

All data were presented as Mean±SEM (standard error of mean). Significant differences in PCV, Hb, WBC and CD4 count were determined by one way analysis of variance (ANOVA). Values of $p < 0.05$ were regarded as significant using SPSS-10.

RESULTS

Table 1 shows the age distribution of the subjects used for the study, with the mode of the three groups fell within the age distribution of 26-30 years of age. Similarly, the majority of the populations were within the age range of 26-50 years of age.

In Table 2 percentage distribution of sexes of subjects used for the experiment were shown with the female sexes forming the highest percentage of the distribution. But when compared they showed no significant difference.

Table 3 shows the hematological changes as observed in the Packed Cell Volume (PCV), Hemoglobin concentration (Hb), White Blood Cell (WBC) count and CD4⁺ count. The three

Table 1: Age distribution of subjects used for the study

Ages (years)	Distribution of HIV		
	Negative subjects	Positive subjects without ARVDS	Positive subjects on ARVDS
11-15	2	0	0
16-20	7	9	5
21-25	8	30	11
26-30	29	46	34
31-35	17	27	23
36-40	22	43	19
41-45	7	27	10
46-50	7	43	4
51-55	1	12	4
Total	100	200	110

Table 2: Percentage distribution of sexes of subjects used for the study

Ages (years)	% Distribution of HIV		
	Negative subjects	Positive subjects without ARVDS	Positive subjects on ARVDS
Male	37.0	40.5	42.8
Female	63.0	59.5	57.2
Total	100	100	100

Show no significance at $p < 0.05$

Table 3: Hematological changes

Groups	PCV (%)	Hb (g dL ⁻¹)	WBC (Total)	CD4 ⁺ count (cell mm ⁻³)
HIV negative subjects (control group 1)	12.24±0.15	6.22±0.33	603.03±20.19	603.03±20.19
HIV positive subjects without ARVDS (group 2)	31.56±0.65 ^a	10.30±0.22 ^a	4.07±0.25 ^{a,b}	412.53±15.23 ^a
HIV positive subjects on ARVDS (group 2)	32.26±0.49 ^a	10.44±0.17 ^a	4.76±0.15 ^{a,b}	422.93±25.73 ^a

^{a,b} Show significance at $p < 0.05$

groups (HIV negative subjects, HIV positive subjects without ARVDS and HIV positive subjects on ARVDS) were compared statistically.

Observation shows that the values of PCV in percentage, which is 36.67 ± 0.45 for HIV negative subjects significantly reduced to 31.56 ± 0.65 in HIV positive subjects without ARVDS treatments but upon administration of ARVDS there was an insignificant increase over HIV positive subjects without ARVDS treatments. The increase observed did not returned the value to the obtained value in control subjects.

The hemoglobin concentration in g dL^{-1} of the subject showed also a significant reduction from 12.24 ± 0.15 to 10.30 ± 0.22 for HIV positive subjects without ARVDS treatments. There was an insignificant increase of 10.44 ± 0.17 when the subjects received ARVDS treatments. This observed increase did not return the value back to the recorded value for HIV negative subjects.

The pattern observed in the WBC count (measured in cells mm^{-3}) showed that there was a significant decrease from 6.33 ± 0.33 in HIV negative subject to 4.07 ± 0.25 in HIV positive subjects without ARVDS treatments. But the observed increase when the subjects received ARVDS treatments was significant (value was 4.76 ± 0.15) when compared with subjects without ARVDS. It was also noted that although the increase was significant, the observed value of 4.76 ± 0.15 was not up to the recorded value for the HIV negative subjects which is 6.22 ± 0.33 cell mm^{-3} found in HIV negative subjects.

Values from the CD4^+ counts showed 603.03 ± 20.19 cells mm^{-3} for HIV negative subjects. The observed values of 412.53 ± 15.23 cell mm^{-3} was measured for HIV positive subjects without ARVDS therapy, this was a reduction which was significant at $p < 0.05$ value. Although, there was an insignificant increase to 422.93 ± 25.73 cells mm^{-3} for subjects that received ARVDS treatments, this was not up to the observed value of 603.03 ± 20.19 found in HIV negative subjects.

DISCUSSION

Despite some side effects that were reported to be associated with the use of antiretroviral drugs in Gboko, Benue state of Nigeria as complained by patients and yet patients who can avoid the cost were still using them (Iornon *et al.*, 2008). The results of this study reemphasize and encourage the use of antiretroviral drugs in Nigeria.

From this study PCV value reduced in both HIV positive subjects (on ARVDS therapy and those not on ARVDS therapy) to levels showing mild anemia, respectively. This confirmed reported generalized effects of HIV/AIDs on hematopoietic and blood cells (Blockman, 1991). But with ARVDS therapy the value of PCV increase over those who were not on ARVDS therapy. This shows that ARVDS therapy has ability to promote blood cells production.

The reported reduction in CD4^+ count in this study was consistent with the established diagnosis of AID (James *et al.*, 1998) this observed reduction was not less than 200 cells mm^{-3} . But during the ARVDS therapy there was an increase in the CD4^+ count, which was consistent with the work of Wei *et al.* (1995), Ho *et al.* (1995) and Chukwurah *et al.* (2007).

The reported significance increase observed in the WBC count and insignificant increase in CD4^+ during this study was an indication of the ability ARVDS to boost the immune system and reduce the risk of an opportunistic infection (Baker *et al.*, 2007). Although, the study of Mosier *et al.* (1995), Mohri *et al.* (1998) and Grossman and Herbarman (1997) suggested that adult immune system might not have capacity for rapid CD4^+ T cell regeneration but there were increase in the lymphoid subset in the blood.

CONCLUSION

In conclusion, the study support the earlier findings of Chukwurah *et al.* (2007) and Wei *et al.* (1995) that the use of ARVDs therapy increase PCV %, Hg, WBC and CD4⁺ count and thus has the ability to boost the immune system of the body amidst the reported side effects. The ability of the drugs boosting the immune system seems to override the reported side effects and encourage the management of HIV/AIDs patients with ARVDs despite the side effects. The drugs effectiveness' will become significant if proper management start at the early stage under qualified personnel.

REFERENCES

- Baker, J., G. Peng, J. Rapkin, D. Abrams and M. Silverberg *et al.*, 2007. HIV-related immune suppression after ART predicts risk of non-opportunistic diseases: Results from the FIRST study. Proceedings of the 14th Conference on Retroviruses and Opportunistic Infections, Feb. 25-28, Los Angeles, pp: 1-2.
- Blockman, D., 1991. HIV related thrombocytopenia. *Br. J. Haematol.*, 99: 350-354.
- Bucy, R.P., R.D. Hockett, C.A. Derdeyn, M.S. Saag and K. Squires *et al.*, 1999. Initial increase in blood CD4⁺ lymphocytes after HIV antiretroviral therapy reflects redistribution from lymphoid tissues. *J. Clin. Invest.*, 103: 1391-1398.
- Chow, Y. and D. Merrill, 1993. Use of evolutionary limitations of HIV-1 multi-drug resistance of optimize therapy. *Nature*, 361: 650-654.
- Chukwurah, F.E., D. Echeobi and R.O. Nneli, 2007. Hematological profile of immunodeficient (HIV) seropositive patients on antiretroviral (ARV) therapy implication of nutrition. *Res. J. Med. Sci.*, 1: 242-244.
- Dimitrov, D.S. and M.A. Martin, 1995. HIV results in the frame CD4⁺ cell turnover. *Nature*, 375: 194-195.
- Essex, M., M.F. McLane, T.H. Lee, L. Falk and C.W. Howe *et al.*, 1983. Antibodies to cell membrane antigen associated with human T-cell virus in patients with AIDS. *Science*, 220: 859-862.
- Graham, N.M., S.L. Zeger, L.P. Park, S.H. Vermund, R. Detels, C.R. Rinaldo and J.P. Phair, 1992. The effects of survival of early treatment of human immunodeficiency virus infection. *N. E. J. Med.*, 326: 1037-1042.
- Grossman, Z. and R.B. Herberman, 1997. T-cell homeostasis in HIV infection is neither failing nor blind: Modified cell counts reflect an adaptive response of the host. *Nat. Med.*, 3: 486-490.
- Ho, D.D., A.U. Neuman, A.S. Perelson, W. Chen, J.M. Leonard and M. Markowitz, 1995. Rapid turnover of plasma virions and CD4 lymphocytes in HIV-1 infection. *Nature*, 373: 123-126.
- Horowitz, W., E. Telzak, A. Sepkowitz and P. Wormser, 1998. Human immunodeficiency virus and AIDS (Review). *Papua New Guinea Med. J.*, 39: 174-180.
- Imarhiagbe, F.A. and E.P. Kubeyinje, 2005. Hypertriglyceridemia in antiretroviral therapy. *Med. Gen. Med.*, 7: 65-65.
- Iornon, T.F., K. John, A.S. Nyitor and A. Terzungwe, 2008. Antiretroviral drug therapy in Benue state, Nigeria a follow up of 20PLWA in private Hosipital in Gboko. *J. Hum. Ecol.*, 23: 267-273.
- James, T., B. Rebecca, G. Heiner, M. Philippe and M. Frank *et al.*, 1997. HIV-associated adult mortality in a rural Tanzanian population. *Official J. Int. Soc. AIDS.*, 11: 801-807.

- James, O., M.D. Kahn, D. Bruce and M.D. Walker, 1998. Acute human immunodeficiency virus type 1 infection. *N. Engl. J. Med.*, 339: 33-39.
- Kelly, P., 1998. Diarrhoea and AIDS recent development in the African setting. *Afr. Health*. 20: 16-18.
- Kovacs, J.A., L. Deyton, R. Davey, J. Falloon and K. Zunich *et al.*, 1989. Combined Zidovudine and interferon-alpha therapy in patients with Kaposi sarcoma and the acquired immunodeficiency syndrome (AIDS). *Annals Int. Med.*, 111: 280-287.
- Lloyd, A., 1996. HIV infection and AIDS (Review). *Papua New Guinea Med. J.*, 39: 174-188.
- Mohri, H., S. Bonhoeffer, S. Monard, A.S. Perelson and D.D. Ho, 1998. Rapid turnover of T lymphocytes in SIV-infected rhesus macaques. *Science*, 279: 1223-1227.
- Mosier, D., J. Sprent and D. Tough, 1995. CD4+ cell turnover. *Nature*, 375: 193-194.
- Pakker, N.G., D.W. Notermans, R.J. de Boer, M.T. Roos and F. de Wolf *et al.*, 1998. Biphasic kinetics of peripheral blood T cells after triple combination therapy in HIV-1 infection: A composite of redistribution and proliferation. *Nature Med.*, 4: 208-214.
- Van Kampen, E.J. and W.G. Zijlstra, 1961. Standardization of hemoglobinometry. II. The hemoglobincyanide method. *Clin. Chim. Acta*, 6: 538-544.
- Wei, X., S.K. Ghosh, M.E. Taylor, V.A. Johnson and E.A. Emini *et al.*, 1995. Viral dynamics in human immunodeficiency virus type 1 infection. *Nature*, 373: 117-122.
- World Health Organization, 2003. Scaling up Retroviral Therapy in Resource Limited Setting. WHO., Rome.