UNIVERSITY of RWANDA

COLLEGE OF MEDICINE AND HEALTH SCIENCES, SCHOOL OF MEDICINE AND PHARMACY, DEPARTMENT OF INTERNAL MEDICINE

HEMATOLOGICAL PROFILE OF HIV SEROPOSITIVE PATIENTS AT THE UNIVERSITY TEACHING HOSPITAL OF KIGALI (CHUK) HIV FOLLOW-UP CLINIC

Final project submitted in partial fulfillment of the requirements for the award of the Masters of medicine in internal medicine

By

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DECLARATION

I, SHUMBUSHO Patrick, to the best of my knowledge hereby declare and certify that the work presented in this dissertation entitled **"HEMATOLOGICAL PROFILE OF HIV SEROPOSITIVE PATIENTS AT THE UNIVERSITY TEACHING HOSPITAL OF KIGALI (CHUK) HIV FOLLOW-UP CLINIC."** is entirely my own and original work and it has never been presented or submitted in whole or in part to any other university.

SHUMBUSHO Patrick Signature: Date: 30/08/2021

Supervisor:

I, hereby declare that this dissertation has been submitted with my approval as the supervisor.

NKESHIMANA Menelas, MBBS, MMed, MRC.

Signature: Date: 30.08.2021

DEDICATION

To God the Almighty

To my Lovely wife

To my parents

To my relatives and friends

To my classmates and other people who contributed to my studies

I dedicate this work

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My special thanks go to Prof. Florence Masaisa and Dr Menelas NKESHIMANA, who despite many engagements, accepted to supervise this work. Their remarks and scientific rigor have been of great importance for this work to be realized.

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Last but not the least; I want to express my gratitude to the University of Rwanda, particularly to the department of Internal Medicine and its devoted staff, staff of CHUK/ HIV clinic, and staff of the teaching hospitals where I did my clinical Rotations, for making our training possible.

May God bless you all!

ABSTRACT

Background: HIV/AIDS is still a major public health concern, especially in sub-Saharan Africa, its manifestations are mainly related to immunosuppression, but also studies have reported various hematological manifestations including cytopenias, mainly anemia, leukopenia and thrombocytopenia. The causes of those cytopenias and its associated factors in HIV patients are multifactorial. In the present study, we aim to know the prevalence of cytopenia in HIV patients and its associated factors during the era of widespread use of HAART

Patients and methods: this is a 2-month (April to June 2021) cross-sectional study. Our participants were adults' HIV patients (18 years and above). Interview and chart review were conducted on patients visiting the HIV follow-up clinic. Blood analysis done include full blood counts and serum iron levels Cytopenia were defined according to WHO standards parameters by gender. Correlation between cytopenia, serum iron and immunological status were made using the Chi-square test and a P value set at < 0.05 for statistical significance

Results: Data were collected for 200 participants; the median age was 50 years (interquartile range 39-50). Anemia and leukopenia were common in our participants (23% and 22% respectively), whereas thrombocytopenia was only found in 6%. Fourteen percent (14%), of our participants had IDA. almost 98% have been on HAART, and 84% with viral suppression. Low CD4 count at diagnosis, low serum iron levels were associated with anemia ($P<0.001$). Both leukopenia and thrombocytopenia were also associated with a baseline CD4 count below 200 ($P=0.015$ and 0.048 respectively), and high viral load at diagnosis (>1000 copies/ml), $P<0.001$). The majority of our participants were HIV stage 1 and 2 (75%), and anemia was common in that category unlike other studies have demonstrated.

Conclusion: Like others found, anemia is still the common cytopenia in HIV patients, low prevalence is noted in patients on HAART. IDA is among the cause of cytopenia in HIV patients which needs special attention and management in our population.

KEY WORDS: antiretroviral, anemia, HIV, cytopenia, immunosuppression

LIST OF ABBREVIATIONS

AIDS: Acquired Immunodeficiency syndrome

ART: Anti-retroviral therapy

BMI: Body Mass Index

CHUK: University Teaching Hospital of Kigali

HAART: Highly active anti-retroviral therapy

HIV: Human immunodeficiency virus

G-CSF: Granulocyte colony stimulating factor

ID/IDA: Iron deficiency/ iron deficiency anemia

NRTI: Nucleoside Reverse Transcriptase Inhibitor

OI: Opportunistic infection

VL: Viral load

WHO: World Health Organization

Table of Contents

List of tables

CHAP I. BACKGROUND AND PROBLEM STATEMENT

HIV remains a major public health concern. Globally, it affects 38 million people, with new infections approaching 1.7 million at the end of 2018.Two third of global HIV infections and new infections are found in Africa, with higher rates in sub-Saharan region. HIV claimed 690.000 deaths globally in 2018(1). The prevalence of HIV in Rwanda is at 2.9% in adult's population, with 87% of ART coverage, 94% know their HIV status, and only 74% were found to have viral suppression(2)

HIV related cytopenias were very common in the pre-ART era, however, they are still common especially in the resource limited settings due to limited access to treatment programs(3). The main hematological manifestations of HIV infection include anemia, leukopenia and thrombocypenia, and they become severe in the advanced stages of the infection. Anemia and granulocytopenia can be more common in AIDS, whereas thrombocytopenia is often a sentinel presentation of HIV infection in the asymptomatic stages(4).Anemia is the predominant cytopenia among HIV patients; it ranges between 1.3 to 95% during the course of the disease, it is associated with an increased mortality and impaired quality of life, and rapid disease progression(5). In Rwanda, the prevalence of anemia in HIV was evaluated in women only, where two groups were compared;anemia was found to be 29%in the group of HIV positive women,but only 25% were on HAART, compared to 8% of HIV negative counterpart, other cytopenias were not reported(6). Kyeyune et al. in Uganda, found that the prevalence of anemia was 47.8% in their cohort of HIV naïve and those initiating HAART not more than 6 months, however, more than 50% were on HAART, leukopenia was found in 24.3% whereas 8.3% were having thrombocytopenia. The female gender, body mass index and CD4 count were associated with any form of cytopenias(7).

A high prevalence of cytopenias was found in an Indian cohort of patients with advanced HIV infection. Anemia, leukopenia and thrombocytopenia was found in 84%,60% and 32% respectively(4). However, in the above studies, all the possible causes of cytopenias apart from HIV were not excluded. There is high prevalence of anemia in HIV patients seeking acute medical care, as it was demonstrated by Kerkhoff et al. in South Africa, where in a cohort of 578 HIV patients seeking acute medical care; 84.8% had anemia, there was a high mortality rate in participants presenting with life threatening anemia (hemoglobin $\leq$ 6.5g/dl) (8). High prevalence

of anemia is also observed in ART naïve patients. Wankah et al. in Cameroun found that in a cohort of 81 ART naive patients, 62.9% (51 patients) had anemia, leukopenia and thrombocytopenia in 28(34.6%) and 22(27.1%) patients respectively(9). In a Nepalese study, 210 HIV patients were studied, and 66.7% of participants had anemia, whereby Two-third of the study population had advanced immunosuppression(10). A low number of cytopenias in HIV patients was found in china. In a group of 4325 ART naïve HIV patients, anemia,neutropenia and thrombocytopenia were found in 287 (6.63%), 306(7.7%), and 69 (1.6%) patients respectively; this low prevalence may be attributed to geographical location and study population(11). In a Korean study, 472 HIV patients were studied to evaluate cytopenias, 82.4% were on HAART, and other potential causes of marrow suppression have been excluded. The results showed a low prevalence of anemia at 3%, neutropenia and thrombocytopenia were 10% and 2.4% respectively, the risk factor for cytopenias was mainly AIDS status at presentation(12). HIV infection itself is associated with an increased risk of leukopenia and neutropenia, and an independent risk of bacterial and fungal infections, due to impaired function of neutrophils(13), 10-30 % of HIV patients are neutropenic during early symptomatic infection, and more than 50% in advanced infection(3). The risk of bleeding associated with thrombocytopenia in HIV patients is not common and thrombocytopenia has an excellent response to antiretroviral medications(14).Hematological abnormalities are common in HIV infection, and they negatively impact the outcomes and quality of life. The burden of cytopenia in HIV patients and its associated factors are not well known in our country, therefore the aim of this study is to determine the prevalence and associated factors of different cytopenias associated with HIV infection in patients attending CHUK HIV clinic.

CHAP I.1.RESEARCH QUESTION

What is the prevalence and associated factors of cytopenias in HIV patients attending CHUK HIV follow-up clinic?

CHAP I.2.OBJECTIVES OF THE STUDY

I.2.1. MAIN OBJECTIVE

Determine the spectrum of hematological manifestations and its correlation with immunological status.

I.2.2. SPECIFIC OBJECTIVES

1. Determine the prevalence of cytopenias in HIV patients at CHUK follow-up clinic.

2. Determine the immunological profile of HIV patients in the follow-up clinic at CHUK.
3. Determine the relationship between cytopenias and immunological status of the patients evidenced by VL, CD4 cells count and clinical staging

CHAP II. LITERATURE REVIEW

CHAP II.1. DEFINITIONS OF CYTOPENIAS

WHO defines standards hematological parameters as follow: anemia as Hemoglobin < 12g/dl for female gender, and hemoglobin <13g/dl for male gender. Leukopenia is defined as an absolute white blood cell counts < 4×10^9/l, and thrombocytopenia as an absolute platelet count < 150×10^9/l(15), and these values will be used in the current study to define cytopenias in HIV seropositive patients.

CHAP II.2. FACTORS ASSOCIATED WITH CYTOPENIAS IN HIV PATIENTS

The cytopenia associated with HIV infection are explained by a direct infection to progenitor cells or by immune dysregulation by cytokine release, thus causing impaired hematopoiesis. In addition to HIV, opportunistic infections, nutritional deficiencies, malignancies and multiple drugs regimen cause cytopenias in HIV patients(3).

Mycobacterium (i.e. avium and tuberculosis) and fungal infections (i.e. cryptococcus and histoplasmosis) are commonly associated with cytopenias(3). Daniel W. Gunda et al. found in Tanzania, an increased risk of having anemia in HIV patients who have also pulmonary TB or disseminated tuberculosis, in the same study, other risk factors to develop anemia include advanced HIV infection as evidenced by low CD4 count < 200 cells and WHO clinical stage 3 or 4, these were also a risk to develop thrombocytopenia. Leukopenia was associated with female gender, in addition to low CD4 count <200 cells and WHO clinical stage 3 or 4(16). Hepatitis C co-infection, and injection drug users are also associated with an increased risk of anemia, and female gender, underweight in the resource limited settings increase the risk of anemia in HIV patients(3).

Tamir Z et al., in a study done in Ethiopia, found that development of any cytopenia was associated with a positive history of opportunistic infections, low BMI, and advanced HIV stage. Anemia in particular, was associated with WHO clinical stage 4, low BMI and history of opportunistic infections (OI). Age > 50 years, was an independent predictor of anemia, and ART naïve HIV patients at stage 4, were more likely to be anemic. Leukopenia is more likely to occur in HIV stage 4, with history of OI, and at young age (18-29 years). thrombocytopenia was

mainly associated with advanced HIV stage 4, but no association with body weight or age(17).Zenebe et al. also found in Ethiopia that isoniazid use and bedridden functional status were associated with anemia(18).

Cytopenias related to drug therapy are currently not common as compared to the initial combined antiretroviral therapy, when zidovudine was the major drug used in the NRTI class and causing anemia, drugs used to treat opportunistic infections also contribute to the hematological manifestation(3). There was a significant association between the use of co-trimoxazole and anemia in a study done in Ethiopia by Fekene et al.(19). It is also associated with the development of neutropenia, however , no serious bacterial infections reported(20). Other commonly prescribed drugs associated with cytopenias include amphotericin B, ganciclovir, zidovudine and cancer chemotherapy which predispose to anemia and leukopenia(3).

CHAP II.3. MECHANISMS AND CAUSES OF CYTOPENIAS IN HIV PATIENTS

The causes of cytopenia in HIV are multifactorial. HIV itself can directly affects hematopoietic cells, thus causing cytopenias, or indirectly by cytokines upregulation causing marrow suppression(3). The direct infection of hematopoietic cells by HIV is linked to the fact that the progenitor cells express the CD4 molecules, C-chemokine receptors(CCR5) and CXR4 receptors which constitute the main receptor for the HIV genome. HIV can also induce hematopoietic cells apoptosis without direct infection. The bone marrow microenvironment (stromal cells) is susceptible to HIV infection and this may lead to structural changes and proliferation of fibroblasts and macrophages like cells in the bone marrow stromal cells with subsequent impaired support milieu for hematopoietic cells, thus impaired hematopoiesis(21). HIV may affect granulocytes and cause endogenous G-CSF depletion. The mechanism of thrombocytopenia is mainly direct infection of megakaryocytes by HIV, or immune thrombocytopenia due to immune reaction between HIV glycoproteins and platelets, thus causing reduced thrombopoiesis(3). Autoimmune hemolytic anemia is rare in HIV infection but can still happen as a result of cross reaction of antibodies to HIV antigen with the erythrocytes, or the anti-erythropoietin antibodies which lead to impaired erythropoiesis and anemia(21). Other hematological manifestations are related to the presence of opportunistic infections, malnutrition, malignancy and polypharmacy in HIV patients(3). Viral hepatitis B and C co-infection, liver cirrhosis can also contribute to the hematological manifestations(12).

Nutritional deficiencies have been also noted to cause cytopenia in HIV patients, with vitamin B12 deficiency occurring in up to 30% of patients living with HIV infection (3).Iron deficiency was demonstrated in HIV infection,by the mechanism of altered iron metabolism with functional block of iron release, instead of reduced iron stores, and this is explained by limited response of anemia to iron supplementation. A true iron deficiency is found in advanced immunosuppression with intestinal malabsorption(22). The main opportunistic infections to cause cytopenias are mycobacterium tuberculosis, mycobacterium avium complex and Cryptococcus neoformans. They infiltrate the bone marrow and cause different cytopenia. Parvovirus B19 was also found in immunosuppressed patients, and should be suspected in isolated anemia. Other viral infections like EBV, HHV8 constitute a major risk for malignancies like Hodgkin lymphoma and Kaposi sarcoma, which are increased in HIV patients, and cause remarkable bone marrow infiltration and cytopenias(23).

CHAP II.4. BURDEN OF CYTOPENIAS IN HIV SEROPOSITIVES PATIENTS

HIV is a chronic disease and has clinical and socio-economic impacts on the affected group and the general population. Cytopenias are one of the major clinical manifestations of HIV infection, and anemia among others is the commonest, and it is associated with impaired quality of life. There is a remarkable disease progression to AIDS state in patients with anemia and it was found to be an independent risk factor for death(5). Anemic HIV patients have poor physical functional status due to chronic fatigue. Despite other causes of fatigue like depression, malnutrition in this population, anemia can be assessed easily. Headache, and dizziness associated with anemia also negatively impact the quality of life in HIV patients(24). There is an increased need for blood transfusion for acutely ill HIV admitted patients and mortality risk associated with transfusion in some western studies (25). However, in a study done by Kerkhoff, et al in SA found an increased need for blood transfusion but no mortality risk after excluding the effect of other comorbidities (8).

R.D. Moore et al. found in a cohort of 498 anemic patients with HIV infection, that the median survival from diagnosis of anemia was 113 days to 265 days depending on the severity of anemia, and the development of anemia was preceded by use of zidovudine, ganciclovir and chemotherapy, and the mycobacterium avium complex infection. However, 106 patients (21%) in that cohort, developed anemia without prior use of the later medications or the mycobacterium

avium complex disease, in this cohort the use of erythropoietin was associated with the increased chance of survival in contrast to blood transfusion(26).

CHAP II.5. MANAGEMENT OF CYTOPENIAS IN HIV PATIENTS

Anemia is the commonest hematological manifestation of HIV infection (5).The general approach to the treatment of anemia in HIV patients consists of treating the HIV infection with combined antiretroviral therapy (3).There is a remarkable increase in hemoglobin levels after 6 months of starting HAART, and decreased risk of developing anemia while on HAART for at least one year(27). Vitamin B12, folate and iron deficiency are potential causes of anemia which need correction. Blood transfusion should be considered in patients with acute symptomatic anemia. HIV patients with no identifiable cause of anemia can be treated with erythropoietin Alfa, but this approach would be problematic in resource limited settings(28).

CHAP III. RESEARCH METHODOLOGY

CHAP III.1 STUDY DESIGN, SETTING AND PERIOD

This was a cross-sectional study involving HIV seropositive patients followed at HIV clinic of the University Teaching Hospital of Kigali (CHUK), it is a national referral hospital serving the four provinces of the country, located in the central city of Kigali with a capacity of 519 beds. The HIV clinic serves around 2000 HIV patients mainly from surrounding districts. Participants were recruited from the HIV follow-up clinic over a 2-month period (April-June 2021).

CHAP III.2. STUDY POPULATION

2.a. Inclusion criteria

The study included Adult HIV patients (18 years and older), who are on ART or ART naïve and accepted to sign the consent for the study were included in the study. Data were collected from patients who come for regular follow-up in the clinic during the study period

2.b. Exclusion criteria

Patients less than 18 years of age, pregnant patients (based on clinical history) or who have an ongoing bleeding and patients who refused to sign the consent have been excluded from the study.

Sample size calculation

The sample size (N) is to be calculated using the formula used in cross-section studies. The level of significance set at 5%, p value at <0.05.

p stands for estimated prevalence, we used the prevalence of anemia in the study by Kerkhoff et.al(8) which was found to be 84.8% in their cohort of 578 patients

q Stands for **1-p**

Z is **1.96** as standard normal variate for p value set at <0.05.

d is the absolute error, which is 0.05

$$\mathbf{N=Z^2pq/d^2}$$

p=0.848

q=0.152

$N=1.96^2 x 0.848 x 0.152/0.05^2=198.066$

Therefore, our estimated sample size is **198 patients.**

CHAP III.3. Data collection procedure and laboratory measurements

The patients' socio demographic data were collected using a structured questionnaire during interview. Clinical information mainly included the history of opportunistic infections, years since diagnosis of HIV, time of initiation of ART, the HAART regimen and Bactrim prophylaxis, the most recent CD4 count and VL. The immunological parameters (CD4 and VL) were retrieved from patient's file by considering the recent one (less than 1 year) as the VL is checked yearly as per national protocol of HIV treatment. These data were retrieved from patient's chart or asked during the interview. The World Health Organization HIV clinical staging was recorded for each patient using medical history or physical examination. Laboratory testing was done for each participant who accepted to sign the consent for the study. A total of 4 milliliters of blood werecollected for the complete blood count and 4 milliliters collected for serum iron. The blood samples were collected by a well-trained nurse in the phlebotomy unit of the outpatient clinic laboratory. Data collectors included the principal investigator, a well-trained nurse and medical doctor from the HIV clinic.

CHAP III.4. STATISTICAL ANALYSIS

The data were collected using a structured questionnaire and then entered electronically in SPSS sheet where they were analyzed using SPSS version 21.0 statistical software for analysis. The mean and interquartile ranges were used to characterize the continuous variables with normal distribution. All the categorical variables were expressed as proportions and percentages, and they were compared using Chi-square test. The relationship of HIV cytopenias and different associated factors were evaluated using the univariate logistic regression with 95% confidence interval(CI) to measure the strength of statistical association. P value < 0.05 was used to determine statistical significance. Missing data were excluded from the analysis

CHAP III.5. ETHICAL CONSIDERATION

The research proposal was presented to both the institutional review board, research and ethics committee of the University of Rwanda and to the University Teaching Hospital of Kigali ethics committee for approval. All the participants have signed the consent forms willingly after thorough explanations of the objectives, assuring them of confidentiality of their data and possible risks if any of participating in the study. There were no expected risks associated with this study apart from mild pain and bleeding during blood sampling but this were managed by a

phlebotomy nurse. However, participants who presented with ongoing bleeding have been excluded during interview. The requested laboratory tests are part of routine follow-up and have been paid by the participants who have accepted to willingly participate in this study, given the benefit of the follow-up of his/her condition and further treatment if need be. The consent form was written in both English and Kinyarwanda. Patients information have been kept confidential, names and other personal identifiers were not revealed; each patient's record were assigned a unique study ID number after completing the data collection.

CHAP. IV OBSERVATIONS AND RESULTS OF THE STUDY

CHAP.IV.1 PATIENTS SOCIO-DEMOGRAPHICS AND BASELINE CLINICAL CHARACTERISTICS

Table 1**. patients socio-demographics and clinical characteristics**

Characteristics	Frequency N	Percentage (%)	Median (IQR)
Age groups (years)			
≤ 20	6	3%	
21-35	36	18 %	
31-60	126	63 %	
61and above	32	16 %	
Median (IQR) age, years			50 [39-58]
Sex			
Male	85	42.5%	
Female	115	57.5 %	
Occupation			
Employed	75	37.5%	
Unemployed	125	62.5	
Past opportunistic infection			
Yes	41	20.5%	
No	159	79.5%	
Current opportunistic infection			
Yes	18	9%	
No	182	91%	
WHO HIV stages			
Stage 1&2	150	75 %	
Stage 3&4	50	25%	
CD4 count at diagnosis			
<200	73	42%	
200-499	74	43%	

>500	26	15%	
Viral load at diagnosis			
Suppressed (<20)	24	18%	
20-200	45	34%	
201-1000	13	10%	
> 1000	51	39%	
Current viral load			
Suppressed (<20)	140	84%	
20-200	15	9%	
201-1000	3	2%	
> 1000	8	5%	
Hemoglobin levels (g/dl), n (%)			14[13-16]
Low Hb level:			
Female < 12 g/dl	28	16%	
Male < 13 g/dl	12	7%	
WBC count (cells/mm3)			5[4-6]
Leucopenia (< 4 x10^9/l)	38	22%	
Platelets count (cells/mm^3)			251[202-302]
Thrombocytopenia (< 150 x 10^9/l)	10	6%	

The median age was 50 years [IQR 39-58]. The majority of our participants were females, 57.5 % and males 42.5%. The majority, 62.5 % were not employed. Twenty percent (20.5%) of our participants had opportunistic infections at the time of HIV diagnosis whereas 9% were found with an opportunistic infection during the time of the study. In addition, most of them 75%, were in HIV stage 1&2 and the remaining in advanced stages (3 or 4). Regarding the immunological status of our participants, the baseline CD4 cell count at diagnosis were below 200 in about 42% of participants. The viral load was recorded both at the diagnosis and currently after several years on HAART; initially, the majority had a higher VL > 1000 copies/ml in about 39% of participants, and only 18% had a suppressed VL (less than 20 copies/ml) as opposed to the recent VL counts showing the majority of viral suppression at 84% in our cohort. The overall

prevalence of anemia was 23% in this study population. Anemia was more prevalent in females, 16% than in males, 7%. Leucopenia was 22% among the study population and thrombocytopenia was found in 6% of the study participants.

Table 2. Correlation between leucopenia with HIV stages, viral load, CD4 as well as opportunistic infections.

Leucopenia			logistic regression	
	Yes, n (%)	No n (%)	95%CI	P value
WHO HIV staging			[1, 1]	0.024
Stage 1	25 (19%)	63 (47%)		
Stage 2	3 (2%)	3 (2%)		
Stage 3	8 (6%)	27 (20%)		
Stage 4	2 (1.5%)	4 (3%)		
Initial viral load			[1, 2]	p<0.001
Suppressed (<20)	2 (2%)	1 (1%)		
20-200	7 (7.5%)	22 (25%)		
201-1000	2 (2%)	6 (6.8%)		
> 1000	16 (18%)	23 (26%)		
CD4 counts at diagnosis			[1, 1]	0.015
<200	15 (13%)	38 (33%)		
200-500	15 (13%)	28 (24%)		
>500	4 (3%)	16 (14%)		
Opportunistic infection			[1, 1]	0.025
Yes	9 (7%)	21 (16%)		
No	29 (21%)	76 (52%)		

Leukopenia were equally distributed among participants having Baseline CD4 count at diagnosis below 200, and 500 respectively, which were 13% in each group, and this were statistically significant (P<0.015). Leukopenia was found in 18% of participants with an initial VL > 1000

copies, P<0.001. a small number of participants had leukopenia and associated OIs (7%, P= 0.025)

Table 3. Correlation between thrombocytopenia with HIV stages, viral load, CD4 and opportunistic infections.

Thrombocytopenia			logistic regression	
	Yes, n (%)	No n (%)	95%CI	P value
WHO HIV staging			[1, 2]	0.073
Stage 1	5 (3%)	114 (65%)		
Stage 2	1 (0.5%)	10 (6%)		
Stage 3	4 (2%)	34 (19%)		
Stage 4	0	7 (4%)		
Initial viral load			[1, 2]	p<0.001
Suppressed (<20)	0	20 (17%)		
20-200	2 (2%)	37 (31%)		
201-1000	1 (1%)	11 (9%)		
> 1000	5 (4%)	43 (36%)		
CD4 counts at diagnosis			[1, 2.06]	0.048
<200	2 (1%)	64 (42%)		
200-500	6 (4%)	56 (36%)		
>500	1(1%)	25 (16%)		
Opportunistic infection			[1, 1]	0.053
Yes	3 (2%)	34 (19%)		
No	7 (4%)	131(75%)		

There was no significant association between thrombocytopenia and WHO clinical stages or the presence of opportunistic infections, however, it does with the initial viral load

Table 4. Relationship between patients' period since diagnosis, opportunistic infections and WHO HIV clinical stages

	Anemia	Linear logistic regression

	Yes (n %)	No n (%)	95%CI	P value
Years since diagnosis			[10, 14]	0.33
< 6 months	4 (2%)	1 (0.5%)		
6 months-2 years	1 (0.5%)	4 (2%)		
2 years-10 years	3 (2%)	20 (11%)		
> 10 years	32 (18%)	109 (63%)		
Past opportunistic infections			[14, 15]	p<0.001
Yes	11 (6%)	26 (15%)		
No	29 (16%)	110 (62.5%)		
Current opportunistic infection			[14, 15]	p<0.001
Yes	6 (3%)	10 (5%)		
No	34 (18%)	136 (73%)		
WHO HIV stages			[1, 2.03]	0.004
Stage 1	15 (8%)	105 (60%)		
Stage 2	4 (2%)	7 (4%)		
Stage 3	5 (3%)	33 (19%)		
Stage 4	4 (2%)	7 (4%)		

The majority of our participants were enrolled in the program and diagnosed with HIV for more than 10 years, in that category, 18% had anemia but this was not statistically significant. Six percent (6%) of our participants had a past history of OI and anemia together, and it was statistically significant (P<0.001). HIV stage 1 and 2 had more participants with anemia in our cohort (8% and 2% respectively) compared to advanced stages (3 and 4), P=0.004. Sixty percent (60%) of participants in HIV stage 1 had no anemia

Table 5. Relationship between patients CD4 at diagnosis, Viral loads, serum iron and anemia

	Anemia		Linear logistic regression	
	Yes (n %)	No n (%)	95%CI	P value
CD4 counts at diagnosis				

		[2, 3]		p<0.001
<200	11 (7%)	55 (36%)		
200-499	13 (8%)	49 (32%)		
>500	8 (5%)	18 (12%)		
Viral load at diagnosis			[14.0, 16.0]	p<0.001
Suppressed (<20)	4 (3%)	15 (13%)		
20-200	6 (5%)	34 (28.5%)		
201-1000	2 (2%)	10 (8%)		
> 1000	13 (11%)	35 (29%)		
Current viral load			[14.0, 15.0]	p<0.001
Suppressed (<20)	25 (17%)	100 (67%)		
20-200	4 (3%)	9 (6%)		
201-1000	2 (1%)	1 (1%)		
> 1000	3 (2%)	4 (3%)		
Serum iron			[6, 8]	p<0.001
< 9 Umol/l	20 (14%)	25 (17%)		
9-30.4 Umol/l	7 (5%)	91 (63%)		
> 30.4 Umol/l	0	1 (1%)		

Baseline lower CD4 count at diagnosis were likely to be more associated with anemia, P<0. 001. The proportion of patients with high VL (>1000 copies) at diagnosis was predominant and associated with higher rates of anemia (11% P<0.001) as opposed to the predominance of anemia in participants with suppressed current viral load (VL<20 copies) who had higher rates of anemia (17% P<0.001). Iron deficiency anemia (IDA) was found in (14%) of our participants, compared to 5% of the participants who had anemia with normal serum iron levels, and this difference was statistically significant, P<0.001, Thus anemia is positively correlated with low serum iron in HIV patients.

CHAP V. DISCUSSION

In the present study, the prevalence of anemia was estimated at 23%, leukopenia and thrombocytopenia in 22% and 6% respectively.

Two previous studies in Rwanda have evaluated anemia in HIV female patients' cohorts. Masaisa et al found anemia prevalence of 29% in female HIV patients(6), whereas, in the study by Mutimura E et al. in Rwanda, the prevalence of anemia was 20.5% (29).

In our study, the proportion of anemia in female was 16%. These differences between our study and the two previous studies may be explained by many factors but one of them being the low percentage of patients on HAART as opposed to the current study where the majority were taking HAART. In the study by Mutimura et al, the prevalence of thrombocytopenia was higher than in our cohort, 13.5% versus 6% in our study, but for leukopenia this was different, as our cohort had a higher number of leukopenia, 22% as opposed to 4.2% in their cohort(29). Higher prevalence of cytopenias were noted in HAART naïve patients in Uganda and Ethiopia(30)(19), nevertheless, in a study done in Tanzania, anemia was still high (40.46%) compared to our study(16). However, anemia prevalence closer to our finding was noted in the study by J.O.Mugisha et .al in Uganda, where they found 18.9 % of anemia despite using lower threshold for defining anemia(hemoglobin < 11mg/dl in female and < 12mg/dl in males)(31).

Cytopenia like anemia and thrombocytopenia may present early in the course of HIV infection, however they are generally common in advanced stages of the infection and severe immunosuppression(32). in our study, the majority of participants had very low baseline CD4 count at diagnosis, in the two categories of low CD4 count(less than 200 and less than 500), anemia was similarly distributed and significantly correlated with low CD4 count($P<0.001$).In the very low baseline CD4 count category(CD4 < 200) , 7% had anemia as opposed to 88.5% of anemia in those with recent CD4count of <200 in the study done in india by Jain L et al(32). they also found that different cytopenia (anemia, leukopenia and thrombocytopenia) are all significantly correlated with low CD4 count($P=0.05$).in our study, a baseline CD4 count of less than 200 was significantly associated with leukopenia and thrombocytopenia, with a P-value 0.015 and 0.048 respectively, similar finding was noted by Jain L. et al

Currently in Rwanda, the follow-up of HIV patients is monitored using the viral load measured every year. In the present study, we used the most recent VL (less than a year) which was compared to the VL at diagnosis. The majority of our participants had a suppressed VL (84%), whereby in our cohort, almost 98% were covered on HAART, this is opposed to 18% of viral suppression at the initiation of HAART and diagnosis of HIV. Anemia was likely to occur in participants whose baseline VL at diagnosis were high and more than 1000 copies/ml, 11% in our cohort and this was statistically significant, P<0.001, and lower rates of anemia in those who were suppressed at diagnosis. This trend was reversed when the recent VL measured, whereby the majority were suppressed (84%), and the anemia prevalence was increased in the group of suppressed VL (VL < 20 copies/ml) at 17%, P<0.001. This may be explained by the fact that the number of participants with a recent VL more than 1000 copies/ml was very low, thus a negligible prevalence of anemia in that group. This was also similar to leukopenia and thrombocytopenia, which were likely to occur when the baseline VL at diagnosis was more than 1000 copies/ml, P<0.001.

Our findings are in contrast with a Nigerian study, where no relationship was found between cytopenia and viral load(33), however, in a retrospective study done at different centers in Malawi and Mozambique, anemia was found to be significantly associated with an elevated VL> 1000copies/ml, P<0.005(34).

In our study we have measured the serum iron levels for HIV patients followed in the HIV clinic. Iron status biomarkers (serum iron, soluble transferrin receptor and ferritin) are greatly affected by inflammation, which is prominent in case of HIV infection. Soluble transferrin receptor is more reliable test in determining the iron status(36). Fourteen percent (14%) of our participants had iron deficiency anemia whereas 17% had ID without anemia. In the anemia category, 5% had anemia with normal iron levels, therefore, anemia was associated with low serum iron, P<0. 001.In a large prospective study in Tanzania, in HIV patients initiating on HAART, IDA was found in 44% and 41% had anemia without iron deficiency, only 4% had ID without anemia, their cohort was bigger than ours in terms of participants, and have a higher prevalence of anemia(35), thus these differences. Frosch et. Al in Kenya found a strong association between soluble transferrin receptor and anemia in cohort of 132 HIV patients (P=0.03), with a prevalence of ID of 18.8%. using the mean cell volume (MCV) criteria, ID was defined as an

MCV less than 80 Fl/ml in females and 81fl/ml in males, and this was also related to the odds of developing anemia in HIV patients, in their cohort, IDA was found in 47%, P<0.001(36). Iron deficiency is one of the major contributing factor for the development of anemia, and its correction and supplementation has been controversial, given the risk of increasing mortality when iron supplements are given in the setting of infections(35). The risk of developing anemia was likely to be associated with the history of opportunistic infections (past or current) in our study which is the same finding by Fekene et .al in Ethiopia,(19).many studies found an association of anemia with an advanced HIV stages(3 or 4),(19)(16). However, in our cohort of HIV patients, anemia was more likely to occur in HIV stage 1 and 2 more than 3 and 4, we thought this may be due to a large number of participants who were found in stage 1 in our study, compared to the rest of stage 3 and 4.

STUDY LIMITATIONS

The main limitations of this study included some missing data, with some information which cannot be recalled by the patient and not found in the medical archive. Our study was conducted on a single center; therefore, our results may not be generalized.

Knowing the prevalence of cytopenia and some associated factors was important in our settings; however, the possible causes were not explored in this study apart from serum iron levels. Being a non-funded study also limited us in terms of laboratory workup to find out different causes of cytopenia.

CHAP VI. CONCLUSION AND RECOMMENDATIONS

VI.1 CONCLUSION

Despite the widespread use of HAART, cytopenias are still common in HIV patients, with anemia being the most common, followed by leukopenia and thrombocytopenia respectively. We have noted IDA in 14% of our participants. The HAART coverage was almost 98% in our cohort with the majority having viral suppression (84%), and this was different with many other studies in the region whereby the majority were ART naïve and initiating HAART at the time of the study. The prevalence of anemia was particularly lower in our study compared to others in the region. Baseline CD4 at diagnosis, history of opportunistic infection was found to be associated with anemia and leukopenia, and low serum iron being also a risk for anemia in this HIV patients' cohort. Unlike others, we found anemia likely to be associated with HIV stage 1 and 2 instead of advanced stages, but we thought this mainly due to a small number of participants found in stage 3 and 4.

VI.2 RECOMMENDATIONS

A nationwide study should be conducted to have more generalizable findings in our settings. The Rwanda biomedical center through the division of infectious disease, should include more laboratory workup in the national HIV treatment guidelines, to facilitate early detection of different cytopenia. Clinicians in the HIV follow-up clinic should consider regular check for the anemia, particularly as it is associated with disease progression and mortality risk, and address some treatable causes like iron deficiency.

REFERENCES

1. UNAIDS. Fact Sheet – World Aids Day 2018. http://www.unaids.org/sites/default/files/media_asset/ UNAIDS_FactSheet_en.pdf. 2018.
2. http://aidsinfo.unaids.org/ country profile:RWANDA. 2019.
3. Vishnu P, Aboulafia DM. Haematological manifestations of human immune deficiency virus infection. 2015;(October):695–709.
4. Kumar MB, Thippeswamy T, Shankar R, Prathima C. Hematological Abnormalities in Early and Advanced HIV Infection Patients. 2016;3(11):1–5.
5. Belperio PS, Rhew DC. Prevalence and Outcomes of Anemia in Individuals with Human Immunodeficiency Virus : A Systematic Review of the Literature. 2004;27–43.
6. Masaisa F, Gahutu JB, Mukiibi J, Delanghe J, Philippé J. Anemia in Human Immunodeficiency Virus – Infected and Uninfected Women in Rwanda. 2011;84(3):456–60.
7. Kyeyune R, Saathoff E, Ezeamama AE, Löscher T, Fawzi W, Guwatudde D. Prevalence and correlates of cytopenias in HIV-infected adults initiating highly active antiretroviral therapy in Uganda. 2014;1–10.
8. Kerkhoff AD, Lawn SD, Schutz C, Burton R, Boulle A, Cobelens FJ. Anemia , Blood Transfusion Requirements and Mortality Risk in Human Immunode fi ciency Virus-Infected Adults Requiring Acute Medical Admission to Hospital in South Africa. 2015;1–10.
9. Wankah PN, Tagny CT, Ngum D, Mbanya S. Profile of blood cell abnormalities among antiretroviral therapy naïve HIV patients attending the Yaounde University Teaching Hospital , Cameroon. 2014;1–6.
10. Care P, Sah SK, Dahal P, Tamang GB, Mandal DK, Shah R, et al. Prevalence and Predictors of Anemia in HIV- Infected Persons in Nepal. 2020;
11. Fan L, Li C, Zhao H. Prevalence and Risk Factors of Cytopenia in HIV-Infected Patients before and after the Initiation of HAART. 2020;2020.
12. Choi SY, Kim I, Kim NJ, Lee S, Choi Y, Bae J, et al. Hematological manifestations of

human immunodeficiency virus infection and the effect of highly active anti-retroviral therapy on cytopenia. 2011;

13. Kuritzkes DR. Neutropenia , Neutrophil Dysfunction , and Bacterial Infection in Patients with Human Immunodeficiency Virus Disease : The Role of Granulocyte Colony-Stimulating Factor. :256–60.
14. Scaradavou A. HIV-related thrombocytopenia. 2002;73–6.
15. Dikshit B, Wanchu A, Sachdeva RK, Sharma A, Das R. Profile of hematological abnormalities of Indian HIV infected individuals. BMC Blood Disord. 2009;9:5.
16. Gunda DW, Godfrey KG, Kilonzo SB, Mpondo BC. Cytopenias among ART-naive patients with advanced HIV disease on enrolment to care and treatment services at a tertiary hospital in Tanzania : A cross- sectional study. 2017;29(March):43–52.
17. Tamir Z, Seid A, Haileslassie H. Magnitude and associated factors of cytopenias among antiretroviral therapy naïve Human Immunodeficiency Virus infected adults in Dessie, Northeast Ethiopia. PLoS One. 2019;14(2):1–15.
18. Care P, Zenebe WA, Anbese AT, Tesfaye TS. Anemia And Associated Factors Among Adult People Living With HIV / AIDS Receiving Anti-Retroviral Therapy At Gedeo Zone , SNNPR ,. 2019;351–6.
19. Fekene TE, Juhar LH, Mengesha CH, Worku DK. Prevalence of cytopenias in both HAART and HAART naïve HIV infected adult patients in Ethiopia : a cross sectional study. 2018;1–11.
20. Toure S, Gabillard D, Seyler C, Gourvellec G, Anglaret X. Incidence of neutropenia in HIV-infected African adults receiving co-trimoxazole prophylaxis : a 6-year cohort study in Abidjan , Cˆ ote d ’ Ivoire. 2006;
21. Durandt C, Immunol M, Potgieter JC, Chb MB, Med MF, Haem M. HIV and haematopoiesis. 2019;109(8):41–6.
22. Rockstroh KKJK. Pathogenesis and pathophysiology of anemia in HIV infection. 1997;179–87.
23. Opie J. Haematological complications of HIV infection. 2012;102(6):465–8.

24. Abrams DI, Steinhart C. Epoetin alfa therapy for anaemia in HIV-infected patients : impact on. 2015;659–65.

25. Sullivan P. Associations of Anemia , Treatments for Anemia , and Survival in Patients with Human Immunodeficiency Virus Infection. 2002;185(Suppl 2):138–42.

26. Richard D. moore, Jeanne C.keruly, Richard E. chaisson. ANEMIA AND SURVIVAL IN HIV INFECTION. J Acquir Immune Defic Syndr retrovilogy. 1998;19(1):29–33.

27. Berhane K, Karim R, Cohen MH, Masri-Lavine L, Young M, Anastos K, et al. Impact of highly active antiretroviral therapy on anemia and relationship between anemia and survival in a large cohort of HIV-infected women: Women's interagency HIV study. J Acquir Immune Defic Syndr. 2004;37(2):1245–52.

28. Volberding PA, Levine AM, Dieterich D, Mildvan D, Mitsuyasu R, Saag M, et al. Anemia in HIV Infection : Clinical Impact and Evidence-Based Management Strategies. 2004;94121.

29. 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. 2012;1–8.

30. Muzoora C, Muwanguzi E, Atuhairwe C, Taremwa IM. Hematological abnormalities in HIV-antiretroviral therapy naïve clients as seen at an immune suppression syndrome clinic at Mbarara Regional Referral Hospital , southwestern Uganda. 2018;105–10.

31. Mugisha JO, Shafer LA, Paal L Van Der, Mayanja BN, Eotu H, Hughes P, et al. Anaemia in a rural Ugandan HIV cohort : prevalence at enrolment , incidence , diagnosis and associated factors. 2008;13(6):788–94.

32. Jain L, Singh AA, Chauhan PS. Peripheral haematological manifestations in HIV infection and its relation to CD4 count. 2019;6(3):681–6.

33. Denue BA, Gashau W, Bello HS, Kida IM, Bakki B, Ajayi B. Relation between some haematological abnormalities , degree of immunosuppression and viral load in treatment-naïve HIV-infected patients. 2013;19(4).

34. Id FC, Lucaroni F, Latagliata R, Morciano L, Mondlane E, Balama M, et al. Hematologic alterations and early mortality in a cohort of HIV positive African patients.

2020;174(Vl):1–14. Available from: http://dx.doi.org/10.1371/journal.pone.0242068

35. Haider BA, Spiegelman D, Hertzmark E, Sando D, Duggan C, Makubi A, et al. Anemia , Iron De fi ciency , and Iron Supplementation in Relation to Mortality among HIV-Infected Patients Receiving Highly Active Antiretroviral Therapy in Tanzania. 2019;100(6):1512–20.

36. Frosch AEP, Ayodo G, Odhiambo EO, Ireland K, Vulule J, Cusick SE. Iron De fi ciency is Prevalent among HIV-Infected Kenyan Adults and is Better Measured by Soluble Transferrin Receptor than Ferritin. 2018;99(2):439–44.

ANNEXES

ANNEX 1. Informed consent form (English version)

SHUMBUSHO Patrick is carrying out a study, to determine the prevalence and risk factors of cytopenias in HIV seropositive patients. This study will look at how many patients, have anemia, leukopenia or thrombocytopenia and what are the possible risk factors associated with them.

You are invited to participate in this study by giving blood on a voluntary basis, and blood will be taken once during the study and it will be enough for the study.

blood draws will be performed by qualified technicians at the hospital, around 8 mls of blood will be withdrawn from a vein in your arm. During the collection of blood, you may experience discomfort and bruising at the site of collection, but the nurse will help you stop and minimize the risk of bleeding.

Although you will not be given money for the study, you will make a major contribution to the information known about cytopenias in HIV patients in our country. The possible benefit is that whoever has the cytopenia will be directed to his physician for treatment and care. the results will also inform us on HIV control, which will subsequently enhance the adherence mechanisms.

A research assistant will keep a record of all blood draws in a secure database. Only the professional staff at the hospital will know the identity of study participants. Your signature on this form means that you understand the information presented, and that you want to participate in the study, you understand that participation is voluntary and you may withdraw from the study at any time.

N.B: You have all the rights to refuse the participation in this study, without any condemnation either about your treatment here or any other consequence. Even after enrollment, you also have right to withdraw your consent at any point without any consequence

Names of the participant: ----------

Signature of the participant: ---------- Dates: --/---/---

Researcher: SHUMBUSHO Patrick,

Signature----------

Tel: 0784105699

Email: johnsonparick65@gmail.com

In case of any concern about the study, feel free to contact the Chairperson of the ethics committee at University teaching hospital of Kigali

Dr Emmanuel K. Rusingiza

Tel: 0785466254 , Email: erkamanzi@gmail.com

Informed consent form (Kinyarwanda version)

Kwemera gukorerwaho ubushakashatsi

Muganga SHUMBUSHO Patrick arimo gukora ubushakashatsi,kureba abantu bagira ikibazo cyo kubura maraso na zimwe mu mpamvu zibitera kubarwayi babana nubwandu bw'agakoko ka SIDA

Tukaba tugusaba ngo ube muri bamwe bakorerwaho ubushakashatsi,turagufata amaraso tujye kuyapima turebe ingano yamaraso yawe, hamwe na vitamin B12, ubutare, biri muri bimwe bishobora gutuma ugira amaraso make.Birasaba kuzagufata amaraso inshuro imwe mugihe cyubushakashatsi kugirango tubashe kubona amakuru akenewe.Ibi ni ku bushake bwawe,ntabwo utegetswe kuza muri ubu bushakashatsi.

Amaraso azajya afatwa n'umukozi ubifitiye ubushobozi n'uburambe,azajya afatwa mu mutsi hakurwemo nka mililitiro 8

Ushobora kumva ububabare mu gihe bagufata amaraso,ushobora no kubona amaraso akomeje kuva aho bateye urushinge cyangwa akipfundika(imfunira).umuforomo azabigufashamo byose kugirango urekere kuva.

Nubwo nta gihembo uzabona kubera ubu bushakashatsi;uzaba ufashije cyane kuko amakuru azava muri ubu bushakashatsi azadufasha kumenya urugero rw'ubudahangarwa bw'umubiri nnuburyo imiti igabanya ubukana ibafashamo, kandi abazatahurwaho ikibazo cy'amaraso make cyangwa ibipimo bidahagije bya za vitamin zavuzwe hejuru bazoherezwa kuri muganga bafashwe.

Amaraso tuzaba twagufashe azajya apimwa n'abakozi b'ibitaro babishinzwe,nta handi azajyanwa.Nta n'undi muntu uzamenya ibijyanye n'ibizamini twagukoreye kuko ni ibanga hagati yawe n'abaganga.

Niba wemeye gukorerwaho ubu ubushakashatsi,urasinya kuri uru rupapuro,bivuga ko wasobanukiwe neza ibijyanye n'ubu bushakashatsi,ko winjiyemo ku bushake bwawe nta gahato, Igihe cyose waba utagishaka gukomeza muri ubu bushakashatsi,wabitumenyesha tukagukuramo,kandi nta ngaruka n'imwe bizakugiraho.

Icyitonderwa: ufite uburenganzira busesuye bwo kwanga gukorerwaho ubu bushakashatsi,kandi ibyo nta ngaruka n'imwe byakugiraho haba mu bijyanye n'uburyo uzavurwa cyangwa indi ngaruka iyo ariyo yose.Igihe kandi waba wabyemeye,wagera nyuma ugashaka kwisubiraho,ufite uburenganzira bwo kuvamo kandi nabwo nta ngaruka n'imwe byakugiraho.

Amazina y'ukorerwaho ubushakashatsi: ----------

umukono w'ukorerwaho ubushakashatsi: ----------Taliki----/---/----

Ukora ubushakashatsi SHUMBUSHO Patrick

Umukono----------

Email:johnsonpatrick65@gmail.com

Telefoni: 0784105699

Ugize ikibazo muri ubu bushakashatsi, wahamagara Uhagarariye ishami ryiga ibirebana nubushakashatsi muri CHUK

Dr Emmanuel K. Rusingiza, Tel : 0785466254, email: erkamanzi@gamil.com

ANNEX 2. Data collection tool

Title: Hematological profile of HIV seropositive patients at CHUK/HIV follow-up clinic

DATA COLLECTION FORM

I. Patient Identification:

Record No_____ HIVCLINIC ID _____

II. Socio-demographic data

A. Age (years): _____

B. **Sex**: □Male (0) □Female (1)

C. Occupation status: employed (1) unemployed (0)

D.**Residence**: Kigali (1) Eastern province (2) Western province (3) Northern province (4) South (5)

III. YEARS ON ART:

1: less than 6months

2: 6-12 months

3: more than 12 months to 2 years

4: more than 2 years

B. YEARS SINCE DIAGNOSIS:

1: less than 6months

2: 6 months to 2 years

3: more than 2 years to 10 years

4: more than 10 years

Hematological profile of seropositive patients at CHUK/HIV follow-up clinic

IV. INITIAL CD4 COUNT

1. **CD4 less than 200**
2. **CD4 200-500**
3. **CD4 more than 500**

V. INITIAL VL 1

1. suppressed (less than 20) copies

2. less than 200 copies

3. 200-1000 copies

4. more than 1000 copies

VI. CURRENT VL 2

1. suppressed (less than 20) copies

2. less than 200 copies

3. 200-1000 copies

4. more than 1000 copies

V. ART REGIMEN:

1. **First line**
2. **second line**
3. **Third line**
4. **AZT containing regimen**

VI. BACTRIM PROPHYLAXIS: YES (1) NO-(0)

VII. UNDERLYING MEDICAL CONDITIONS: ----------

1. **Past Opportunistic infections: ----------**

2. **Current opportunistic infections: ----------**

VIII. History of blood transfusion: YES (1) NO (1)

IX. HIV clinical stage (details on the annexes):

stage 1□□

stage 2□□

stage 3 □□

stage 4 □□

X. Laboratory measurements

1. hemoglobin: ------g/dl

2. white blood cells: ---------cells/µl

3. platelet count: ----------×10⁹

4. vitamin B12 levels : --------

5. Serum iron: ----------

XI. management options :

1. **Iron. Supplementation**
2. **Vitamin B12 supplementation**
3. **Erythropoietin injection**
4. **Granulocyte colony stimulating factor**
5. **Blood transfusion**

ANNEX 3. IRB APPROVAL

UNIVERSITY of RWANDA

COLLEGE OF MEDICINE AND HEALTH SCIENCES

DIRECTORATE OF RESEARCH & INNOVATION

CMHS INSTITUTIONAL REVIEW BOARD (IRB)

Kigali, 2nd / February /2021

Dr Shumbusho Patrick
School of Medicine and Pharmacy, CMHS, UR

Approval Notice: No 020/CMHS IRB/2021

Your Project Title *"Hematological Profile of HIV Seropositive Patients At CHUK/ HIV Follow-Up Clinic "A Cross-Sectional Study of Patients Followed at The University Teaching Hospital of Kigali (CHUK)/ HIV Clinic"* has been evaluated by CMHS Institutional Review Board.

Name of Members	Institute	Involved in the decision		
		Yes	No (Reason)	
			Absent	Withdrawn from the proceeding
Prof. Kato J. Njunwa	UR-CMHS	X		
Dr Stefan Jansen	UR-CMHS	X		
Dr Brenda Asiimwe-Kateera	UR-CMHS	X		
Prof. Ntaganira Joseph	UR-CMHS	X		
Dr Tumusiime K. David	UR-CMHS	X		
Dr Kayonga N. Egide	UR-CMHS	X		
Mr Kanyoni Maurice	UR-CMHS		X	
Prof Munyanshongore Cyprien	UR-CMHS	X		
Mrs Rozindana Landrine	Kicukiro district		X	
Dr Gashoma Darius	UR-CMHS	X		
Dr Donatilla Mukamana	UR-CMHS	X		
Prof. Kyamanywa Patrick	UR-CMHS		X	
Prof. Condo Umutesi Jeannine	UR-CMHS		X	
Dr Nyirazinyoye Laetitia	UR-CMHS	X		
Dr Nkeramihigo Emmanuel	UR-CMHS		X	
Sr Malibobi Marie Josee	CHUK	X		
Dr Mudenge Charles	Centre Psycho-Social	X		

After reviewing your protocol during the IRB meeting of where quorum was met and revisions made on the advice of the CMHS IRB submitted on 27th January 2021, **Approval has been granted to your study.**

Please note that approval of the protocol and consent form is valid for **12 months**.

Email: researchcenter@ur.ac.rw P.O Box 3286 Kigali, Rwanda www.ur.ac.rw

CENTRE HOSPITALIER UNIVERSITAIRE
UNIVERSITY TEACHING HOSPITAL

Quality Health Care Training & Research

Ethics Committee / Comité d'éthique

08,Apr,2021 *Ref.:EC/CHUK/038/2021*

Review Approval Notice

Dear PATRICK SHUMBUSHO,

*Your research project: **"HEMATOLOGICAL PROFILE OF HIV SEROPOSITIVE PATIENTS AT CHUK/ HIV FOLLOW-UP CLINIC "***

During the meeting of the Ethics Committee of University Teaching Hospital of Kigali (CHUK) that was held on 08,Apr,2021 to evaluate your request for ethical approval of the above mentioned research project, we are pleased to inform you that the Ethics Committee/CHUK has approved your research project.

You are required to present the results of your study to CHUK Ethics Committee before publication by using this link:www.chuk.rw/research/fullreport/?appid=289&&chuk.

PS: Please note that the present approval is valid for 12 months.

Yours sincerely,

Dr Emmanuel Rusingiza Kamanzi
The Chairperson, Ethics Committee,
University Teaching Hospital of Kigali

ETHICS COMMITTEE
CHUK

Scan code to verify