Original Research Article

Effects of Highly Active Antiretroviral Treatment on Complete Blood Count parameters

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ABSTRACT

Aim: This study assesses the effects of HAART on complete blood count parameters among HIV infected participants.
Study design: Case control study
Place and Methods: This study was conducted in Tamale, Ghana from August, 2015 to November 2017.
Methodology: A total of 300 HIV infected participants with ages ranging from 19–79 years, administered with HAART for at least 6 months were recruited. Pre-HAART administration (baseline) demographic and clinical information, with initial full blood count results were retrieved from the medical records of the participants. Post HAART administration blood sample (5mLs) was taken from each participant into an EDTA vacutainer tube and complete blood count (CBC) performed using URIT 5250 haematology analyser. Participants transfused with blood for the last 4 months were excluded from the study.
Results: The study recorded significant decreases in WBC and Neutrophil % post HAART administration. Lymphocyte (%), Haemoglobin, Haematocrit, MCV, MCHC, RDW-SD were all significantly higher post HAART administration. Total Platelets count, MPV, PDW-SD, PCT and P-LCR were significantly lower post-HAART administration. A comparison of the effects of EFV and NVP administered with AZT/3TC backbone yielded the following results. The NVP group recorded a significantly higher HCT compared with the EFV group (**p-0.0073).** A significantly higher mean PCT, MPV, P-LCR, PLCC, PDW-SD were recorded in the EFV group compared to the NVP group respectively.
Conclusion: The administration of HAART is associated with significant improvements in erythroid and lymphoid lineages, reduce anaemia, improves immunity and general patient well-being. NVP improve erythroid cell indices while EFV ameliorate platelet indices. HAART regimen should be chosen based on the pre-HAART laboratory tests conducted on the individual.

Keywords: Highly Active Antiretroviral Therapy, HIV infection, haematological abnormalities

1. INTRODUCTION

HIV infection results in severe systemic disorder, with characteristic impairment and progressive damage to both humoral and cellular immune responses [1]. Haematological abnormalities may be the first laboratory findings in HIV infection and may involve all cell lines and noted to be strong independent predictors of morbidity and mortality in HIV infected persons [2, 3]. Calis and colleagues reported a prevalence of 3-38% moderate anaemia (Hb 8.0-9.9g/dL) and 50-91% mild anaemia (Hb10.0-12.0g/dL) among people HIV infected individuals in tropical areas, which increases as the disease progresses and varies with age, gender and the definition used to establish anaemia [2]. The causes of anaemia in HIV infected individuals included decreased erythropoietin production, ineffective erythropoiesis, opportunistic infections, neoplasia and micronutrient deficiency [4]. Iron deficiency has also

been reported as the commonest cause of nutritional anaemia among HIV infected individuals [3]. The type of anaemia serves as a guide to the choice of HAART and treatment option for opportunistic infections. Neutropenia was reported in 10% more of HIV infected individual with advanced immunosuppression than in non-advanced HIV infected individuals [5, 6]. Asymptomatic thrombocytopenia was reported in 20%-33% of HIV infected individuals but increased with progression of the disease [6, 7].

Kibaru (3) reported that the use of zidovudine, lamivudine and stavudine was associated with significant amelioration in hemoglobin concentration and after 12 months of HAART use, the prevalence of anaemia reduced from 65.5 % to 46% [3]. In another study, after 3 months of HAART administration, Huang (8) documented significant increases in mean Hb from 13.9 to 14.1 g/dl [8]. Huang (8) reported improvements in mean cell volume (MCV) from 55 to 98.9fl to 105.5fl and 106fl at 3, 6, 9, 12 months respectively after HAART use [8].

The current regimens used in Ghana comprise two nucleotide reverse transcriptase inhibitors (NRTI) plus one nonnucleotide reverse transcriptase inhibitor (NNRTI) or two NRTI and one protease inhibitor (PI) [9]. The WHO recommends HAART for all HIV infected individuals since it improves morbidity and mortality associated with HIV infection, and offers better life expectancy [10, 11]. Despite the beneficial effects associated with HAART use, studies have shown that steps must be taken to prevent life threatening side effects and HAART related haematotoxicity [12]. In resource constrained developing countries, based on availability, safety and efficacy, the WHO has made efavirenz, tenofovir in addition to lamivudine or emtricitabine plus nevirapine as the preferred first line antiretroviral medications, though so much information is not available on HAART use in these areas [13]. Nevirapine remains the NNRTI of choice when efavirenz cannot be used. Better rates of HIV replication suppression is achieved in patients administered with efavirenz-based HAART who received tenofovir-emtricitabine compared with patients who received zidovudine-lamivudine [14]. In order to avoid the toxicities associated with Zidovudine use, especially in individuals with anaemia, global access to tenofovir has been increased [15]. Not many studies on the haematological parameters abnormalities in HIV infected persons have been conducted in sub Saharan Africa. This study examines the effect of HAART on complete blood count parameters.

2. MATERIAL AND METHODS / EXPERIMENTAL DETAILS / METHODOLOGY

Study Design

This was a cross sectional study carried out from 12th August 2016 to 21st December 2017.

Study population

A total of 300 HIV infected participants with ages ranging from 19 to 79years and have been on HAART for at least 6 months were recruited. Participants who have been transfused with blood for less than 4 months were excluded from the study.

Data Collection

Pre-HAART administration (baseline) information such as weight, systolic and diastolic blood pressure, age, date of HAART initiation and initial complete blood count results were retrieved from the medical records of the participants. Post HAART information such as age, weight, blood pressure measurement, HAART type and duration of HAART use were recorded using questionnaire which had been pre-tested among 10 HIV infected individuals administered with HAART to clear possible ambiguity and difficulty in answering the questions. Data from the pre-tested questionnaires were however not included in the results analysis.

Blood samples (5mLs) was taken into an EDTA vacutainer for Complete Blood Count (CBC) analysis. The CBC was performed using URIT 5250, a 5-part differential, 28 parameters

haematology analyser, from URIT Medical Electronic (group) Co., LTD, China, http://www.urit.com/index.aspx. The HAART comprised two Nucleotide Reverse Transcriptase Inhibitor (NRTI) plus one Nonnucleotide Reverse Transcriptase Inhibitor (NNRTI) or two NRTIs and a Protease Inhibitor (PI). The participants were further stratified into short term (<52 months), medium term (≥52 but ≤104months), long term (>104months) based on the duration of HAART.

Statistical analysis

Data was entered into Microsoft excel 2016 and exported to GraphPad prism version 6.0 (www.graphpad.com) for analysis. Data was presented as number, percentages, means and standard deviation. Means were compared between groups using student paired t-test and ANOVA and $p<0.05$ was considered statistically significant.

3. RESULTS AND DISCUSSION

Table 1 shows the demographic data of the study population. Out the 300 participants, majority (80.7%) were females, 176 (58.7%) were short-term HAART users, 96 (32%) were medium-term HAART users while 28 (9.3%) were long-term HAART users.

Table 1: Demographic characteristics of the study population

Variables	Pre-HAART (n=300)	Post-HAART (n=300)
Age (years)*	35.4 ± 9.4	**39.7 ± 10.0**
Weight (Kg)*	58.8 ± 12.8	**64.3 ± 25.6**
Age Group (years)		
10-19	10 (3.3%)	3 (1%)
20-29	76 (25.3%)	36 (12%)
30-39	125 (41.7%)	120 (40%)
40-49	64 (21.3%)	96 (32%)
50-59	20 (6.7)	34 (11.3%)
60-69	5 (1.7%)	13 (4.3%)
70-79	0	1 (0.3%)
Gender		
Male	58 (19.3%)	58 (19.3%)
Female	242 (80.7%)	242 (80.7%)
HAART Duration (Months)		
Short term	0	176 (58.7%)
Medium term	0	96 (32%)
Long term	0	28 (9.3%)

*Data are presented as frequencies and percentages, * - comparison between pre and post HAART administration, with p-value of paired t-test <0.001. P-values 0.05 were considered significant.*

Distribution of HAART in the Study Population

HAART regimen was distributed as follows, TDF+3TC+EFV (72%), AZT+3TC+NVP (13%), TDF+3TC+NVP (6.7%), TDF+3TC+LPV/r (6.7%), AZT+3TC+EFV (1%) and TDF+FTC+EFV (0.7%) regimen.

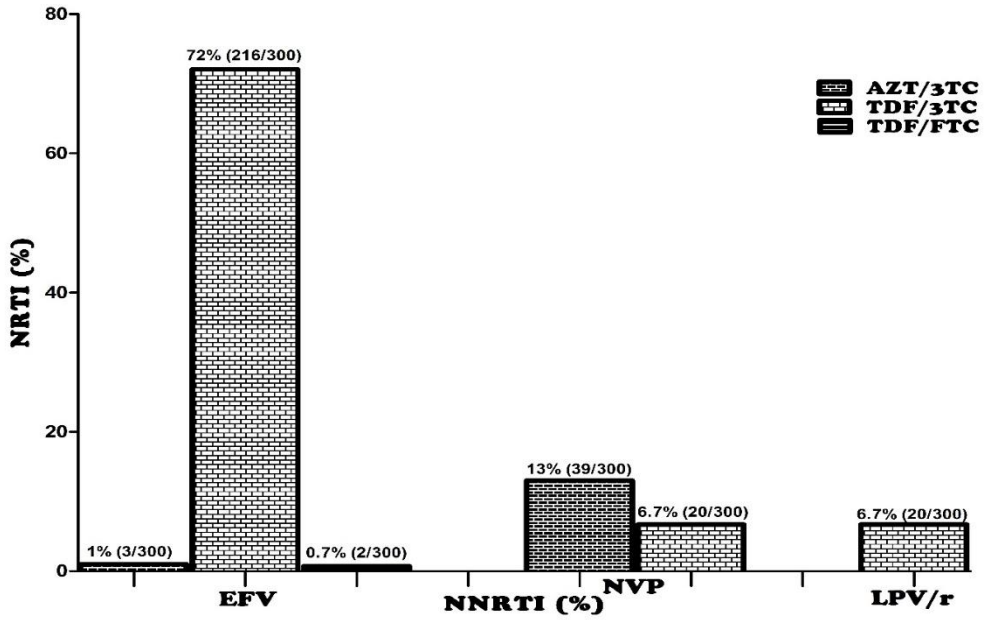

Figure 1 shows the percentage distribution of the various types of HAART regimen adminstered at the ART centers

Table 2 compared CBC parameters in the study population pre and post-HAART administration. WBC (%) 7.446±5.066 vrs 4.733±2.008, neutrophil (%) 51.52±18.37 vrs 44.26±14.46, basophils (%) 4.0±0.2 vrs 3.9±0.06 were significantly higher in pre-HAART administration while lymphocyte (%) 33.11±14.05 vrs 43.94±12.87 increased significantly post-HAART administration.

Haemoglobin (g/dL) 10.88±2.255 vrs 11.63±2.401, haematocrit (%) 32.75±6.239 vrs 34.85±6.932, MCV 81.96±10.77 vrs 88.0±12.96, MCHC 33.52±1.651 vrs 34.50±5.368, RDW-SD 44.26±11.78 vrs 68.69±42.64 were significantly higher post-HAART administration (Table 2).

Again, thrombocytopenia was significantly pronounced post-HAART administration, with PLT 284.7±148.1 vrs 254.4±145.7, MPV 9.028±1.773 vrs 6.840±1.601, PDW 14.55±6.180 vrs 8.881±4.37, PCT 0.260±0.140 vrs 0.169±0.085 and P–LCR 28.87±9.586 vrs 20.60±15.12 significantly decreased post-HAART administration (Table 2).

Table 2: Complete blood count tests parameters pre and post HAART administration

Parameters	Pre-HAART (n-300)	Post-HAART (n-300)	*P* – value
White blood cell count (10^9/L)	**7.5 ± 5.1**	4.7 ±2.0	**< .00**
Lymphocytes %	33.1 ± 14.1	**43.9 ± 12.9**	**< .00**
Monocytes %	10.0 ± 4.9	9.8 ± 5.7	.31
Neutrophils %	**51.5 ± 18.4**	44.3 ± 14.5	**.00**
Eosinophils %	**4.2 ± 3.7**	3.7 ± 3.4	.63
Basophils %	**0.4 ± 0.2**	0.08 ± 0.06	**.00**
Red Blood Cell Count (10^{12}/L)	4.0 ± 0.9	3.9 ± 0.7	.79
Haemoglobin (g/dL)	11.0 ± 2.6	**11.6 ± 2.4**	**.04**
Haematocrit (HCT, %)	32.8 ± 6.3	**34.9 ± 6.9**	**.01**
Mean Cell Volume (MCV, fL)	82.0 ± 10.8	**88.0 ± 13.0**	**.00**
Mean Cell Haemoglobin (MCH, pg)	29.4 ± 18.1	30.5 ± 5.3	.78
MCHC (g/dL)	33.5 ± 1.7	**34.5 ± 5.4**	**.03**
RDW-SD (fL)	44.3 ± 11.8	**68.7 ± 42.6**	**.00**

RDW-CV (%)	13.9 ± 4.9	15.7 ± 10.7	.13
Platelets (10^9/L)	**284.7 ± 148.1**	254.4 ± 145.7	**.00**
MPV (fL)	**9.0 ± 1.8**	6.8 ± 1.6	**< .00**
PDW (fL)	**14.6 ± 6.2**	8.9 ± 4.4	**< .00**
Platelet crit (PCT, %)	**0.3 ± 0.1**	0.2 ± 0.1	**< .00**
P–LCR (%)	**28.9 ± 9.6**	20.6 ± 15.1	**< .00**
P–LCC (10^9/L)	72.8 ± 45.7	48.4 ± 27.7	0.32

Data are presented as mean ± SD. Table shows paired t-test comparison of complete blood count parameters before and after HAART administration. P-values 0.05 were considered significant.

Table 3 shows the influence of duration of HAART usage on CBC parameters. Neutrophil (%) and basophils (%) decreased significantly ($p<0.05$) from short-term HAART users, medium-term through to long-term HAART users. The significant reduction in neutrophil (%) was from 46.36±14.26 in short-term HAART users to 39.53±15.13 in long-term HAART users while basophils (%) were from 0.065±0.049 to 0.053±0.032 to 0.002±0.001 in short-term, medium-term to long-term HAART users respectively.

However, lymphocytes (%), haemoglobin concentration, haematocrit, mean cell volume (MCV) and mean cell haemoglobin (MCH) increased significantly ($p<0.05$) with duration on HAART uses. Haemoglobin concentration increased significantly from 11.31±2.394, 12.25±2.172 and 12.93±7.352 in short-term, medium-term and in long-term HAART users respectively. While for lymphocytes, the significant increased were between 42.13±13.18 in short-term to 48.74±11.50 in long-term HAART users and from 46.03±12.04 in medium-term to 48.74±11.50 in long-term HAART users. For haematocrit, there was a significant increased between 33.93±5.945 in short-term to 36.49±8.026 in medium-term HAART users only but for MCV and MCH, significant increased were observed between short-term (86.56±13.02fL and 29.60±5.132ng) and median-term (91.20±12.43fL and 31.64±5.612ng) HAART users as well as short-term (86.56±13.02fL and 29.60±5.132ng) and long-term (92.25±14.67fL 33.04±5.172ng) and HAART users respectively.

Table 3 Complete Blood Count based on the duration of HAART usage

PARAMETER	DURATION OF HAART			F test	*P* - value
	Short-term n-176	Medium-term n-96	Long-term n-28		
White blood cell count (10^9/L)	4.7 ± 1.6	4.5 ± 1.7	4.9 ± 2.0	0.8	.46
Lymphocytes %	42.1 ± 13.2	46.0 ± 12.0$^+$	48.7 ± 11.5*	5.1	**.01**
Monocytes %	9.4 ± 5.5	10.7 ± 6.4	10.7 ± 8.3	1.7	.18
Neutrophils %	46.4 ± 14.3	41.7 ± 14.0	39.5 ± 15.1*	5.0	**.01**
Eosinophils %	3.4±2.8	3.4 ± 2.6	3.0±2.8	0.1	.91
Basophils %	0.07 ± 0.05$^@$	0.05 ± 0.03$^+$	0.002 ± 0.001*	11.4	**< .00**
Red Blood Cell Count (10^{12}/L)	4.0 ± 0.7	4.0 ± 0.6	3.748 ± 0.7	1.2	.29
Haemoglobin (g/dL)	11.3 ± 2.4$^@$	12.3 ± 2.2$^+$	12.9 ± 7.4*	4.9	**.01**
Haematocrit (HCT, %)	33.9 ± 6.0$^@$	36.5 ± 8.0	35.6 ± 8.1	4.5	**.01**
Mean Cell Volume (MCV, fL)	86.6 ± 13.0$^@$	91.2 ± 12.4	92.3 ± 14.7*	5.2	**.01**
Mean Cell Haemoglobin (MCH, pg)	29.6 ± 5.1$^@$	31.6 ± 5.6	33.0 ± 5.2*	7.9	**.00**
MCHC (g/dL)	34.4 ± 6.0	34.8 ± 4.8	35.0 ± 3.7	0.3	.76
RDW-SD (fL)	65.7 ± 13.4	66.9 ± 12.6	68.9 ± 11.8	0.8	.46
RDW-CV (%)	14.7 ± 5.1	14.2 ± 2.8	15.4 ± 7.1	0.5	.78
Platelets (10^9/L)	251.1 ± 102.9	254.8 ± 213.4	227.8 ± 82.2	0.5	.61

MPV (fL)	6.9 ± 1.6	6.8 ± 1.7	6.8 ± 1.7	0.3	.72
PDW (fL)	9.0 ± 4.5	8.8 ± 4.5	8.0 ± 2.7	0.7	.52
Platelet crit (PCT, %)	0.2 ± 0.1	0.19 ± 0.13	0.16 ± 0.07	0.5	.61
P –LCR (%)	20.3 ± 9.5	19.2 ± 8.2	21.2 ± 9.4	0.7	.49
P –LCC (10^9/L)	50.6 ± 30.1	44.4 ± 22.2	47.8 ± 26.3	1.6	.20

*Data presented as mean ± SD. Shows One-way anova comparison of Complete Blood Count parameters in short, medium and long-term HAART users. @ - comparison between short and medium term, * - comparison between short and long term, + - comparison between medium and long term HAART users. P-values 0.05 were considered significant.*

Table 4 considered the effects of EFV and NVP administered with a common backbone AZT/3TC. Haematocrit 32.50±5.328 vrs 33.87±5.559 was significantly higher in the NVP group compared with EFV group. However, PCT 0.263±0.124 vrs 0.158±0.062, MPV 8.667±1.290 vrs 6.479±1.502, P-LCR 34.70±9.930 vrs 17.32±8.894, P-LCC 111.0±78.89 vrs 41.64±21.54 and PDW-S 12.97±3.083 vrs 7.567±2.255 were significantly higher in the EFV group compared with the NVP group. The EFV group had a more favourable effect on platelet indices compared with the NVP group. Comparatively, there were no significant variations in the effects of EFV, LPV/r and NVP administered with a TDF/3TC back bone on CBC parameters

175 ***Table 4 Effects of EFV, NVP and LPV/r with common backbones (AZT/3TC and TDF/3TC)***

	AZT/3TC BACKBONE			TDF/3TC BACKBONE			
PARAMETER	**EFV GOURP**	**NVP GROUP**	***P* - value**	**EFV GROUP**	**LPV/r GROUP**	**NVP GROUP**	***P* - value**
White blood cell count (10^9/L)	3.9±1.6	4.6±1.4	.38	4.7±1.7	5.2±2.5	5.1±4.3	.39
Lymphocytes %	35.5±27.0	45.8±13.5	.24	43.8±12.9	44.1±11.3	43.7±10.4	.99
Monocytes %	2.7±1.9	3.6±2.7	.59	3.8±3.7	1.7±0.9	3.7±1.9	.28
Neutrophils %	0.07±0.02	0.06±0.03	.66	0.06±0.04	0.05±0.02	0.08±0.06	.43
Eosinophils %	8.9±2.0	10.1±6.2	.73	9.5±5.2	10.9±7.7	10.8±7.3	.39
Basophils %	55.3±25.7	41.8±17.1	.21	44.6±14.0	43.4±13.1	44.1±13.0	.93
Red Blood Cell Count (10^{12}/L)	3.5±0.3	3.5±0.7	.98	4.0±0.7	4.0±0.7	4.01±0.6	.97
Haemoglobin (g/dL)	10.5±2.4	11.8±2.08	.33	11.6±2.4	11.86±2.5	11.4±3.5	.86
Haematocrit (HCT, %)	32.5±5.3	**33.9±5.6**	**.01**	34.6±5.7	34.9±7.5	39.8±15.45	.01
Mean Cell Volume (MCV, fL)	92.6±13.5	97.4±13.6	.55	87.0±12.1	87.0±13.9	92.0±13.3	.22
Mean Cell Haemoglobin (MCH, pg)	30.1±6.6	34.3±5.4	.21	29.9±4.8	29.4±4.3	31.4±8.1	.39
MCHC (g/dL)	32.1±2.7	35.2±3.7	.17	34.5±5.5	33.6±4.4	33.8±7.8	.68
RDW-SD (fL)	71.9±9.8	72.9±13.9	.90	68.7±49.7	64.7±11.9	65.2±12.2	.89
Platelets (10^9/L)	321.3±182.0	242.9±71.6	.11	254.4±161.9	267.3±112.5	247.1±112.5	.91
Platelet crit (PCT, %)	**0.3±0.1**	0.2±0.1	**.01**	0.17±0.09	0.2±0.1	0.2±0.1	.51
MPV (fL)	**8.7±1.3**	6.5±1.5	**.02**	6.8±1.6	7.1±1.7	6.7±2.0	.75
P –LCR (%)	**34.7±9.9**	17.3±8.9	**.00**	21.0±17.0	21.7±8.3	18.8±6.9	.81
P –LCC (10^9/L)	**111.0±78.9**	41.6±21.5	**.00**	46.9±23.0	55.3±30.2	46.7±28.1	.33
PDW-S (fL)	**13.0±3.1**	7.5±2.3	**.00**	9.0±4.5	10.2±6.9	8.6±2.0	.46

176 *Data are presented as mean ± SD. Shows a comparison of the individual influences of EFV and NVP (with AZT/3TC backbone), EFV and LPV/r (with*
177 *TDC/3TC backbone) on Complete Blood Count parameters (CBC). P-values 0.05 were considered significant.*
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Results in Table 6 shows the effects of AZT and TDF administered with 3TC/EFV or 3TC/NVP. In comparing AZT with TDF (administered with 3TC/EFV), P-LCC 111.0±78.89 vrs 46.88±22.97 was significantly higher in the AZT group compared with the TDF group. In comparing the AZT group with TDF group (administered with 3TC/NVP), RBC 3.525±0.651 vrs 4.008±0.614 and HCT 33.87±5.559 vrs 39.80±15.48 were significantly higher in the TDF group compared with the AZT group. However, RDW-SD 33.87±5.559 vrs 39.80±15.48 was significantly higher in the AZT group compared with the TDF group.

Table 5 Comparison of the individual effects of AZT and TDF (administered with 3TC/EFV and 3TC/NVP) on Complete Blood Count parameters

	3TC/EFV			3TC/NVP		
PARAMETER	**AZT**	**TDF**	***P* = value**	**AZT**	**TDF**	***P* = value**
WBC	3.9±1.6	4.7±1.7	.42	4.6±1.4	5.1±4.3	.52
Lymphocyte (%)	35.5±27.0	43.8±12.9	.28	45.8±13.5	43.7±10.4	.55
Eosinophil (%)	2.7±1.9	3.8±3.7	.64	3.6±2.7	3.7±2.0	.94
Basophil (%)	0.07±0.03	0.06±0.04	.81	0.06±0.03	0.08±0.05	.22
Monocyte (%)	8.9±2.0	9.6±5.2	.83	10.1±6.2	10.8±7.3	.71
Neutrophil %	55.3±25.7	44.6±14.0	.20	41.8±17.1	44.1±13.0	.61
RBC	3.5±0.3	4.0±0.7	.20	3.5±0.7	**4.0±0.6**	**.01**
HBG	10.5±2.4	11.6±2.4	.42	11.8±2.1	11.4±3.5	.65
HCT	32.5±5.3	34.6±5.7	.53	33.9±5.6	**39.8±15.5**	**.04**
MCV	92.6±13.5	87.0±12.1	.43	97.4±13.6	92.0±13.3	.16
MCH	30.1±6.6	29.9±4.8	.93	34.3±5.4	31.4±8.1	.11
MCHC	32.1±2.7	34.5±5.5	.44	35.2±3.7	33.8±7.8	.36
RDW-CV	16.2±1.6	14.0±7.5	.61	13.9±3.5	14.4±3.0	.60
RDW-SD	71.9±9.8	68.7±49.7	.91	**72.9±13.9**	65.2±12.2	**.04**
PLT	321.3±182.0	254.4±161.9	.48	242.9±71.6	247.1±112.5	.85
PCT	0.3±0.1	0.2±0.1	.05	0.2±0.1	0.2±0.1	.33
MPV	8.7±1.3	6.8±1.6	.05	6.5±1.5	6.7±2.0	.57
P - LCR	34.7±9.9	21.0±17.0	.17	17.3±8.9	18.8±6.9	.52
P - LCC	**111.0±78.9**	46.9±23.0	**< .00**	41.6±21.5	46.7±28.1	.45
PDW-S	13.0±3.1	9.0±4.5	.12	7.6±2.3	8.6±2.0	.10

Shows a comparison of the effects of AZT and TDF (administered with 3TC/EFV and 3TC/NVP) on Complete Blood Count. Data are presented as mean ± SD. P = values 0.05 were considered significant.

Discussion

The findings in this study show that, the percentage of short, medium and long-term HAART users increased gradually from 9.3% in long-term HAART users through 32.0% in medium-term HAART users to 58.7% in short-term users. This reflects a gradual increase in the number of individuals enrolled on HAART. This shows that more HIV infected individuals are being recruited unto HAART. This results are in agreement with the findings of Atuyambe (16) and Nii-Trebi (15) who also recorded an increased number of HIV infected individuals on HAART.

The mean duration of HAART is denoted by the mean difference between Post HAART age and pre-HAART age. The participants have been on HAART for a long duration as the post-HAART age is significantly higher than the pre-HAART age. This shows that the participants have been on HAART long enough for HAART to elicit its effect on CBC parameters.

There was a significant increase in the body weight of the study population post HAART administration. This indicates an improvement in the general health status of the individuals or the absence of frequent illness in the study population as a result of immune restoration

indicated by improvement in lymphocyte count. Guillén (17) and [18] reported increases in the body weight of people living with HIV post HAART administration.

The study found significant decline in total WBC post HAART administration and a consistent decline in neutrophil and basophil counts from short-term through to long-term among post HAART users post HAART administration. This indicates gradual development of severe leucopenia with time. Other studies also found leucopenia in HIV infected individuals who commenced HAART [19-21]. Leucopenia may be largely due to neutropenia caused by HIV suppression of the bone marrow, leading to ineffective granulopoiesis [21, 22]. Kimura (22) observed neutropenia may also be caused by the presence of antigranulocyte antibodies which attack and destroy granulocytes. Many of the HAART drugs are considered as myeloid suppressive, especially Zidovudin, hence should be reviewed for patients who already have cytopenias [23]. The leucopenia in the present study may possibly be due to the presence of inflammation in the tissues as a result of exposure to the drug. There is direct leucopenic inhibitory effect on matured granulocytes in the peripheral system or on the myeloid progenitor cells in the bone marrow. Consolini (5) reported leucopenia after six months of AZT based HAART [5, 24, 25]. However, the findings of this study contradicted the findings of [3] Kibaru and his colleagues who did not record leucopenia post HAART administration [3].

Lymphocyte count post HAART administration increased significantly in a time dependent manner. This is accounted for by the sturdy state equilibrium in favour of endogenous cell provisions over virus mediated cell killing. In the tap and drain model proposed by Wei (26), decreased viral killing of lymphocytes quickly turn the balance in favour of lymphocyte production and survival which allows at least partial immune reconstitution to occur. This signifies a shrinkage in the myeloid lineage in the favour of the lymphoid lineage [27]. Many other studies also found an increase in lymphoid tissue activity after HAART administration [28-30]. Studies suggest that, the observed increase in lymphoid activity was a response from the immune system following HAART administration [28-30].

This study also recorded significant improvements in erythroid cell line and indices. HGB, HCT, MCV and RDW-SD were significantly higher post HAART administration in a time dependent manner. The present study findings are consistent with studies by [4] and [31] who also found increases in red cell indices post-HAART administration. These findings are also consistent with the findings of Ogunbusuyi (32) who reported the prevalence of anaemia as higher in treatment naïve patients compared with those on HAART. Other studies reported a decline in the erythroid lineage due to the toxic effect of medications on the bone marrow, nutritional deficiency especially B12, iron deficiency, decreased erythropoietin release, gastrointestinal bleeding, malabsorption, autoimmune antibodies to haemopoietic precursors etc [33] while other studies attribute the increased incidence of anaemia to the direct effect of HIV on bone marrow stroma as a prelude to bone marrow failure [23].

Thrombocytopenia was recorded as an early haematological abnormality in HIV infected individuals in sub-Saharan Africa [19]. The incidence of thrombocytopenia post HAART administration in this study was significant. This finding is consistent with the findings of Akinbami (23) who also recorded higher incidence of thrombocytopenia post HAART administration. The possible explanation may be due to increased platelet destruction by the deposition of immune complexes on platelets and decreased platelet production, which results in decreased MPV and plateletcrit [27]. Thrombocytopenia is also a consequence of HIV's direct infection and destruction of megakaryocytes [34]. Amegor (27) reported that thrombocytopenia increased as immunological incompetence of the participants worsens. The presence of anti-platelet antibodies which leads to an increased destruction of platelets has also been hypothesized [4]. However, the results of this study is not in line with the findings of a study conducted in Kenya which recorded a decrease in thrombocytopenia from 20% to 6.5% after 6 months of ART [3, 35].

The predominant HAART regimen in this study was the TDF+3TC+EFV which is the WHO recommended alternate first line HAART regimen in some resource limited areas [36, 37]. Majority, (72%) of the study population were on TDF+3TC+EFV, 13% were on AZT+3TC+NVP (which is the standard WHO recommended first line HAART regimen in resource limited settings), while 6.7% were on TDF+3TC+NVP which is also an alternate first line regimen [36, 37]. TDF+3TC+LPV/r was the commonest second line HAART regimen recorded in this study. This implies that 6.7% of the HIV infected individuals experienced treatment failure and have switched to a second line therapy. Also, 0.7% of the study population were administered with TDF/FTC/EFV, which is an alternate first line HAART regimen in resource rich areas. According to the WHO guidelines on HAART issued in 2003, the formulation of first line HAART includes the combination of AZT/3TC plus stavudine (d4T) or NVP or EFV [37]. In 2006, this recommendation was revised to include TDF or ABC as alternative first-line NRTIs while encouraging health care givers not to include (d4T) base combinations in order to minimize its possible accumulation in the mitochondria leading to d4T associated complications [36]. Majority of the regimen in this study included AZT, 3TC and either EFV or NVP or LPV/r.

Comparison of lymphocyte values in NVP and EFV groups showed higher counts in the NVP group compared with the EFV group. These findings are consistent with findings of a Kenyan study which recorded higher lymphocyte values in NVP group compared to the EFV group [38]. The higher lymphocyte count signifies restoration of immunity following HAART administration. Comparison of AZT and TDF, both administered with a 3TC/NVP shows that RBC and HCT were both higher in the TDF group. AZT/3TC/NVP had better result on erythroid cell indices compared to AZT/3TC/EFV. The worst decrease in both erythroid and myeloid cell lines were recorded in the AZT/3TC/EFV. This demonstrated the compensatory effect of NVP over AZT when administered together, and showed AZT's toxicity on progenitor cells in the bone marrow stroma [23]**.** This was consistent with a study by Hema, 2011 who also found NVP more favourable to erythroid cell indices compared with AZT or EFV.

The AZT/3TC/EFV group recorded the highest platelet large cell count (PLCC). This shows increased variation in the sizes of thrombocytes. This corroborates with the findings of a study conducted by Munyazesa (19) in sub-saharan Africa who found increased variation in platelet sizes post HAART administration. From the findings of this study, a comparison of EFV and NPV administered with AZT/3TC backbone showed that EFV improved platelet indices as opposed to NVP which did not improve platelet indices. This may probably be the reason why the 2013 WHO HIV treatment guidelines recommended EFV as the first line choice of NNRTIs (http://www.who.int/hiv/pub/guidelines/arv2013). Thrombocytic indices; PLT, PCT, MPV, PLCR, P-LCC and PDW-S were all higher in the EFV group compared with the NVP group. The results of this study show that EFV has an ameliorative influence on platelet indices compared to NVP.

There was no significant difference in the effect of AZT and TDF administered with 3TC/EFV on complete blood count parameters. A comparison of AZT and TDF administered with 3TC/NVP shows a more positive influence on erythroid cell lines in the TDF group compared with the AZT group. Again, this study TDF/FTC/EFV which is the gold standard first line regimen in resource rich area had the best effect on platelet indices [36].

CONCLUSION AND RECOMMENDATION

In conclusion, the administration of HAART is associated with significant improvements in erythroid and lymphoid lines, which reduces anaemia, improves immunity and general patient well-being. Cumulatively, NVP has a much more significant improvement on erythroid cell indices while EFV significantly improves ameliorated platelet indices. As found in this study, NVP favoured lymphoid lineage growth compared with EFV. TDF favoured RBC indices compared with AZT and EFV improved platelet indices as opposed to NVP which did

not improve platelet indices**.** AZT/3TC/NVP, TDF/3TC/LPV/r, TDF/3TC/NVP should be considered for improvement in erythroid cell indices. AZT/3TC/EFV and TDF/FTC/EFV should be considered in clients with thrombocytopenia. This makes HAART a suitable choice over its side effects in the management of people living with HIV to prevent the development of AIDS especially when started early. This study therefore provides basic information to encourage health workers to intensify the effectiveness of HAART campaign to get HIV infected individuals to initiate HAART early. Also, ART should be chosen base on the results of the initial laboratory tests conducted on the patient.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

Consent

Written informed consent was obtained from all participants for publication of this case control study. A copy of the written consent is available for review by the Editorial office of your journal.

Ethical considerations

This study was approved by the Committee for Human Publication and Research Ethics of the Kwame Nkrumah University of Science and Technology, Kumasi Ghana. Written informed consent was obtained from all participants before recruiting them into the study. Consent form was given to each participant to sign or thumb-print and confidentiality was assured.

References

1. Brenchley JM, Price DA, Schacker TW, Asher TE, Silvestri G, Rao S, et al. Microbial translocation is a cause of systemic immune activation in chronic HIV infection. Nature medicine. 2006;12(12):1365.
2. Calis JC, van Hensbroek MB, de Haan RJ, Moons P, Brabin BJ, Bates I. HIV-associated anemia in children: a systematic review from a global perspective. Aids. 2008;22(10):1099-112.
3. Kibaru EG, Nduati R, Wamalwa D, Kariuki N. Impact of highly active antiretroviral therapy on hematological indices among HIV-1 infected children at Kenyatta National Hospital-Kenya: retrospective study. AIDS research and therapy. 2015;12(1):26.
4. Thulasi RR, Manimaran D, Hemanathan G, Afroz T, Sagar R. Hematological abnormalities in HIV infected individuals in correlation to CD4 counts and art status. Asian Journal of Medical Sciences. 2016;7(4):14-8.
5. Consolini R, Bencivelli W, Legitimo A, Galli L, Tovo P, Gabiano C, et al. A pre-HAART follow-up study of the hematologic manifestations in children with perinatal HIV-1 infection: suggestions for reclassification of clinical staging. Journal of pediatric hematology/oncology. 2007;29(6):376-83.

6. Adetifa I, Temiye E, Akinsulie A, Ezeaka V, Iroha E. Haematological abnormalities associated with paediatric HIV/AIDS in Lagos. Annals of tropical paediatrics. 2006;26(2):121-5.
7. Karpatkin S, Nardi M, Green D. Platelet and coagulation defects associated with HIV-1-infection. Thrombosis and haemostasis. 2002;87(03):389-401.
8. Huang SS, Barbour JD, Deeks SG, Huang JS, Grant RM, Ng VL, et al. Reversal of human immunodeficiency virus type 1-associated hematosuppression by effective antiretroviral therapy. Clinical infectious diseases. 2000;30(3):504-10.
9. Daugas E, Rougier J-P, Hill G. HAART-related nephropathies in HIV-infected patients. Kidney international. 2005;67(2):393-403.
10. Aboulafia DM, Bundow D, Waide S, Bennet C, Kerr D. Initial observations on the efficacy of highly active antiretroviral therapy in the treatment of HIV-associated autoimmune thrombocytopenia. The American journal of the medical sciences. 2000;320(2):117-23.
11. Ajayi A, Ajayi E, Fasakin K. CD4+ T-Lymphocytes cell counts in adults with human immunodeficiency virus infection at the medical department of a tertiary health institution in Nigeria. Annals of African medicine. 2009;8(4).
12. Nubila T, Ukaejiofo EO, Nubila NI, Okorie GI. Examination of haematotoxicity of fixed-dose highly active antiretroviral drug in albino wistar rats. ISRN pharmacology. 2012;2012.
13. WHO. Consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection: recommendations for a public health approach: World Health Organization; 2016.
14. Darin K, Scarsi K, Meloni S, Rawizza H, Chang C, Chaplin B, et al., editors. Clinical and virologic outcomes of six first-line regimens in a large ART program in Nigeria. XVIII International AIDS Conference: Abstract no THPE01172010; 2010.
15. Nii-Trebi NI, Ibe S, Barnor JS, Ishikawa K, Brandful JA, Ofori SB, et al. HIV-1 drug-resistance surveillance among treatment-experienced and-naive patients after the implementation of antiretroviral therapy in Ghana. PLoS One. 2013;8(8):e71972.
16. Atuyambe L, Neema S, Otolok-Tanga E, Wamuyu-Maina G, Kasasa S, Wabwire-Mangen F. The effects of enhanced access to antiretroviral therapy: a qualitative study of community perceptions in Kampala city, Uganda. African health sciences. 2008;8(1):13.
17. Guillén S, Ramos JT, Resino R, Bellón JM, Muñoz MA. Impact on weight and height with the use of HAART in HIV-infected children. The Pediatric infectious disease journal. 2007;26(4):334-8.
18. Newell M-L, Borja M-C, Peckham C. Height, weight, and growth in children born to mothers with HIV-1 infection in Europe. Pediatrics. 2003;111(1):e52-60.
19. Munyazesa E, Emile I, Mutimura E, Hoover DR, Shi Q, McGinn AP, et al. Assessment of haematological parameters in HIV-infected and uninfected Rwandan women: a cross-sectional study. BMJ open. 2012;2(6):e001600.
20. Mugisha JO, Shafer LA, Paal D, Van L, Mayanja BN, Eotu H, et al. Anaemia in a rural Ugandan HIV cohort: prevalence at enrolment, incidence, diagnosis and associated factors. Tropical medicine & international health. 2008;13(6):788-94.
21. Firnhaber C, Smeaton L, Saukila N, Flanigan T, Gangakhedkar R, Kumwenda J, et al. Comparisons of anemia, thrombocytopenia, and neutropenia at initiation of HIV

antiretroviral therapy in Africa, Asia, and the Americas. International Journal of Infectious Diseases. 2010;14(12):e1088-e92.
22. Kimura S, Matsuda J, Ikematsu S, Miyazono K, Ito A, Nakahata T, et al. Efficacy of recombinant human granulocyte colony-stimulating factor on neutropenia in patients with AIDS. AIDS (London, England). 1990;4(12):1251-5.
23. Akinbami A, Oshinaike O, Adeyemo T, Adediran A, Dosunmu O, Dada M, et al. Hematologic Abnormalities in Treatment-naïve HIV patients. Infectious Diseases: Research and Treatment. 2010;3:IDRT. S6033.
24. Gallicchio V, Hughes N, Tse K. Prevention of hematopoietic myeloid and megakaryocyte toxicity associated with zidovudine in vivo in mice with recombinant GM-CSF. Growth regulation. 1994;4(2):41-7.
25. Ukoha UU, Umeasalugo KE, Dimkpa U, Ndukwe G, Anyabolu AE, Emefo LE. Effects of zidovudine on hemostatic and hematologic parameters in adult rats. J Exp Integr Med. 2015;5(2):85.
26. Wei X, Ghosh SK, Taylor ME, Johnson VA, Emini EA, Deutsch P, et al. Viral dynamics in human immunodeficiency virus type 1 infection. Nature. 1995;373(6510):117.
27. Amegor O, Bigila D, Oyesola O, Oyesola T, Buseni S. Hematological changes in HIV patients placed on anti retroviral therapy in markurdi, Benue State of Nigeria. Asian J Epidemiol. 2009;2:97-103.
28. Baker J, Peng G, Rapkin J, Abrams D, Silverberg M, Cavert W, et al., editors. HIV-related immune suppression after ART predicts risk of nonopportunistic diseases: results from the FIRST Study. 14th Conference on Retroviruses and Opportunistic Infections; 2007.
29. Grossman Z, Herberman RB. T-cell homeostasis in HIV infection is neither failing nor blind: modified cell counts reflect an adaptive response of the host. Nature medicine. 1997;3(5):486.
30. Mohri H, Bonhoeffer S, Monard S, Perelson AS, Ho DD. Rapid turnover of T lymphocytes in SIV-infected rhesus macaques. Science. 1998;279(5354):1223-7.
31. Sullivan PS, Hanson DL, Chu SY, Jones JL, Ward JW, Group AASoD. Epidemiology of anemia in human immunodeficiency virus (HIV)-infected persons: results from the multistate adult and adolescent spectrum of HIV disease surveillance project. Blood. 1998;91(1):301-8.
32. Ogunbusuyi B, ESAN AYODELE. J;1 OMISAKIN C. T;1 FASAKIN, Kolawole, OYEDELE Titilayo E, OYEGUE KELVIN OGUNBUSUYI, Bolawatife. 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. 2015;4(1):54-61.
33. Schmaier AH, Lazarus HM. Concise guide to hematology: John Wiley & Sons; 2011.
34. Kasturi A, Sanjeevan S, Kar P. A study of hematological manifestations of HIV infection. Indian Journal of Sexually Transmitted Diseases. 2006;27(1):9.
35. Enawgaw B, Alem M, Addis Z, Melku M. Determination of hematological and immunological parameters among HIV positive patients taking highly active antiretroviral treatment and treatment naïve in the antiretroviral therapy clinic of Gondar University Hospital, Gondar, Northwest Ethiopia: a comparative cross-sectional study. BMC hematology. 2014;14(1):8.

36. Wester CW, Bussmann H, Koethe J, Moffat C, Vermund S, Essex M, et al. Adult combination antiretroviral therapy in sub-Saharan Africa: lessons from Botswana and future challenges. HIV therapy. 2009;3(5):501-26.
37. WHO U. Treating 3 million by 2005. Making it happen The WHO strategy Geneva: WHO, UNAIDS. 2003.
38. Naluande PK. A Comparison of Effectiveness of Efavirenz and Nevirapine-Based First-Line HIV Treatment in Patients Attending Coast Provincial General Hospital, Mombasa County, Kenya: Kenyatta University; 2017.

DEFINITIONS, ACRONYMS, ABBREVIATIONS

Short term HAART users = Participants who have been on HAART for less than or equal to 52 months.

Medium term HAART users = Participants who have been on HAART for more than 52 months but less than or equal to 104 months.

Long term HAART users = Participants who have been on HAART for more than 104 months.