MEDWIN PUBLISHERS
Committed to Create Value for Researchers

Haematology International Journal
ISSN: 2578-501X

Evaluation of Haematoimmunological, Erythropoietic Growth Factor and Virological Status in HIV-Patients

ESAN Ayodele J [1]*, OYEGUE Kelvin[2], OYEDELE Titilayo E[3] and OGUNBUSUYI Bolu[4]

[1]Hematology and Blood Transfusion Department, Federal Teaching Hospital, Nigeria
[2]Hematology and Blood Transfusion Department, Federal Medical Centre, Nigeria
[3]Department of Medical Laboratory Science, Achievers University, Nigeria
[4]Department of Medical Laboratory Science, Afe Babalola University, Nigeria

Research Article
Volume 5 Issue 2
Received Date: October 26, 2021
Published Date: November 11, 2021
DOI: 10.23880/hij-16000193

***Corresponding author:** Esan Ayodele J, Hematology and Blood Transfusion Department, Federal Teaching Hospital, Ido-Ekiti, Nigeria, Tel: +2348035477756; Email: ayodelejacob4u@gmail.com

Abstract

Background: Human Immunodeficiency Virus reduces immune status and diminishes haematological values causing decreased or ineffective haematopoiesis in HIV-infected individuals.
Aim: To evaluate haematoimmunological, erythropoietic growth factor and virological status in HIV-patients.
Methodology: This study was carried out at Federal Teaching Hospital, Ido-Ekiti. One hundred samples each were collected from HIV positive subjects on ART and ART-naïve, one hundred samples were collected from apparently healthy individuals as control. Six milliliters of whole blood were collected from each subject; 3mls of whole blood was dispensed into K2EDTA bottle for immediate analysis of haematological parameters using haematology analyzer, CD4 and CD8 count were analyzed using flow cytometer. The remaining 3ml of blood was dispensed into plain bottle, serum was extracted for erythropoietin analysis using enzyme-linked immunosorbent assay technique and viral load using polymerase chain reaction.
Results: Mean values of RBC indices CD4, CD4/CD8, EPO, TWBC and LYM among ART-naïve were significantly lower ($p<0.05$) compared to ART and control subjects. Mean values of CD8, VL, NEU, MONO, EOSIN and BASO in ART-naïve were significantly higher ($p<0.05$) compared to ART and control subjects.
Conclusion: HIV infection suppresses erythropoietic growth factor, haematoimmunological, and virological parameters as observed in the study. However, there is an improvement in HIV subjects on ART compared with ART-naïve, this suggested that there is positive response to antiretroviral therapy in HIV patients.

Keywords: Immunohaematological; Virological; Erythropoietin and HIV-infection

Abbreviations: HCT: Haematocrit; LYM: Lymphocytes; NEU: Neutrophlis; MONO: Monocyte; EOSIN: Eosinophil; BASO: Basophil; EPO: Erythropoietin; VL: Viral Load; CD4: Cluster Of Differentiation 4; CD8: Cluster Of Differentiation 8; MCV: Mean Cell Volume; MCH: Mean Cell Haemoglobin; MCHC: Mean Cell Haemoglobin Concentration; RDW: Red Cell Distribution Width;, HB: Haemoglobin Concentration; RBC: Red Blood Cell; TWBC: Total White Cell Count; K_2EDTA: Di-Potassium Ethylene Enthylene-Diamine Tetra-Acetic Acid; SD: Standard Deviation: ART: Antiretroviral Therapy.

Introduction

The amount of Human Immunodeficiency Virus (HIV) in the blood (specifically the number of copies of HIV-RNA) is called viral load. Human Immunodeficiency Virus

(HIV) infection reduces immune status and diminishes haematological values causing decreased or ineffective haematopoiesis in HIV-infected individuals [1]. Viral load represents how quickly HIV is replicating, when people are first infected with HIV infection, the HIV viral load increases rapidly [2] after about 3 to 6 months, even without treatment, it drops to a lower level, which remains constant, called the set point. HIV-RNA viral load indicates how contagious the infection is, how fast the CD4 count is likely to decrease and how fast symptoms are likely to appear [3]. During successful treatment, the viral load decreases to very low or undetectable levels (less than about 20 to 40 copies per microliter of blood). However, inactive (latent) HIV infection is still present within cells and if treatment is stopped, HIV starts replicating and the viral load increases. An increase in the viral load during treatment may indicate that HIV has developed resistance to drug treatment; the person is not taking the prescribed drugs or both [4]. Absolute CD4+ lymphocytes are a primary target of the human immunodeficiency virus (HIV), which helps to determine how well the immune system can protect the body from infections and how severe the damage done by the HIV infection, CD4 count falls below about 200 cells per microliter of blood make the immune system becomes less able to fight certain infections. However, CD4 counts below 50 cells per microliter of blood are particularly dangerous because additional opportunistic infections that can rapidly cause severe weight loss, blindness, or death commonly occur. (CD8) T cell is a cytotoxic T Lymphocytes that destroy virally infected cells and remain inactivated when there is no foreign antigen. It contributes to the eradication of intracellular infections and to the control of many chronic infections like HIV/AIDS [5].

In HIV infected patients, CD4/CD8 ratio and CD8+ T-lymphocyte counts have been suggested as prognostic markers for mortality, in addition to viral load and CD4 count. During HIV infection, CD8 cells increases as HIV is progressing in response to HIV infection. HIV replication leads to activation of the innate and adaptive immune system, generating an inflammatory environment making CD8 T cell increasing [6]. An elevated CD8 cell count is associated with an increased risk of HIV treatment failure especially for patients who initially achieve an undetectable viral load [7,8]. The CD4/CD8 ratio is considered a marker of disease progression in HIV/AIDS, and is often found to be inverted meaning that there are less CD4 cells than CD8 cells, resulting in a ratio of less than 1. Low CD4/CD8 ratios were also found to be associated with increased morbidity and mortality in HIV infection [9,10]. CD8 cells are often increased, especially in less advanced stages of AIDS. Combination of lowered CD4 counts and increased CD8 counts are commonly thought to occur only in people diagnosed HIV positive [11,12]. The primary action of Erythropoietin (EPO) is to promote the proliferation and differentiation of the colony-forming unit-erythroid (CFU-E) and other erythroid progenitors. Haematological abnormalities are common occurrence in individuals diagnosed with human immunodeficiency virus, the commonest of these haematological abnormalities reported by several studies include: anaemia, thrombocytopenia and leucopenia [13]. Associated risk factors for these haematological abnormalities both prior to starting ART and while on ART could include HIV-related bone-marrow suppression, myelosuppression from antiretroviral drugs such as zidovudine and opportunistic infections [14].

Erythropoietin level in HIV-infected patients showed that the levels of erythropoietin failed to rise commensurate with increasing anaemia, suggested that insufficient amounts of erythropoietin cause anaemia due to direct effect of HIV infection on marrow progenitor cells [15]. Adebola, et al. reported that non-HIV infected anaemic subjects had an expected EPO rise whereas the HIV infected anaemic subjects showed no significant expected rise in serum EPO levels, this confirmed that there is an inappropriate EPO response to anaemia in HIV infected patients. There is blunted response to EPO in HIV infected patients who have anaemia, this suggested that a blunting of the EPO response may be involved in the pathogenesis of the HIV-related anaemia [16]. The primary goal of ART is to suppress HIV RNA lower than the detection level of the assay within six months on treatment to restore immunologic and haematological function, reduces morbidity and mortality and vertical transmission [7]. Positive effect of ART in the reduction of viral load, decreased destruction of mature haematopoietic cells of multiple lineages, an improvement in the blunted erythropoietin response and decreased incidences of opportunistic infections while on ART will improve overall quality of life expectant among HIV patients [17]. The aim of this study was to evaluate haematoimmunological, erythropoietic growth factor and virological status in HIV-patients.

Materials and Methods

Study Design

This study was carried out at Federal Teaching Hospital, Ido Ekiti, Nigeria. One hundred samples each was collected from HIV positive subjects on ART and HIV positive subjects ART naïve. One hundred samples were collected from apparently healthy individuals as control for the study. Consented subjects were re-screened for HIV infection for the purpose of the study to confirm their HIV status using serial algorithm method. Subject's consent was sort for through an informed consent form and ethical approval was

obtained from Federal Teaching Hospital, Ido-Ekiti.

Sample Collection and Sample Preparation

Six milliliters (6ml) of whole blood was collected from each consented subject, 3ml was dispensed into K_2EDTA bottle for immediate analysis of haematological parameters, CD4 count, CD8 count and HIV screening. The remaining 3ml of blood was dispensed into plain bottle, allowed to clot and centrifuged at 2500 revolution per minute for 5minutes to extract the serum into another plain vial, stored at -40^{0}C for the analysis of erythropoietin and viral load.

Methodology

HIV Screening Test

Human immunodeficiency virus was diagnosed using serial algorithm method. Determine HIV-1/2 (Abbott Diagnostic Division, Belgium/Luxemburg), Uni-Gold HIV Kit (Trinity Biotech, Wicklow Bay, Ireland) and Chembio HIV ½ Stat-PakTM Assay. Patients reactive to antibody screening tests were considered positive and recruited into the study; the test was carried out according to the manufacturer's instruction.

Haematological Parameters

Haematological parameter was analyzed using Haematology Analyzer (Sysmex XN 350 five parts) following Manufacture's instruction.

Analysis Of CD4 and CD8 Count Using Flow Cytometry (Cyflow Counter)

Research samples for CD4 and CD8 count was prepared and run on the Partec cyflow counter (Partec flow cytometer, GMBH, Munster, Germany) according to the manual instructions.

Viral Load Analysis

Extracted plasma was used to estimate HIV-RNA viral load analysis using polymerase chain reaction (PCR), the procedure was follow as describe in the manual.

Erythropoietin

Erythropoietin (EPO) was estimated using enzyme-linked immunosorbent assay (ELISA) kit; the procedure was followed as described in the manual ALPCO (2018).

Results

Groups	RBC(×10^9/l)	HB(g/dl)	HCT(%)	MCV(fl)	MCH(pg)	MCHC(g/dl)	RDW(%)
Control N=100	5.03±0.42	13.87±1.12	40.37±3.71	89.49±4.87	30.34±2.00	34.65±0.63	16.4±1.18
Art-Naïve N=100	3.28±0.79	8.18±2.55	27.03±32.50	83.48±9.67	28.37±3.14	32.32±1.54	18.5±4.21
Art N=100	4.34±1.25	12.05±4.31	39.38±32.17	97.92±14.61	32.21±3.75	33.79±2.75	15.72±3.10
F(P-Value)	99.50(0.00*)	96.14(0.00*)	7.87(0.00*)	47.67(0.00*)	14.58(0.00*)	40.17(0.00*)	21.45(0.00*)
Control Vs Art-Naïve	0.00*	0.00*	0.00*	0.00*	0.00*	0.00*	0.00*
Control Vs Art	0.00*	0.00*	0.95	0.00*	0.71	0.01*	0.01*
Art- Naïve Vs Art	0.00*	0.00*	0.02*	0.00*	0.00*	0.00*	0.00*

Table 1: Mean±SD of Red Cell indices in HIV Infected and Control Subjects.

Table 1 shows comparison of mean±SD of red cell indices in control, ART-naïve and ART subject. The parameters include red blood cell count (RBC), haemoglobin (Hb) haematocrit (HCT), mean cell volume (MCV), mean cell haemoglobin (MCH), mean cell haemoglobin concentration (MCHC) and red cell distribution width (RDW). The mean±SD of RBC 3.28± 0.79 in ART- naïve was significantly lower ($p<0.05$) compared to 5.03± 0.42 and 4.34± 1.25 in control and ART respectively (F-value 99.50; p-value 0.00). The mean±SD of Hb 8.18± 2.55 in ART naïve was significantly lower ($p <0.05$) compared to13.87± 1.12 and 12.05± 4.31 in control and ART respectively (F value 96.14: p-value 0.00). The mean±SD of HCT 27.03± 32.50 in ART-naïve was significantly lower ($p< 0.05$) compared to 40.37± 3.71 and 39.38±32.17 in control and ART respectively (F-value 7.87; p-value 0.00). The mean±SD of MCV 83.48± 9.67 in ART naïve was significantly lower ($p<0.05$) compared to 89.49± 4.87 and 97.92 + 14.61 in control and ART respectively (F-value 47.67; p-value 0.00). The Mean ± SD of MCH 28.37± 3.14 in ART-naïve was significantly lower ($p<0.05$) compared to 30.54 ± 2.00 and 30.21 ± 3.75 in control and ART respectively (F value 14.58; p-value0.00). The mean±SD of MCHC 32.32± 1.54 in ART-naïve was significant lower ($p<0.05$) compared to 34.65± 0.63 and 33.79± 2.75 in control and ART respectively (F-value 40.17;

p-value 0.00). The mean±SD of RDW 15.72± 3.10 in ART was significantly lower (p<0.05) compared to 16.40±1.18 and 18.50± 4.29 in control and ART- naïve respectively (F-value 21.45; p-value 0.00). However, multiple comparison between ART-naïve and control shows that mean±SD of RBC, Hb, HCT, MCV, MCH and MCHC in ART-naïve were significantly lower (P<0.05) compared to control. Mean±SD of RDW in control was significantly lower (p<0.05) in ART-naive. Multiple comparison between control and ART shows that, mean±SD of RBC, Hb and MCHC in ART were significantly lower (p<0.05) compared to control, however mean± SD of HCT, MCH, and RDW in ART were lower compare to control, the comparison shows no significant difference (P<0.05). Mean± SD of MCV in ART was significantly higher (P<0.05) compare to control. Multiple comparison between ART- naïve and ART shows that mean±SD of RBC, HB, HCT, MCV, MCH and MCHC in ART were significantly higher (p<0.05) compared to ART-naïve. However, mean±SD of RDW in ART was significantly lower (p<0.05) compared to ART-naïve.

Mean values of RBC indices among ART-naïve were lower compared to ART and control subjects. p≤0.05 was considered significant, p>0.05 was considered not significant, F-value = mean±SD of parameters was compared using ANOVA. RBC($\times 10^9$/l).

Table 2 shows the mean±SD of CD4, CD8, CD4/CD8, VL and EPO in control, ART-naïve and ART subject.The mean± SD of CD4 298.54±123.24 in ART-naïve was significantly lower (p<0.05) compared to 7746.22±67.29 and 422.52± 187.54 in control and ART respectively (F-value 292.04; p-value 0.00). The mean±SD of CD8 794.81±225.68 in ART-naïve was significantly higher (p<0.05) compared to 591.01± 56.87 and 654.55±190.21 in control and ART respectively (F-value 36.11; p-value 0.00). The mean±SD of CD4/CD8 0.38±0.08 in ART-naïve was significantly lower (p<0.05) compared to 1.27±0.09 and 0.59±0.16 in control and ART respectively (F-value 1663.00; p<0.00). The mean±SD of VL 130610.00±86647.32 in ART-naïve was significantly higher (p<0.05) compared to 91518.00±30807.97 in ART (F-value 159.35; p value 0.00). The mean± SD of EPO 2.18±0.81 in ART-naïve was significantly lower (p<0.05) compared to 7.26±0.87 and 3.32± 0.94 in control and ART respectively (F-value 924.58; p-value 0.00). Multiple comparison between control and ART-naïve shows that mean±SD of CD4, CD4/CD8 and EPO in ART-naïve were significantly lower (p<0.05) compared to control, however; mean±SD of CD8 and VL in ART-naïve were significantly higher (p<0.05) compared to control. Multiple comparison between control and ART show that, mean±SD of CD4, CD4/CD8 and EPO in ART were significantly lower (p<0.05) compared to control however; mean±SD of CD8 and VL in ART were significantly higher (p <0.05) compared to control mean±SD of CD4, CD4/CD8 and EPO in ART were significantly higher (p<0.05) compared to ART-naïve, however mean± SD of CD8 and VL in ART were significantly lower (p<0.05) compared to ART- naïve.

Groups	CD4(cells/µl)	CD8(cells/µl)	CD4/CD8	VL (copies/ml)	EPO (lU/L)
Control N=100	746.22±67.29	591.01±56.987	1.27±0.09	-	7.26±0.87
Art- Naïve N=100	298.54±123.24	794.81±225.68	0.38±0.08	130610.00±86647.32	2.18±0.81
Art N=100	422.52±187.54	654.55±190.21	0.59±0.16	91518±30807.97	3.32±0.94
F (P-Value)	292.04(0.00*)	36.11(0.00*)	1663.00(0.00*)	159.35(0.00*)	924.58(0.00*)
Control Vs Art-Naïve	0.00*	0.00*	0.00*	0.00*	0.00*
Control Vs Art	0.00*	0.01*	0.00*	0.00*	0.00*
Art-Naïve Vs Art	0.00*	0.00*	0.00*	0.00*	0.00*

Table 2: Mean±SD of CD4, CD8, CD4/CD8, VL and EPO in HIV Infected and Control Subjects.

Mean values of CD4, CD4/CD8 and EPO in ART-naïve were lower compared to ART and control subjects. Mean values of CD8 and VL in ART-naïve were higher compared to ART and control subjects. p≤0.05 was considered significant, p>0.05 was considered not significant, F-value = mean±SD of parameters was compared using ANOVA.

Table 3 shows comparison of mean±SD of total white blood cell (TWBC), neutophil (NEU), Lymphocyte (LYM), monocyte (MONO), eosinophil (EOSIN) and basophil (BASO) in control, ART-naïve and ART subject. The mean ±SD of TWBC 4.18± 1.41 in ART-naïve was significantly lower (p<0.05) compared to 6.27± 0.98 and 5.13± 1.34 in control and ART respectively (F-value68 .95; p-value 0.00). The mean±SD of NEU 38.03± 10.78 in ART was significantly lower (p<0.05) compared to 57.16± 5.56 and 54.65± 11.11 in control and ART-naive respectively (F-value 11985; p value0.00). The mean± SD of LYM 37.40± 9.03 in ART- naïve was significantly lower (p<0.05) compared to 41.50± 5.58 and 58.25±9.76 in control and ART respectively (F-value 176.97; p-value 0.00). The mean± SD of MONO in ART-naive was significantly higher (p<0.05) compared to 1.90± 0.77 and 2.92± 2.41 in control and ART respectively (F value 29.23; p-value 0.00). The mean± SD of EOSIN in ART was significantly higher (p<0.05)

compared to 1.36± 0.50 and 3.45± 3.19 in control and in ART-naïve respectively (F value 3.78; p-value 0.00). The mean± SD of BASO in ART-naïve was not significantly higher (p>0.05) compared to 1.00± 0.00 and 1.17± 0.39 in control and ART respectively (F-value 0.24; p-value 0.79). Multiple comparison between control and ART-naïve showed that mean±SD of TWBC and LYM in ART-naïve were significantly lower (p<0.05) compared to control. However, mean±SD of NEU in ART-naïve was not significantly lower (p>0.05) compared to control. Mean±SD of MONO and EOSIN in ART-naïve were significantly higher (p<0.05) compared to control. Mean±SD of BASO in ART-naïve was not significantly higher (p>0.05) compared to control.Multiple comparison between control and ART shows that mean±SD of TWBC and NEU in ART were significantly lower (p<0.05) compared to control. Mean±SD of LYM, MONO and EOSIN in ART were significantly higher (p<0.05) compared to control. Mean±SD of BASO in ART was not significantly higher (p>0.05) compared to control. Multiple comparison between ART and ART-naïve shows that mean±SD of TWBC and LYM, in ART-naïve were significantly higher (p<0.05) compared to ART. Mean± SD of NEU and MONO in ART were significantly lower (p<0.05) compared to ART- naïve. Mean± SD of EOSIN in ART was not significantly lower (p>0.05) compared to ART-naïve.

Groups	TWBC((×109/l)	NEU(%)	LYM(%)	MONO(%)	EOSIN(%)	BASO(%)
Control N=100	6.27±0.98	57.16±5.56	41.50±5.58	1.90±0.50	1.36±0.50	1.00±0.00
Art- Naïve N=100	4.18±1.41	54.65±11.11	37.40±9.03	5.96±4.98	3.45±3.19	1.25±0.62
Art N=100	5.13±1.34	38.03±10.78	58.25±9.76	2.92±2.41	4.11±3.73	1.17±0.39
F (P-Value)	68.95(*0.00)	119.85(0.00*)	176.97(0.00*)	29.23(0.00*)	3.78(0.00*)	0.24(0.79)
Control Vs Art-Naïve	0.00*	0.11	0.00*	0.00*	0.00*	0.38
Control Vs Art	0.00*	0.00*	0.00*	0.00*	0.00*	0.34
Art- Naïve Vs Art	0.00*	0.00*	0.00*	0.00*	0.63	0.92

Table 3: Mean±SD of White Blood Cell Counts in HIV Infected and Control Subjects.

Mean values of TWBC and LYM in ART-naïve were lower compared to ART and control subjects. Mean values of NEU, MONO, EOSIN and BASO in ART-naïve were higher compared to ART and control subjects. p≤0.05 was considered significant, p>0.05 was considered not significant, F-value = mean±SD of parameters was compared using ANOVA.

Discussion

In this present study, mean value of red cell indices in HIV-infected ART-naïve subjects were significantly lower compared to HIV-infected on ART and control subjects. Findings in this study were similar to Gedefaw, and Okafor report. They reported that decrease in red cell indices in ART-naïve subjects compared to ART and control subjects were due to effect of HIV infection causing decrease in red blood cell production, increase in red blood cell destruction and ineffective production of red cells [18,19]. Supporting findings in this study, Ballah reported that HIV infection alters red blood cell membrane fluidity these changes disrupt erythrocyte membrane stability, thus promoting haemolysis and ultimately anaemia [4]. Percentage of anaemia in HIV ART-naïve is higher compared to HIV subjects on ART and control subjects.Similar to the findings in this study, Volberding reported that the degree of anaemia in HIV-infected subjects is fairly related to immunosuppression and HIV disease stages. Haemoglobin concentrations decrease significantly with increasing markers of disease progression [20]. In this study, absolute CD4 count, CD4/CD8 ratio and erythropoietin were lower in ART-naïve subjects compared to ART and control subjects, while CD8 and viral load were higher in ART-naïve subjects compared to ART and control subjects. Findings in this present study was consistent with Wiredu report, he reported that the pathogenic effect of HIV virus resulted in significantly low mean levels of CD4 count and CD4/CD8 ratio among HIV patients ART naïve compared to ART and control group [21]. Findings in this study was supported with the fact that, in early HIV infection CD8+ T-cell numbers tend to increase reflecting expansion of memory CD8+ T cells. HIV patients ART-naive had decreased CD4 cell counts and increased CD8 cell, making the CD4/CD8 ratio lower. However, after treatment, the majority of patients will experience CD4 cell recovery but not followed by CD8 cell decline [10]. As observed in this study, CD8 cell expansions persist until far advance stage of HIV disease, CD8+ T cell expand more extensively than CD4+ T cells during immune response. High viral load reported in this study among ART-naïve compared to HIV subjects on ART indicate that, HIV-virus is at work making copies of it causing the disease to progress quickly. CD4/CD8 ratio is predictive of subsequent disease progression, a favorable ratio (>1.0) is a clear sign of immunologic health that is strongly associated with a delayed course to severe CD4 deficiency [22]. Supporting findings in this study, decrease in CD4/CD8 ratio was reported lower in HIV ART-naïve compared to HIV subjects on ART. Erythropoietin level in HIV-infected

patients showed that the levels of erythropoietin failed to rise commensurate with increasing anaemia, confirming the finding in this present study that insufficient amounts of erythropoietin cause anaemia due to direct effect of HIV infection on marrow progenitor cells [15].

Supporting the findings in this study, HIV infected anaemic subjects showed no significant rise in serum EPO levels, this confirmed that there is an inappropriate EPO response to anaemia in HIV infected patients, that there is blunted response to EPO in HIV infected patients who have anaemia and suggested that ablunting of the EPO response may be involved in the pathogenesis of the HIV-related anaemia. The severity of anaemia was found to increase with the severity of the HIV infection but the level of EPO failed to increase commensurately, suggesting that one of the reasons for anaemia in HIV subjects was erythropoietin deficiency [23]. EPO level decline with advancing HIV disease in WHO stage 2 and stage 3 as reported in this present study. The mechanism of anaemia in this study was due to depressed bone marrow function by HIV infection leading to low production of erythropoietin as reported in this study, which resulted into ineffective production of RBC. Supporting the findings in this study, it was reported that viral load predicts how fast the disease will progress, while CD4 count, indicate how much damage the virus has already caused to immune system HIV. The more HIV in the blood (the higher the HIV viral load), the faster the CD4 cell count will fall, and the greater the risk of becoming ill because of HIV infection [24]. In this present study, total white cell count and differential white cell count were lower in HIV ART-naïve compared to ART and control subjects. It was observed in this study that, HIV-infected subjects on ART had increase leucopenia and neutropenia compared to ART-naïve and control subjects. Similar to early report by Esan that, when patient's CD4 count decreases prevalence of leucopenia and lymphopenia increases [25]. In supporting the findings in this study, may be due to suppression of bone marrow and direct infection of T cells. This condition reduces the body's resistance to many opportunistic infections and the patient becomes more susceptible to other infections, this condition may become life-threatening due to low immunity [26].

Conclusion

Low erythropoietin (EPO) level reported in this study among HIV subjects compared to control subjects confirmed that there is an inappropriate EPO response to anaemia in HIV infected patients causing decrease and ineffective production of red blood cells (RBC). Improvements observed in virological, immunological and haematological parameters on ART subjects suggested that there is positive response to antiretroviral therapy despite the reported side effects. However, drug compliance should be ensuring among HIV-infected patients to prevent HIV-virus resistance to drugs. This study also provides alternative surrogate maker for monitoring progression of HIV/AIDS disease.

References

1. Ugbeni OC and Eruotor OH (2018) Profile of Micronutrients, Electrolytes, Haematology and CD4 Count in HIV Infected Subjects on Highly Active Antiretroviral Therapy. Trop J Nat Prod Res 2(1): 42-46.

2. Margaret CA, Ani A, Attah DI, Mora M (2018) Comparison of viral load and CD4 values of ARV naive and ARV challenged HIV patients in Taraba State Nigeria. Virology 9(3): 55-56.

3. Germanaud D, Derache A, Traore M, Madec Y, Toure S, et al. (2010) Level of viral load and antiretroviral resistance after 6 months of non-nucleoside reverse transcriptase inhibitor first-line treatment in HIV-1-infected children in Mali. J Antimicrob Chemother 65(1): 118-124.

4. Denue BA, Yusuf I, Bello HS, Abja AU, Bukar AA (2013) Changes in blood profile of human immunodeficiency virus (HIV)-infected patients on highly active antiretroviral therapy (HAART) in North Eastern Nigeria. Academic Journals of AIDS and HIV Research 5(8): 284-291.

5. Kellie NS, Robbie BM, Paolo AP, Fischer W, Bette TK, et al. (2016) Effective Cytotoxic T Lymphocyte Targeting of Persistent HIV-1 during Antiretroviral Therapy Requires Priming of Naive CD8 T Cells. mBio 7(3): 473-516.

6. Trickey A, May MT, Schommers P, Tate J, Ingle SM, et al. (2017) CD4:CD8 Ratio and CD8 Count as Prognostic Markers for Mortality in Human Immunodeficiency Virus–Infected Patients on Antiretroviral Therapy: The Antiretroviral Therapy Cohort Collaboration (ART-CC). Clin Infect Dis 65(6): 959-966.

7. Villar SS, Sainz T, Lee SA, Hunt PW, Sinclair E, et al. (2014) HIV-Infected Individuals with Low CD4/CD8 Ratio despite Effective Antiretroviral Therapy Exhibit Altered T Cell Subsets, Heightened CD8+ T Cell Activation, and Increased Risk of Non-AIDS Morbidity and Mortality. PLoS Pathog 10(5): e1004078.

8. Krantz EM, Hullsiek KH, Okulicz JF, Weintrob AC, Agan BK, et al. (2011) Elevated CD8 counts during HAART are associated with HIV virologic treatment failure. J Acquir Immune Defic Syndr 57(5): 396-403.

9. Sauter R, Huang R, Ledergerber B, Battegay M, Bernasconi E, et al. (2016) CD4/CD8 ratio and CD8 counts predict CD4 response in HIV-1-infected drug naive and in

patients on cART. Medicine (Baltimore) 95(42): e5094.

10. Saracino A, Bruno G, Scudeller L, Volpe A, Caricato P, et al. (2014) Chronic inflammation in a long-term cohort of HIV-infected patients according to the normalization of CD4:CD8 ratio. BMC Infect Dis 30(12): 1178-1184.

11. Chong XL, Yu YL, Li PH, Jing K, Jin SB, et al. (2019) The predictive role of CD4+ cell count and CD4/CD8 ratio in immune reconstitution outcome among HIV/AIDS patients receiving antiretroviral therapy: an eight- year observation in China. BMC Immunol 20(1): 31.

12. Jianming T, Xuelin L, Matthew AP, Eduard JS, Omu A, et al. (2015) CD4:CD8 lymphocyte ratio as a quantitative measure of immunologic health in HIV-1 infection: findings from an African cohort with prospective data. Front Microbiol 6: 670.

13. Devi CS, Suchitha S, Gupta M (2016) A study of haematological profile in human immune deficiency virus infection: correlation with CD4 counts. Ann Pathol Lab Med 3: 484-489.

14. Mathews SE, Srivastava D, Balayadav R, Sharma A (2013) Association of hematological profile of human immunodeficiency virus-positive patients with clinicoimmunologic stages of the disease. J Lab Physicians 5(1): 34-37.

15. Sule A, Kishanrao R, Kinikar A, Valvi C, Rajput U, et al. (2018) Anaemia in HIV infected HAART naïve and HAART exposed children. International Journal of Contemporary Pediatrics 5(5): 1962-1965.

16. ALPCO (2018) Quantitative determination of erythropoietin in human serum by ELISA; Catalog Number: 21-EPOHU-E01 pp: 1-12.

17. Enawgaw B, Alem M, Addis Z, Melku M (2014) Determination of hematological and immunological parameters among HIV positive patients taking highly active antiretroviral treatment and treatment naive in the antiretroviral therapy clinic of Gondar University Hospital, Gondar, Northwest Ethiopia: a comparative cross-sectional study. BMC Hematol 14(1): 1-8.

18. Gedefaw L, Yemane T, Sahlemariam Z, Yilma D (2013) Anemia and Risk Factors in HAART Naıve and HAART Experienced HIV Positive Persons in South West Ethiopia: A Comparative Study. PLoS ONE **8**(8): e72202.

19. Okafor AO, Akwiwu EC, Akpotuzor JO (2019) Prevalence of Anaemia after Initiation of Antiretroviral Therapy among HIV-infected Patients Attending University of Calabar Teaching Hospital Calabar, Nigeria. International Journal of Tropical Disease and Health 35(1): 1-7.

20. Volberding P (2002) The impact of anaemia on quality of life in human immunodeficiency virus-infected patients. J Infect Dis 185(Suppl 2): 110-114.

21. Wiredu OK, Edzeamey FJ, Dompreh A, Awuah M, Ako AK, et al. (2018) Lymphocyte Subset (CD3, CD4 and CD8 Cells) and their Ratios in HIV patients on Highly Active Antiretroviral Therapy (HAART) and HAART Naïve Patients. Int J Microbiol Adv Immunol 6(2): 92-95.

22. Ferede G, Wondimeneh Y (2013) Prevalence and related factors of anemia in HAART-naive HIV positive patients at Gondar University Hospital, Northwest Ethiopia. BMC Hematol 13(8): 1-5.

23. Gatukui DK, Oyoo GO, Rajab J, Kayima J, Omonge E, et al. (2014) Serum erythropoietin in patients with anaemia on HAART attending the Kenyatta National Hospital, Comprehensive Care Centre. East African Journal of Pathology 1(1): 2-6.

24. Mocroft A, Phillips AN, Ledergerber B, Smith C, Bogner JR, et al. (2010) Estimated average annual rate of change of CD4 (+) T-cell counts in patients on combination antiretroviral therapy. Journal of Antiviral Therapy 15(4): 563-570.

25. Esan Ayodele J, Omisakin CT, Fasakin Kolawole, Oyedele Titilayo E, Oyegue Kelvin, et al. (2015). Assessment of Some Haematological and Immunological Parameters in HIV-infected Patients on HAART and HAART- Naïve in Ekiti State. British Journal of Advance Academic Research 4(1): 54-61.

26. Bashorun A, Nguku P, Kawu I, Ngige E, Ogundiran A, et al. (2014) A description of HIV prevalence trends in Nigeria from 2001 to 2010: what is the progress, where is the problem? Pan Afr Med J 18(Suppl 1): 1-3.