



# **Haematological and Immunological Abnormalities in HIV-Infected Adults: A Comparative Study of ART-treated and ART-naive Patients in Kiambu County, Kenya**

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## **Authors' contributions**

*This work was carried out in collaboration among all authors. Author EWM conceptualized the idea, structured the study, collected the data, supervised the study, contributed to statistical interpretation, writing – review of the manuscript. Authors SKW and SE participated in its design and reviewed the manuscript. All authors read and approved the final manuscript.*

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## ABSTRACT

**Aims:** Globally, haematological and immunological abnormalities in HIV infection are associated with a higher risk of HIV disease progression, morbidity and mortality. This study aim was to assess the magnitude of haematological and immunological abnormalities in ART- treated and ART- naïve HIV infected adult patients and their comparative analysis.

**Study Design:** Cross – sectional study.

**Place and Duration of Study:** Thika Level Five Hospital Comprehensive Care Centre in Kiambu County, Kenya from July 2022 to December 2023.

**Methodology:** We enrolled 237 participants (122 males and 115 females) which comprised of 106 ART- treated, 51 ART- naïve and 80 HIV Sero-negative controls. Blood samples were collected using EDTA tubes to prevent clotting. Complete blood count (CBC) was performed using DYMIND DF-52 automated haematology analyser while CD4+ T (Cluster of Differentiation 4) cell counts determined using FACS Calibur system. Sociodemographic information and clinical characteristics were collected by use of a structured questionnaire and review of patient medical records. Comparative analysis was performed using an unpaired T-test with Welch's correction.

**Results:** Leucopenia was the most prevalent haematological abnormality followed by anemia and thrombocytopenia; 18.9%, 15.2% and 2.5% respectively. Prevalence of leucopenia, anemia and thrombocytopenia were higher in ART- treated than in ART- naïve. The mean  $\pm$  SD of PLT, ALC, HB, MCV, MCH, PCV of ART- treated was significantly higher than mean  $\pm$  SD of ART- naïve ( $p < 0.05$ ). The mean  $\pm$  SD CD4 count of ART- treated was higher compared to mean of ART- naïve but not significantly different ( $p = 0.5045$ ).

**Conclusions:** HIV infected patients ought to be routinely monitored for haematological and immunological abnormalities followed by appropriate therapeutic interventions so as to improve quality of life, reduce morbidity and mortality. Kenyan ministry of health should devise new strategies and strengthen the existing programs that encourage earlier HIV testing and treatment so as to reduce the magnitude of the abnormalities in ART- naïve patients.

**Keywords:** HIV-infected; antiretroviral therapy; Cytopenias; Anaemia; Leucopenia; Thrombocytopenia; CD4 count.

## 1. INTRODUCTION

The human immunodeficiency virus (HIV) virus, a lentivirus, and a member of the retroviridae family of viruses is the cause of the HIV/AIDS epidemic [1] that infects cells and disrupts the immune system. It causes malignancies, opportunistic infections, secondary infections, immunological and haematological abnormalities [2].

As of 2023, there were about 39.9 million HIV-positive individuals in the world. More than half of cases worldwide are found in Sub-Saharan Africa [3]. Globally, more than 30.7 million people living with HIV (PLWHIV) were on antiretroviral therapy (ART) by 2023 [4]. Despite the improved access to ART, more than 630,000 global HIV-associated deaths were reported in 2023 with three in five deaths occurring in the African region [4]. Besides, Sub Saharan Africa (SSA) remains the most affected region by the pandemic where more than 20.8 million HIV-infected individuals, accounting for two thirds of the global HIV infections are found [3]. In Kenya, approximately 1,400,000 people were living with

HIV, 17,000 were newly infected and 21,000 had died due to HIV/AIDS by the end of 2023 [4]. HIV-associated comorbidities continue to be a concern, however starting ART significantly improves prognosis and longevity and lowers HIV transmission, even for HIV positive patients with advanced disease. [5].

The most prominent immunologic characteristic of HIV infection is increasing decline in Cluster of Differentiation 4 (CD4) T cells which consequently results to immunodeficiency [6]. The CD4 T cells are attacked by the HIV virus leading to their destruction. CD4 cells, known as T helper cells, are responsible for initiating the body's immune response against infectious agents and are a crucial part of the body's defenses. Declining CD4 T cells is the characteristic feature of HIV infection and prognosticates a person's susceptibility to opportunistic infections and other HIV associated complications [7-8].

Haematological abnormalities are said to be one of the most frequent HIV associated complications. These abnormalities affect nearly

every type of cell found in the bone marrow, which is demonstrated by low levels of red blood cells, white blood cells, neutrophils and platelets in the peripheral blood as well as clotting disorders [9]. These issues can lead to severe clinical outcomes, such as a higher rate of advancement of Acquired Immunodeficiency Syndrome (AIDS) and higher death rates due to anaemia. [10] along with higher likelihood of bacterial infections [11] and bleeding [12] due to decreased levels of granulocytes and platelets, respectively. Findings from a systematic literature review has documented that the prevalence of anaemia, leucopenia and thrombocytopenia vary according to geographical location. Anemia is more prevalent in HIV-infected individuals compared to thrombocytopenia or leucopenia, with rates varying between 1.3% and 95% based on the HIV/AIDS disease stage and how anemia is defined [10,13]. Thrombocytopenia can be detected in 3–40% of HIV infected individuals and may develop at any stage during the course of HIV infection. [14,15-17] while the prevalence of Leucopenia also varies widely, with rates ranging from 10% to 50%. [18,19,20].

In most developing countries like Kenya, haematological complications in HIV infected patients still remains a concern, greatly impacting the quality of life of the patients. Regular monitoring of the haematological and immunological parameters in HIV infected patients for early detection of the abnormalities is critical for prompt clinical interventions so as to reduce the HIV – related morbidity and mortality. Although studies have been conducted to evaluate the haematological and immunological abnormalities among HIV- infected patients especially in developed countries, published data on the magnitude of haematological and immunological abnormalities in both ART-treated and ART- naïve HIV- infected patients are scarce in our setting. Thus, the objectives of this study were: 1) To assess the magnitude of haematological and immunological abnormalities in both ART- treated and ART- naïve patients at Thika Level Five Comprehensive Care Centre in Kiambu County, Kenya and 2) To compare the magnitude of the haematological and immunological abnormalities between the ART-treated and ART- naïve patients.

## 2. MATERIALS AND METHODS

### 2.1 Study Site

This study was conducted at the HIV Comprehensive Care Centre (CCC) of Thika

Level Five Hospital (TL5H) in Kiambu County, Kenya. Thika Level Five Hospital is a county referral hospital located in Thika West District, Thika Municipality Division, Biashara sub-location along General Kago Road. The hospital has a 467-bed capacity and is situated in Thika, approximately 50 km north-east of Nairobi, in Central Province, Kenya. Kiambu County, the second most populous county after Nairobi, has a population of 2,417,735 and covers an area of 2,539 km<sup>2</sup>, with a population density of 952.4/km<sup>2</sup>. Thika Level Five Hospital serves as an inter-county referral facility for a wide catchment area, including Machakos, Kitui, Murang'a, and Nairobi. It is recognised as a Centre of Excellence, providing comprehensive HIV and Tuberculosis (TB) prevention, care, and treatment services, including HIV testing, care and treatment, prevention of mother-to-child transmission of HIV, and maternal and child health services. Besides, existing data shows that Kiambu County has an estimated 59,016 people living with HIV (PLWHIV), with an overall prevalence of 4.0%, with 2.1% prevalence in men and 5.9% in women. By 2018, approximately 34,417 adults and 1,972 children were on ART, with ART coverage of 61% and 82% for adults and children, respectively.

### 2.2 Study Design, Period, and Population

This was a cross-sectional study conducted from July 2022 to December 2023 at Thika Level Five Hospital Comprehensive Care Centre. The study population included all HIV-infected patients who visited and were newly diagnosed at the Thika Level Five Hospital CCC, as well as those already enrolled for treatment and care at the CCC during the study period and who met the eligibility criteria. The population was divided into ART-treated, ART-naïve and the HIV sero negative groups.

### 2.3 Eligibility Criteria

#### Inclusion Criteria:

- HIV-infected individuals
- Aged 18 years and above
- willing to give informed consent

#### Exclusion Criteria:

- HIV patients with severe concomitant diseases (e.g. TB, cancer)
- Patients with known haematological diseases/disorders

- Patients on medications other than cotrimoxazole prophylaxis
- Patients who had received a recent blood transfusion within three months
- Those taking vitamins and iron supplements at the time of enrolment,
- Pregnant women and lactating mothers
- Those not consenting to the study.

## 2.4 Sample Size

The sample size was calculated using a population proportional formula with a 95% confidence level, a 5% margin of error, a 16% prevalence of cytopenia from a previous study, a population size of 56,622 and a 15% non-response rate

Sample Size = 237 Subjects

## 2.5 Sampling Method

Simple random sampling.

## 2.6 Data Collection

### 2.6.1 Sociodemographic information and clinical characteristics

A pretested structured questionnaire as well as review of patient medical records were used to gather socio-demographic data and clinical characteristics of the study participants. This was done by a clinician at the ART clinic, two experienced laboratory technologists, and the principal investigator, who supervised the entire process.

### 2.6.2 Blood sample collection

After obtaining written informed consent from the participants, 4 mL Ethylenediaminetetraacetic Acid (EDTA)-anticoagulated venous blood samples were collected from each participant by the laboratory technologists. The tubes were gently inverted about six times to ensure proper mixing of the blood with the anticoagulant. This was used for complete blood count (CBC) analysis and CD4 cell counts.

### 2.6.3 Laboratory procedures

#### Haematological (Complete blood count) testing using the fully automated DYMIND DF-52 Haematology Analyzer:

**Principle:** This equipment conducts haematological analysis through several methods which include Impedance method for

Red Blood Cells (RBCs) and platelets (PLT) counting, cyanide free reagent for hemoglobin test and flow cytometry (FCM) + Tri-angle laser scatter method for White Blood Cells (WBCs) 5-part differential analysis and WBC counting.

#### Procedure for using DYMIND DF-52 Hematology Analyzer:

The appropriately labeled samples in EDTA tubes were properly mixed, the tube cap was carefully removed and the sample firmly held under the probe so as to aspirate the sample automatically for analysis. When the analysis is complete, the analyzer indicator returns to constantly-on green. Within 60 seconds, the result was obtained in a printed format. The analyser generated data on the WBCs including the 5-part differentials (neutrophils, lymphocytes, monocytes, basophils and eosinophils), RBCs, haemoglobin (HB) level, haematocrit (HCT), Mean Cell Volume (MCV), Mean Cell Haemoglobin (MCH), Mean Cell Haemoglobin Concentration (MCHC), Red Cell Distribution Width (RDW), platelet (PLT) counts, Mean Platelet Volume (MPV), Platelet Distribution Width, (PDW), Plateletcrit (PCT).

#### CD4 Count Analysis using the Becton Dickinson FACS Calibur system:

**Principle:** When whole blood is added to the reagent, the fluorochrome-labelled antibodies in the reagent bind specifically to lymphocyte surface antigens. During acquisition, the cells travel past the laser beam in the flow cell and scatter the laser light. The stained cells fluoresce. These scatter and fluorescence signals, detected by the instrument, provide information about the cell's size, internal complexity and relative fluorescence intensity.

#### Procedure of using the Becton Dickinson FACSCalibur System:

Sample information was entered at the Worklist view. Each sample tube was gently vortexed and placed in the rack according to the rack Manifest. On the FACSCalibur monitor, the assign rack icon was clicked and the rack number was assigned as per the rack number from the rack, then OK icon clicked. The RUN icon was clicked. On the machine, the HI and PRIME icon were clicked from the fluid control panel. The RUN and HI button were pressed. The tests were run and results imported. The rack was loaded with tubes containing 3ml of BD

FACS clean solution or 1:10 dilution of bleach and 3ml containing distilled water. RUN and HI were then pressed on the control panel so that the analyzer performs the cleaning procedure automatically. The fluid control was set to STNDBY. A tube containing no more than 1ml of distilled water was placed onto the SIP. The computer was turned off followed by turning off the analyzer.

## 2.7 Operational Definitions

Anaemia was defined and graded according to the World Health Organization (WHO) guidelines. For males, anaemia was defined as HB <13 g/dL (mild: 11.0–12.9 g/dL; moderate: 8.0–10.9 g/dL; severe: <8.0 g/dL). For females, anaemia was defined as HB <12.0 g/dL (mild: 11.0–11.9 g/dL; moderate: 8.0–10.9 g/dL; severe: <8.0 g/dL). Leucopenia was defined as leucocyte count <4.0 × 10<sup>3</sup>/μL, with 4–11 × 10<sup>3</sup>/μL considered normal and >11 × 10<sup>3</sup>/μL as leucocytosis. Neutropenia was defined as ANC <1.5 × 10<sup>3</sup>/μL. Lymphopenia was defined as ALC <1 × 10<sup>3</sup>/μL. Thrombocytopenia was defined as platelet count <150 × 10<sup>3</sup>/μL, further classified into mild (100–149 × 10<sup>3</sup>/μL), moderate (50–99 × 10<sup>3</sup>/μL), and severe (<50 × 10<sup>3</sup>/μL) categories. Types of anaemia were classified as normocytic (MCV 80–100 fL), microcytic (MCV <80 fL), macrocytic (MCV >100 fL), normochromic (MCH ≥27 pg), and hypochromic (MCH <27 pg). HIV-infected patients were classified into three groups based on CD4 counts: stage 1 (>500 cells/mm<sup>3</sup>), stage 2 (200–499 cells/mm<sup>3</sup>), and stage 3 (<200 cells/mm<sup>3</sup>) according to the Center for Disease Control and prevention (CDC) staging system.

## 2.8 Data Quality Control

To ensure data quality, laboratory Standard Operating Procedures (SOPs) were strictly followed during specimen collection and laboratory testing. Quality control for haematology analyzers and CD4 machines was checked daily by running the three levels of quality control samples that is low, normal and high before and during the analysis of the patient samples. To ensure validity of the data collection instruments, the questionnaire was reviewed by the principal investigator to ensure they were valid and was also pre-tested before the actual data collection. Routine quality control checks were performed according to manufacturer instructions. Data collectors were trained before the study, with regular supervision and follow-up

by the principal investigators. Data was checked daily for completeness and consistency.

## 2.9 Data Management and Statistical Analysis

The collected data were coded, cleaned, edited, and exported to GraphPad Prism version 10.2 for analysis. Descriptive statistics were performed and parametric variables were presented as mean ± SD and frequency (%). The results were then displayed in tables. Unpaired T – test with Welch’s correction were used to compare the haematological and immunological parameters between the ART-treated and ART-naïve patients. A P-value <0.05 was considered statistically significant with a confidence level of 95%.

## 3. RESULTS AND DISCUSSION

### 3.1 Sociodemographic and clinical Characteristics of the Study Participants

The sociodemographic and clinical characteristics of the study participants are presented in (Table 1). A total of 237 participants were enrolled in this study (122 males and 115 females). The study participants comprised of 106 ART-treated HIV-infected adults, 51 ART-naïve HIV-infected adults, and 80 HIV-seronegative adult controls. The participants included newly diagnosed HIV infected individuals prior to ART initiation or those who had been on ART treatment and care for at least six months at the Thika Level Five Hospital Comprehensive Care Center between July 2022 and December 2024. Out of the total 237 study participants 122 (51.48%) were males compared to 115 females (48.52%), with a male-to-female ratio of 1.06:1. The ages of the study participants ranged from 18 to 66 years, with majority of the participants (88.18%) being 50 years or younger. The predominant age group was 18-25 years (31.65%), and the age bracket of 66 years and above was the least (0.42%). Most of the study participants were single (57%), with 43.88% married, 6.33% were divorced, and only 4.22% were widowed. Majority of the participants (65.1%) had a normal Body Mass Index (BMI), while 3.36% were underweight, 28.18% overweight, and 3.36% obese.

The study participants were taking any of the five different ART regimens with majority of them (79.25%) being placed on),

Tenofovir/Lamivudine/Dolutegravir (TDF/3TC/DTG) regimen. Those who were on TDF- based ART regimens were more (90.57%) than those on Azidothymidine (AZT) – based regimens (8.49%) and Abacavir (ABC)- based regimens (0.94%). Most of the study participants (76.42%) were on ART treatment for more than 6 yrs.

**Table 1. Demographic characteristics of the study population**

Patient Factor		Number (n)	Percentage (%)
Gender (n = 237)	Male	122	51.48
	Female	115	48.52
Age group (Years) (n = 237)	18-25	75	31.65
	26-35	64	27.00
	36-45	53	22.36
	46-55	27	11.39
	56-65	17	7.17
	≥66	1	0.42
Marital status (n = 237)	Single	108	45.57
	Married	104	43.88
	Divorced	15	6.33
	Widowed	10	4.22
BMI (Kg/M <sup>2</sup> ) (HIV +ve only; n = 157)	<20	26	16.56
	21-25	84	53.50
	26-30	42	26.75
	>30	5	3.18
HAART regimen	AZT/3TC/ATV/r	7	6.60%
	TDF/3TC/DTG	84	79.25
	TDF/3TC/ATV/r	12	11.32%
	ABC/3TC/ATV/r	1	0.95%
	AZT/3TC/DTG	2	1.88%
HAART duration	6 months - 5 Yrs	25	23.58%
	6-10 Yrs	41	38.68%
	11-15 Yrs	33	31.13%
	16- 20 Yrs	7	6.60%

Abbreviations: AZT: Zidovudine; 3TC: Lamivudine; ATV/r: Atazanavir/Ritonavir; TDF: Tenofovir Disoproxil Fumarate; DTG: Dolutegravir; ABC: Abacavir; BMI: Body Mass Index; HAART: Highly Active Antiretroviral Therapy

**Table 2. Comparative analysis of Haematological and Immunological Parameters of ART – Treated and ART – Naïve Patients**

Parameter	ART-Treated	ART-Naïve	t (df)	P value
WBC (× 10 <sup>3</sup> /μL)	5.40±1.46	5.24±2.71	0.4843 (155)	0.628
RBC (× 10 <sup>3</sup> /μL)	5.05±0.61	4.80±1.13	1.407 (155)	0.161
PLT count (× 10 <sup>3</sup> /μL)	410.80±217.10	309.30±147.90	3.016 (155)	0.003
ANC (× 10 <sup>3</sup> /μL)	2.89±1.48	3.55±2.55	1.720 (66.26)	0.090
ALC (× 10 <sup>3</sup> /μL)	2.03±0.66	1.50±0.66	4.643 (98.57)	<0.0001
HB (g/dL)	13.96± 2.01	12.63±2.99	2.868 (72.41)	0.005
MCV (fL)	90.35±10.48	82.92±9.42	4.461 (109.0)	<0.0001
MCH (pg)	27.76±3.18	25.83±3.50	3.3290 (90.85)	0.001
PCV (%)	45.53±6.29	40.57±9.13	3.50 (73.62)	0.0008
AMC (× 10 <sup>3</sup> /μL)	0.41±0.13	0.43±0.32	0.4317 (58.43)	0.667
RDW-CV (%)	14.44±2.00	15.07±2.20	1.7390 (90.83)	0.085
CD <sub>4</sub> count (cells/μL)	378.50±317.7	348.50±256.90	0.6697 (108.4)	0.504

Abbreviations: WBC: White Blood Cell; RBC: Red Blood Cell; PLT: Platelet Count; ANC: Absolute Neutrophil Count; ALC: Absolute Leucocyte Count; HB: Hemoglobin; MCV: Mean Cell Volume; MCH: Mean Cell Hemoglobin; PCV: Packed Cell Volume; RDW-CV: Red Cell Distribution Width –Coefficient of Variation; CD<sub>4</sub> – Cluster of Differentiation 4

**Table 3. Magnitude of Haematological and Immunological Abnormalities in ART –Treated, ART –Naïve and Controls**

Parameter	Abnormality	ART-Treated	ART-Naïve	Control
		(n = 106) n (%)	(n = 51) n (%)	(n = 80) n (%)
WBC (x 10 <sup>3</sup> /µL)	Leukopenia (n= 45)	9(8.5%)	25(49.0%)	11(13.7%)
	Normal WBC (n = 189)	86(81.13%)	29(56.86%)	74(92.5%)
	Leukocytosis (n = 3)	1(0.94%)	2(3.92%)	0(0.00%)
RBC (x 10 <sup>3</sup> /µL)	Erythropenia (n = 9)	3(2.83%)	6(11.8%)	0(0.00%)
	Normal RBC (n = 218)	98(92.45%)	42(82.35%)	78(97.5%)
	Erythrocytosis (n= 10)	5(4.7%)	3(5.9%)	2(2.5%)
PLT (x 10 <sup>3</sup> /µL)	Thrombocytopenia (n = 6)	1(0.94%)	4(7.84%)	1(1.25%)
	Moderate thrombocytopenia (n = 3)	1(0.94%)	2(3.92%)	0 (0.00 %)
	Mild thrombocytopenia (n =3)	0 (0.00 %)	2(3.92%)	1(1.25%)
	Normal PLT (n =190)	77(72.64%)	43(84.31%)	70(87.5%)
Neutrophils (x 10 <sup>3</sup> /µL)	Thrombocytosis (n=41)	28(26.4%)	4(7.84%)	9(11.25%)
	Neutropenia (n= 29)	16(15.1%)	9(17.6%)	4(5%)
	Mild Neutropenia (n= 21)	12(11.3%)	7(13.72%)	2(2.5%)
	Moderate Neutropenia (n= 8)	4(3.77%)	2(3.92%)	2(2.5%)
	Normal neutrophil count (n=200)	88(83.01%)	37(72.54%)	75(93.75%)
Lymphocytes (x 10 <sup>3</sup> /µL)	Neutrophilic leukocytosis (n=8)	2(1.9%)	5(9.8%)	1.25%
	Lymphopenia (n=18)	4(3.8%)	23.6%	2(2.5%)
	Normal lymphocyte (n=218)	101(95.28)	39(76.47)	78(97.5%)
Monocytes	Lymphocytosis (n=1)	1(0.94%)	0(0.00%)	0(0.00%)
	Monocytopenia (n =12)	0 (0.00%)	7(13.7%)	5(6.25%)
	Normal Monocyte count (n= 219)	105(99.05%)	39(76.47)	70(87.5%)
HB (g/dL)	Monocytosis (n=6)	1(0.94%)	5(9.8%)	0 (0.00 %)
	Anemia (n= 36)	16(15.1%)	20(39.2%)	0 (0.00 %)
	Severe Anemia (n= 4)	3(2.83%)	1(1.96%)	0 (0.00 %)
	Moderate Anemia (n=18)	6(5.66%)	12(23.6%)	0 (0.00%)
	Mild Anemia (n= 14)	7(6.60%)	7(13.72%)	0 (0.00%)
PCV (%)	Normal HB (n=201)	93(87.73%)	33(64.71%)	75(93.75%)
	Low PCV (n=53)	27(25.4%)	26(50.9%)	0 (0.00%)
	Normal PCV (n=171)	61(57.55%)	38(74.51)	72(2.5%)
MCV (fL)	High PCV (n=13)	8(7.55%)	3(5.88%)	2(2.5%)
	Microcytosis (n=32)	14(13.2%)	14(27.5%)	4(5%)
	Normocytic Anemia (n= 172)	60(56.60%)	36(70.59%)	76(95%)
MCH (pg)	Macrocytosis (n= 33)	23(48.3%)	10(19.6%)	0 (0.00%)
	Normochromia (n =140)	63(59.43%)	21(41.18%)	56(80%)
	Hypochromia (n = 88)	34(32.1%)	30(58.8%)	24(30%)
RDW-CV (%)	Hyperchromia (n = 9)	8.5%	0 (0.00%)	0 (0.00%)
	Normal RDW (n= 208)	96(90.57%)	37(72.55%)	75(93.75%)
	High RDW (n= 29)	10(9.4%)	14(27.5%)	5(6.25%)
CD <sub>4</sub> count (cells/MI)	>500cells/µL(n=125)	44(41.5%)	8(15.6%)	73(91.3%)
	200 to 499 cells/ µL (n= 88)	53(50%)	28(54.9%)	7(8.75%)
	<200 cells/ µL (n=24)	8(7.5%)	16(31.4%)	0 (0.00%)

Abbreviations: WBC: White Blood Cell; RBC: Red Blood Cell; PLT: Platelet; HB: Hemoglobin; MCV: Mean Cell Volume; MCH: Mean Cell Hemoglobin; PCV: Packed Cell Volume; RDW-CV: Red Cell Distribution Width – Coefficient of Variation; CD4 – Cluster of Differentiation 4

### 3.2 Haematological and Immunological Parameters of ART –Treated and ART – Naïve Patients

There was a statistically significant difference in the mean  $\pm$  SD of the PLT, ALC, HB, MCV, MCH and PCV of the ART – treated compared to the mean  $\pm$  SD of ART – naïve HIV infected patients ( $p < 0.05$ ). The mean  $\pm$  SD of PLT, ALC, HB, MCV, MCH, PCV, of ART – treated was significantly higher compared with mean  $\pm$  SD of ART – naïve. ( $p < 0.05$ ). However, there was no statistically significant difference in the mean  $\pm$  SD of the WBC, RBC, ANC, AMC, RDW and CD4 count of ART-treated and ART- naïve HIV infected patients; ( $p > 0.05$ ) as shown in (Table 2).

### 3.3 Magnitude of the Haematological and Immunological Abnormalities in ART – Treated, ART – naïve and Controls

Leucopenia was the most common haematological abnormality among the study participants followed by anemia and thrombocytopenia with an overall prevalence of 18.9%, 15.2% and 2.5% respectively. prevalence of leucopenia varied among ART – naïve and ART – treated patients, with a prevalence of 49.0% and 8.5% respectively. Overall, prevalence of Leukocytosis was 1.3%, with 3.9% in ART- naïve patients and 0.94% in ART- treated patients.

Lymphopenia was seen in 18(7.6%) of study participants but was higher in ART- naïve than in ART- treated with a prevalence of 12(23.6%) and 4(3.8%) and respectively.

Overall, 29(12.23%) of the cases had neutropenia with a 16(15.1%) among ART- treated and 9(17.6%) in ART- naïve patients. A total of 12(11.3%) cases of mild neutropenia were seen in ART- treated and 7(13.72%) cases in ART- naïve. Moderate neutropenia was seen in 4(3.77%) cases in ART- treated and in 2(3.92%) cases in ART- naïve patients.

The total prevalence of thrombocytopenia was 6(2.53%) but it was higher in ART- naïve 4(7.84%) than in ART- treated 1(0.94%) moderate thrombocytopenia was observed in 1(0.94%) cases of ART- treated and in 2(3.92%) cases of ART- naïve patients, while mild thrombocytopenia was seen in 2(3.92%) cases of ART- naïve. There was not any case of mild thrombocytopenia in ART- treated patients.

Total prevalence of anaemia in the study participants was 36(15.18%) with a higher prevalence in ART- naïve 20(39.3%) than in ART- treated patients 16(15.1%). Severe anemia was seen in 3(2.83%) cases in ART- treated while only 1(1.96%) in ART- naïve patients. Moderate anaemia was the most common grade of anemia with 6(5.66%) cases in ART- treated and 12(23.6%) cases in ART- naïve. Prevalence of mild anemia was higher in ART- naïve 7(13.72%) than in ART- treated 7(6.60%).

Prevalence of microcytosis was 14(13.2%) in ART- treated and 14(27.5%) in ART- naïve while macrocytosis was 23(48.3%) in ART- treated and 10(19.6%) in ART- naïve patients.

A total of 34(32.1%) cases in ART- treated and 30(58.8%) cases in ART- naïve had hypochromia. A high number of case in ART- naïve had elevated RDW 14(27.5%) than in ART- treated 10(9.4%).

Most of the study participants 125 (52.7%) had CD4 count  $> 500$  cells/ $\mu$ L (Stage I) with a frequency of 44 (35.20 %), 8 (6.40 %) and 73 (66.00 %) in ART- treated, ART- naïve and controls respectively. A total of 37.1% of the study participants had CD4 count between 200 - 499 cells/ $\mu$ L (Stage II) which also varied among the ART- treated, ART- naïve and the control with a frequency of 53 (60.23 %), 28 (31.82 %) and 7 (7.95 %). Only 24 (10.1%) of the study participants had CD4 count of  $< 200$  cells/ $\mu$ L with a frequency of 8 (33.33 %) and 16 (66.67 %) in ART- treated and ART- naïve patients respectively. There was no any case of immunosuppression (CD4 count of  $< 200$  cells/ $\mu$ L) in the control group.

## 4. DISCUSSION

Haematological abnormalities especially the cytopenias have been widely reported among HIV- infected patients and have been identified as powerful predictors of illness and death in HIV patients [21]. While haematological abnormalities are typically identified in the middle or advanced stages of the HIV infection, anaemia and thrombocytopenia can also occur even in early stages of HIV disease [22].

In resource limited settings like Kenya, measurement of the haematological parameters and detection of the haematological abnormalities is paramount, as these abnormalities can be used as markers for HIV



disease progression and prognosis. The current study aim was to assess the haematological and immunological abnormalities in both ART-treated and ART- naïve HIV- infected patients and their comparative analysis. Accordingly, this study showed that cytopenias (anaemia, leucopenia and thrombocytopenia) were common haematological abnormalities in both ART- treated and ART- naïve HIV infected patients attending Thika Level Five Hospital CCC, Kiambu County.

Leucopenia was the most common haematological abnormality among the study participants followed by anemia and thrombocytopenia. Our study findings agree with those of previous studies that reported that leucopenia was the most prevalent hematological abnormality [16, 23-24]. However, our findings differ with other studies that reported the most frequently observed haematological abnormality in HIV infected patients was anemia [25,26]. The overall leucopenia prevalence of 18.9% reported in the current study is less than 22% reported in India [27] and higher than 13% reported in Ethiopia [28]. In addition, prevalence of leucopenia was higher in ART- naïve than in ART- treated which agrees with findings of Mathews et al who found a higher prevalence of leucopenia in ART- naïve than in ART- treated in a study conducted among HIV infected individuals in New Delhi, India [29]. However, the present study findings differ with others that reported a higher prevalence of leucopenia in ART- treated than in ART- naïve patients [30, 31]. These disparities may result from variations in the study populations, variations in clinical conditions of the study participants, differences in ART status across the studies and use of different cut – offs for leucopenia. The probable causes for leucopenia in HIV – infected patients are the toxic effect of antiretroviral drugs for HIV or HIV- associated conditions. Other theories that have been suggested are autoimmune mechanisms involving antigranulocyte antibodies, decreased granulopoiesis and infiltration of the bone marrow with infections or malignancy [32].

There was a higher prevalence of leukocytosis in ART- naïve (12.79%) than 6.93% in ART- treated patients which is in line with the findings of Mathews et al in a study conducted in India [29].

The present study reported a slightly higher total prevalence of lymphopenia than reported in Ethiopia [28] and the prevalence of lymphopenia

was higher among the ART- naïve (23.6%) than in the ART- treated (3.8%) patients. Our findings concur with those of Kaur et al who reported a higher prevalence of lymphopenia in ART- naïve patients than in ART- treated patients in a study conducted in Patiala, India [27].

There was a higher neutropenia prevalence among ART- naïve patients than among ART- treated patients. The high prevalence of neutropenia in ART- naïve patients could be attributable to the untreated HIV infection. Infection with HIV virus itself inhibits bone marrow function, causing a reduction in granulocyte colony-stimulating factor levels and impacts the development of granulocytes and macrophages, leading to decreased white blood cell and neutrophil levels [33].

In the present study, there were only 6 cases of thrombocytopenia with an overall prevalence of 2.53%, similar to Thulasi et al who reported only 5 cases of thrombocytopenia in the cohort [31]. Prevalence of thrombocytopenia was higher in ART- naïve than in ART- treated and the present study findings collaborate those of Kaur et al who reported a higher prevalence of thrombocytopenia in ART- naïve than in ART- treated patients [27]. The improvement of HIV disease in the ART- treated following the start of antiretroviral therapy could be the most probable cause for this variation between the two groups. The 0.94% thrombocytopenia prevalence in ART- treated patients reported in the present study is lower than 4.5% in ART – treated patients reported by Duguma et al in Gondar, Ethiopia [34]. Similarly, prevalence of 7.84% in ART- naïve patients reported in the present study is higher than 1.6% prevalence in ART- naïve HIV patients in a study conducted in China [24].

The present study revealed a higher prevalence of anaemia in ART- naïve than in ART- treated patients. The present study findings align with earlier studies which reported a higher prevalence of anaemia in ART- naïve than in ART- treated patients [27, 29,31]. The possible explanation for the decreased prevalence of anemia in ART- treated HIV patients is probably due to restoration of haemopoiesis in the bone marrow after the initiation of antiretroviral therapy. It has been reported that the reason for the decline in anemia rates following the start of HAART is the treatment's beneficial impact on RBC differentiation and survival, viral load suppression, and decrease in occurrences of

opportunistic infections [18,35]. The anaemia prevalence of 39.32% in ART- naïve patients reported in the present study is higher than 31.8%, reported by Duguma et al in Ethiopia [34] and 36.6% reported in ART- naïve adult HIV-infected Patients in Mehal Meda hospital Ethiopia [36]. However, it is lower than 89.5% reported in Patiala India [27]. Similarly, 15.1% prevalence of anaemia in ART – treated patients in the present study, was lower than 23.2% reported in North Shewa Zone, Ethiopia [37], but is slightly higher than 14.6% reported in Southeast Ethiopia [34].

Evaluation of the haematological and immunological parameters revealed that the mean  $\pm$  SD of most of the haematological parameters in ART- treated group were significantly higher than the mean  $\pm$  SD of the ART- naïve group. In the present study, the mean HB of ART- treated patients was significantly higher than the mean HB level of ART- naïve patients ( $p =$  of 0.005). Our study findings agree with those of Denué et al, who reported a higher mean HB levels in ART-treated than in ART- naïve individuals [18]. Similarly, the mean levels of PLT, ALC, MCV, MCH, PCV, of ART- treated was significantly higher than mean levels of PLT, ALC, MCV, MCH, PCV, in ART- naïve HIV- infected patients. The present study findings are in agreement with other studies [9,27,29,30,31,38].

Our study did not find a statistically significant difference in the mean  $\pm$  SD of total WBC, RBC, CD4 count for ART- treated and ART- naïve patients, which differs with findings of others that have reported a statistically significant higher total WBC in ART- naïve than in ART- treated and a significantly higher CD4 count in ART-treated than in ART- naïve patients [27,30]. This could be due to the variations in the clinical and HIV disease stages of the study participants across the studies.

The mean level of RDW in ART- naïve was higher than for ART- treated though not significantly different ( $p=$  0.085). This could be as a result of high degree of anisocytosis observed among HIV seropositive subjects due to decreased RBC production or ineffective erythropoiesis. The present study findings agree with those of Kaur et al., 2017 [27] though our findings did not find a statistically significant difference between the mean RDW for two study groups.

In conclusion, the current study has assessed the haematological and immunological abnormalities associated with HIV in both ART-treated and ART- naïve patients and revealed a substantial burden of these abnormalities in HIV-infected patients. Though effective use of antiretroviral therapy helps to keep the virus under control, restores the immune system and prevents HIV transmission, it is associated with several adverse events such as drug toxicity and consequent poor adherence and drug resistance, liver toxicity as well as failure to access potential sources of infection, notably the central nervous system (CNS) and lymph nodes among other adverse effects [39]. Due to these drawbacks related to antiretroviral therapy, there is need to explore other novel interventions in order to overcome the limitations of ART. Additionally, in order to achieve a functional cure for HIV infection and eradicate the HIV viral reservoirs, there is need to develop novel interventions such as gene-based therapies, therapeutic T-cell vaccines, immune therapeutic interventions using broadly neutralising antibodies (bNAb) among others [39,40,41]. Therefore, further studies exploring these areas of novel approaches to HIV treatment strategies and HIV eradication need to be conducted.

## 5. CONCLUSION AND RECOMMENDATIONS

Cytopenias (anaemia, leucopenia and thrombocytopenia) were common haematological abnormalities in both ART – treated and ART – naïve HIV infected patients with leucopenia being the most prevalent haematological abnormality followed by anemia and thrombocytopenia. Higher frequency of these abnormalities was seen in the ART – naïve HIV infected patients than in the ART-treated group. The mean blood cell counts of most of the haematological parameters (PLT, ALC, HB, MCV, MCH and PCV) of ART – treated was significantly higher compared with mean blood cell counts of ART – naïve HIV infected patients but the mean CD4 count of ART – treated was not significantly different between ART- treated and ART- naïve. HIV-infected patients on ART should be regularly monitored for haematological and immunological abnormalities for prompt detection and development of these abnormalities and consequent treatment so as to reduce morbidity and mortality. Additionally, it is important that ART initiation is done early enough so as to reduce the magnitude of haematological and

immunological abnormalities in the newly diagnosed ART – naïve HIV infected patients. Therefore, the Kenyan Ministry of Health should devise new strategies and strengthen the existing programs as well as allocate more resources so as to encourage early HIV testing followed by appropriate treatment so as to reduce the burden of these haematological and immunological abnormalities in the HIV- infected patients especially for the ART- naïve patients. It is recommended that future studies should focus on the exploration of long-term impact of these abnormalities on patient quality of life as well as conduction of large scale longitudinal studies so as to understand the long-term effects of ART on haematological and immunological parameters.

## 6. STUDY LIMITATIONS

The major limitation of this study is its cross-sectional design that was employed in this study which does not allow causal relationships between independent variables and cytopenias to be drawn. Other limitations are the small sample size used in this study and the lack of coverage of other haematological abnormalities such as the coagulation profile abnormalities. Therefore, it is recommended that large scale longitudinal studies covering several HIV comprehensive care centers within Kiambu County and even in different counties of Kenya be done so as to extrapolate the relevant findings from this study. In addition, studies that evaluate other haematological and immunological abnormalities other than the cytopenias and CD4 count abnormalities should be conducted in future.

## DISCLAIMER (ARTIFICIAL INTELLIGENCE)

Author(s) hereby declare that NO generative AI technologies such as Large Language Models (ChatGPT, COPILOT, etc.) and text-to-image generators have been used during the writing or editing of this manuscript.

## CONSENT

Authors declare that written informed consent was obtained from each and every participant before the study.

## ETHICAL APPROVAL

Ethical clearance for this study was obtained from Mount Kenya University's Institutional Ethics Review Board (MKU/ERC/1013). Further

approvals were also granted by the hospital management of Thika Level Five Hospital and the Health Research and Development Unit of Kiambu County, Kenya. The study adhered to all protocols for human subjects research as outlined in the 1964 Declaration of Helsinki.

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## COMPETING INTERESTS

Authors have declared that no competing interests exist.

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