



HEMATOLOGIC ABNORMALITIES AMONG HIV INFECTED CHILDREN ON HAART IN ST. PAUL'S HOSPITAL MILLENNIUM MEDICAL COLLEGE

BY: Tigist Belete(Pediatric Resident)

ADVISORS: Dr. Hilina (pediatrician and Pediatric cardiologist)

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ACRONYMS

SPHMMC.....ST. PAUL'S
HOSPITAL MILLENNIUM MEDICAL COLLEGE

G.C.....GREGORIAN
CALENDER

USA.....UNITED STATES OF
AMERICA

WHO.....WORLED HEALTH
ORGANIZATION

PI PRIMARY INVESTIGATOR

HIV.....Human
Immunodeficiency Virus

AIDS.....Acquired
Immunodeficiency Syndrome

MTCT.....Mother-to-Child
Transmission

VCT.....Voluntary Counseling and
Testing

UNAIDS United Nation's Programme
on AIDS

G-CSF.....Granulocyte Colony-
Stimulating Factor

GM-CSF Granulocytes Myeloid
Colony-Stimulating Factor

IVIG.....Intravenous
Immunoglobulin

Gp Glycoprotein

HAART Highly Active
Antiretroviral Treatment

AZT Zidovudine

NVP.....Nevirapine

RNA Ribonucleic Acid

DNA.....Deoxy-Ribonucleic Acid

ELISA.....Enzyme Linked Immuno
Assay

PCR Polymerase Chain
Reaction

NASBA..... Nucleic Acid Sequence
Based Amplification

PCR Polymerase Chain Reaction

Hb..... Hemoglobin

PCV..... Packed Cell Volume

RBC..... Red Blood Cell

ANC..... Absolute Neutrophil Count

ALC.....Absolute lymphocyte count

TWBC.....Total White Blood Cell
Count

DWBC.....	Differential White Blood Cell Count
CLWHAS	Children Living with HIV/AIDS
ART.....	Antiretroviral Treatment
CHBCS.....	Community Home Base Care Services
PMTCT	Prevention of Mother to Child Transmission
TB-DOTS.....	Tuberculosis Directly Observed Therapy short course
M & E.....	Monitoring and Evaluation

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1. ABSTRACTS

Background: In individuals infected with human immunodeficiency virus, hematological abnormalities are associated with increased risk of disease progression and death. The magnitude and severity of hematological abnormalities in those patients who are taking antiretroviral drugs have been studied previously . However this study will be conducted to determine the magnitude and severity of anemia, neutropenia, and thrombocytopenia in HIV infected children who are taking highly active antiretroviral therapy in St. Paul's hospital millennium medical college.

Objective: : The aim of this study was to determine the magnitude and severity of anemia, neutropenia and thrombocytopenia in HIV-infected children after initiation of ART .St. Paul hospital millennium medical collage

Material and methods: A cross sectional retrospective study was conducted for the study period from March 2021 to July 2021 G.C. Data was collected using a pretested and structured questionnaire. Patient card review was done.

Conclusion: ART positively or negatively affects the hematologic profile of HIV- infected children. The current study demonstrated the hematologic profile of this patients who took ART minimum of 6 months.

Keywords : anemia ,HIV, pediatrics, SPHMMC.

2. Introduction

2.1 Background :- The annual rate of new HIV infections globally was believed to be 1.7 million in 2019. 150,000 infections were among children <15 years of age (1). In both antiretroviral-treated and untreated individuals, different types of hematological abnormalities were documented, the most important being pancytopenia. These changes are related with increased risk of morbidity and mortality. Anemia is a common finding in patients with HIV infection and it is more prevalent in patients with advanced retroviral infection. Its prevalence ranges from 11.7% to 92% depending on the stage of HIV disease, sex, age, pregnancy status, and presence of opportunistic infections (OIs). As HIV disease progresses, the prevalence and severity of anemia also increases(2). Thrombocytopenia is a frequent complication of HIV infection, which is found in 4%–40% of the cases and can occur at any stage of the infection (3). Leukopenia, specifically neutropenia, is the third most prevalent hematologic abnormality in HIV-infected individuals. It may occur in 2%–30% of HIV patients with advanced disease (4) . Other causes include myelosuppressive drugs and OIs. Furthermore, HIV infection causes a decrease in cluster of differentiation (CD4+) lymphocytes as the infection progresses. This can directly result in lymphopenia. (5) Antiretroviral treatment (ART) is known to profoundly suppress viral replication. It increases CD4 cell count, delays disease progression and death; patients on highly active antiretroviral therapy commonly suffer from side effects of the drugs.(6) Each antiretroviral (ARV) drug is associated with specific adverse effects. Among the ARV drugs, zidovudine (AZT) remains the most widely used drug, resulting in myelosuppression. (7) There are studies on the hematologic effects of HIV infection in Ethiopia.

2.2. Statement of the problem

Altered hematopoiesis (blood cell production) occurs in patients with HIV infection. This change affects all three cell lines (red blood cells, white blood cells, and platelets) and consequently, HIV-infected patients may suffer from anemia, leucopenia, thrombocytopenia, or any combination of these three. They are common throughout the course of HIV infection and may be the direct result of HIV; at the stem cell level or the mature blood cell level; manifestations of secondary infections and neoplasms, or side effects of therapy. The use of cART could positively or negatively affect these parameters, depending on the choice of combination used. But generally, it will reverse most of the complications that are the direct result of HIV infection (8).

Anemia is the most commonly encountered hematologic abnormality, occurring in approximately 30% of patients with asymptomatic HIV and in as many as 75% to 80% of those with clinical AIDS; making it more common than thrombocytopenia or leucopenia in patients with AIDS (9). Its prevalence is significantly higher among HAART naive patients than those on HAART (10). Anemia is associated with progression to AIDS and shorter survival times and it is a predictor of poorer prognosis for HIV infected patients independent of the CD4 count.

Leucopenia and neutropenia and/or lymphopenia often accompany HIV, and their prevalence increases from asymptomatic HIV-infected individuals to individuals with AIDS. Severe uncommon infections such as spontaneous bacterial infections, and rare fungal infections like aspergillosis or mucormycosis may occur in the course of HIV infection due to neutropenia, which may be seen in half of HIV-infected patients. The commonest cause of neutropenia is the result of drugs such

as Zidovudine (AZT), the anti-CMV drug gancyclovir, or drugs used to treat cancers and tumors (10)

Thrombocytopenia is a common finding in individuals infected with HIV, occurring in about 40% of HIV-infected patients and the degree is generally mild to moderate; however, severe reduction of platelet count below 50,000/ μ L also occurs. With the advent of HAART, thrombocytopenia is more commonly seen in the setting of uncontrolled HIV infection and Hepatitis C co-infection. Thrombocytopenia in HIV infection can be due to either primary HIV-associated thrombocytopenia or secondary thrombocytopenia.

2.3 Rationale of the study

In individuals infected with human immunodeficiency virus, hematological abnormalities are associated with increased risk of disease progression and death. The magnitude and severity of hematological abnormalities in those patients who are taking antiretroviral drugs have been studied in Ethiopia. However this study was conducted to determine the magnitude and severity of anemia, neutropenia and thrombocytopenia in HIV infected children who are taking highly active antiretroviral therapy in SPHMMC ART follow up clinic.

4. Objectives

4.1 General objective

- To assess the hematologic abnormalities among HIV infected children on HAART following in St. Paul hospital millennium medical college.

4.2 Specific objectives

- To assess the post ART hematologic parameters in HIV patients
- To identify the associated factors

- **Methodology**
- **Study design**

A cross-sectional study was conducted from March 1 to April 30 2021 GC on 75 HIV- infected children.

4.1 Study area

This study was conducted in St. Paul's hospital millennium medical college ART clinic. St. Paul millennium medical college is the leading teaching and tertiary referral hospital under the federal ministry of health of Ethiopia. It's built in 1961 by emperor Haile Selassie in collaboration with German evangelical church, as a source of medical care for underserved populations.

4.2 Study design and period

Descriptive cross sectional retrospective study was conducted for the study period from January 1, 2015 to December 30, 2020 G.C. Data was collected from patient charts from March 1- April 30, 2021 G.C. Patient card review was done regarding the clinical evidences and investigations done and anthropometric assessment was done for each participants.

4.3 Source population

All HIV- infected children who has follow-up at pediatrics ART clinic in St. Paul hospital millennium medical collage.

4.4 Study population

All HIV-infected children who had follow-up at pediatrics ART clinic in St. Paul hospital millennium medical collage in the study period who fulfills the inclusion criteria's.

4.5 Inclusion criteria

- All pediatric HIV patients on follow up at ART clinic who took HAART for more than 6 month.
- Age less than 18 years

4.6 Exclusion criteria

- Patients who had traumatic injury or surgical interventions resulting in blood loss during the study period or within 3 months prior to the study period were excluded.
- Those children without complete chart.
- Patient who has hematologic malignancies.

4.7 Sample Size Determination and Sampling Technique

Since the study is a retrospective cross-sectional study. Using Purposive sampling technique, all pediatric HIV patients who are on follow up at our ART clinic, whose charts are available, from Jan.1, 2015 to Dec.30 2020, was included in the study.

4.8 Data collection

Data collection Was done by using structured and pre- tested questionnaire. It was collected from inpatient charts . Was prepared in English and was modified based on the pretest results before the study period. Relevant laboratory results was also included by revising the patient's medical records. The primary investigator has recheck the data collection forms to ensure their completeness and accuracy.

4.9 Dependent and independent variables

Dependent variable

Hematologic profile

Independent variable

Age

Sex

Weight

RBC

Hemoglobin

MCV

MCHC

RDW

Platelet count

Absolute Neutrophil count

Total Lymphocyte count

4.10 Data processing & analysis

After data collection, each data was checked for completeness based on the code given during data collection. The data was entered in to SPSS version 20 statistical package. Coding of individual questionnaires was checked before data entry into the software. Further data cleaning was performed to check for outliers, missed values and any inconsistencies before the data were analyzed using the software. Descriptive statistics was used to describe the independent variable. Bivariate analysis was done to see the association between dependent and independent variables using the binary logistics regression. These associations was analyzed A confidence limit of 95% and p- value less than 0.05 was considered statistically significant. A draft of the results was submitted to the advisors for approval.

4.11 Data Quality Assurance

- The questionnaire was pretested and the pretest results was not included in the study
- The main investigator supervised the data collection.
- Each day the collected data was checked for accuracy and completeness.

4.12 Result Dissemination Plan

After the data is analyzed, the results of the research will be presented to SPHMMC's department of pediatrics and child health. The findings will be published in a relevant scientific journal and disseminated online so that they can be of use for other academic researchers and clinical practitioners. It will also be presented on different conferences, and professional society meetings. The data can also serve as a base line for future studies.

4.13 Ethical Consideration

The proposal was submitted and clearance was sought from the ethical committee of SPHMMC.

5. Operational definition

Anemia, neutropenia and thrombocytopenia were defined based on WHO grading of hematologic toxicity.¹⁵ Accordingly, anemia was defined as hemoglobin (Hgb) concentration ≤ 10.5 g/dL for all children and further severity was classified into grades as follows:

- Grade 1: Hemoglobin level of 8.5–10.5 g/dL (mild anemia)
 - Grade 2: 7.5–<8.5 g/dL (moderate anemia)
 - Grade 3: 6.5–<7.5 g/dL (severe anemia)
 - Grade 4: <6.5 g/dL (severe life-threatening anemia)
- Thrombocytopenia: defined as platelet count <150,000/mm³ Thrombocytosis: defined as platelet count >450,000/mm³

Leukopenia: defined as white blood cell (WBC) count
<4000/mm³

Leucocytosis: defined as WBC count >12,000/mm³

Lymphopenia: defined as lymphocyte count <1500/mm³

Neutropenia: defined as absolute neutrophil count (ANC) of <1500/mm³, severity further classified as follows:

- Grade 1: 750–1500/mm³; mild neutropenia
- Grade 2: 500–750/mm³; moderate neutropenia
- Grade 3: <500/mm³; severe neutropenia
- Grade 4: <250/mm³; severe life-threatening neutropenia.

6. Results:- from a total of 208 HIV patients following at st'paul Hospital ART clinic 75 of them have fulfilled the inclusion criteria , with a complete charts were selected.

Median age of the subjects was 10years with interquartile range of (IQR 5,11) ,

More than half 39 (53%) of children were in early adolescents.

Female to male ratio 1:1.41

Majority of the participants were 58(72%) resided in an urban area. Almost half 42(56%) of children had lost either or both parents.

1/3rd of care givers were illiterate 23(30.7%), and 16(21.3) were collage graduates.

Half of participants 37(49.3%) were not disclosed their HIV status .

The proportion of study participants who received AZT- based regimen was 60(82%), Tenofovir (TDF) based regimen was 6(8%) , abacavir (ABC) based regimen was 4(5.3%) and 2nd line 5(6.7%).

Clinical parameters

:- we used WHO clinical staging to grade severity of disease, accordingly 48 (64%) were stage 1 and 2, whereas 27(36%) participants were in clinical stage 3&4.

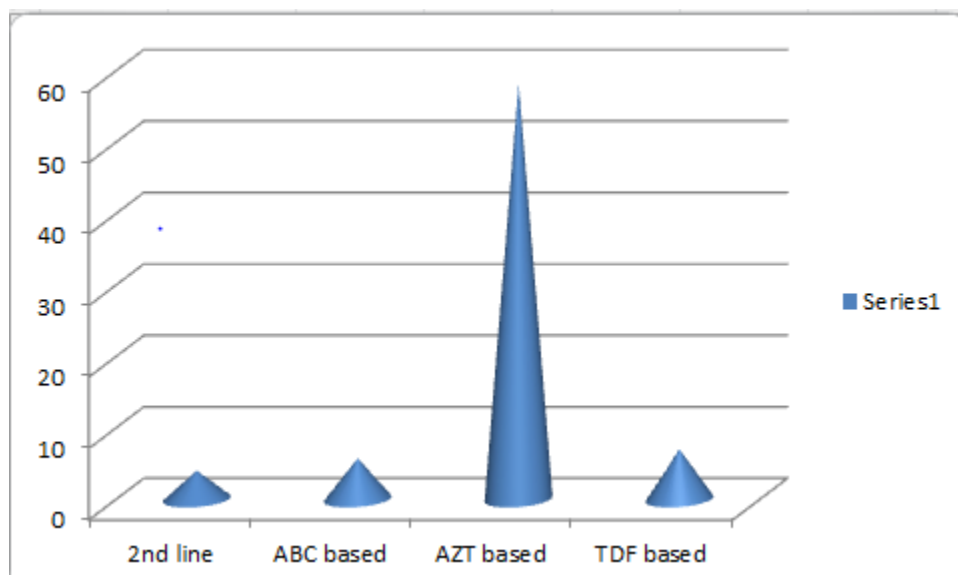
Upon evaluation of nutritional status 36 (48%) and 41 (54.7) were found to be underweight and stunted respectively.

Sever malnutrition using CDC Z score was identified in 14 (18.7%) of the participants.

In the current study pneumonia (33 (44%) and TB 4 (5.3%) were the top identified OI'S

The overall prevalence of OI's was 26 (34.7%).

Table 1 socio-demographic characteristics of of HIV -infected children having fo	Column	Column
variables	N%	
Age(years)		
<1.5	6(2.7)	
1.5-5	25(11.3)	
	10-May 71(32)	
	21-Jan 120(54.3)	
Sex		
Female	117(52.7)	
Male	105(47.3)	
Residency		
Urban	181(81.5)	
Rural	41(18.5)	
Parent status		
Both alive	112(50.5)	
Mother alive	70(31.5)	
Father alive	19(8.6)	
Both died	21(9.5)	
Educational status of caregivers		
Illiterate	75(33.8)	
Primary school	56(25.2)	
Secondary school	55(24.8)	
College/university	36(16.2)	
Employment status of caregivers		
Employed	159(71.6)	
Unemployed	63(28.4)	



Hematologic parameters

The median Hgb was 11 with IQR of (9.9, 14)

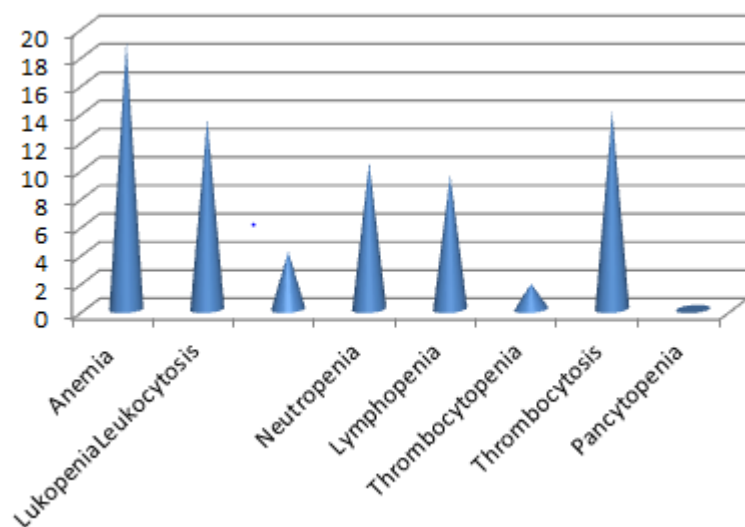
The prevalence of anemia was 24% figure 2 and table 2 , of 24% of study subject with anemia ,80% were taking AZT based regimen and 7.14% of them were on TDF based regimen.

Based on MCV 53(70.7) of patients had normocytic anemia and 2 (2.7%) participants had macrocytic anemia

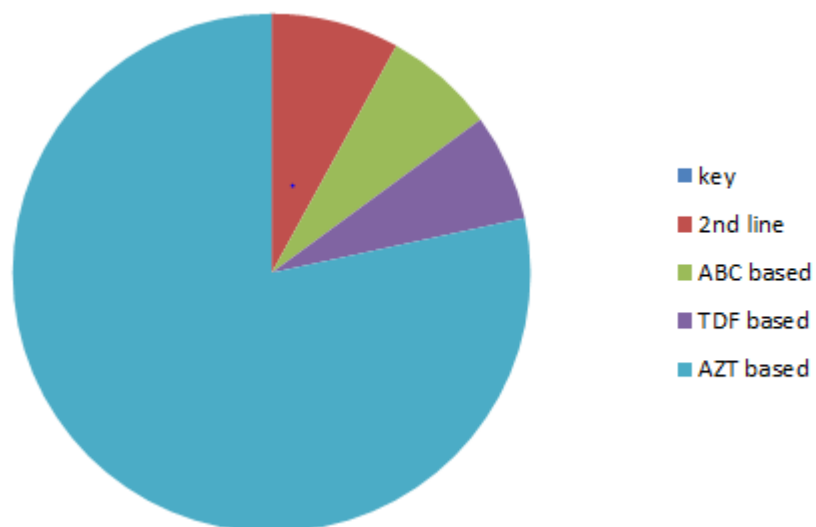
The median of ANC was 3 thousand with IQR of (1.5 , 3.9).

Table 2 clinical and laboratory characteristics of		HIV - infected children during follow up SPHMMC ,2021
variables	n%	p- value
Weight for age		
<0 SD	66(29.7)	
>0 SD	156(70.3)	
Height for age		
<0 SD	74(33.3)	
>- 0 SD	148(66.7)	
Weight for height, %		
<-3SD	5(6.7)	
b/n -3& -2	18(24)	
b/n -2&-1	23(30.7)	
b/n -1 & 0	29(38.7)	
opportunistic infections		
Tuberculosis	5(6.6)	
Persistent diarrhea	2(2.7)	
pneumonia	18(24)	
PCP	1(1.3)	
Other opportunistic infections	19(25.3)	
No opportunistic infection	30(40)	
Anemia		
Yes	38(50.7)	
leukocytes		
Leukopenia	24(32)	
Leukocytosis	5 (12.1)	
Normal	46(61.3)	
Neutrophil count		
Neutropenia	23(30.7)	
Lymphocyte count		

Lymphopenia	21(28)
Thrombocytes	
Thrombocytopenia	2(2.8)
Thrombocytosis	11(14.6)
Normal	62(82.2)



Hematologic profiles among HIV- infected children, SPHMMC 2021



Discussion

The current study investigated the occurrence of hematologic abnormalities among HIV-infected children. The most commonly identified were immune suppression, anemia and thrombocytopenia. The impact of HIV infection that can be found in the peripheral blood and bone marrow includes anemia, leukopenia, thrombocytopenia and thrombocytosis. These could be because of direct effects of the virus on the bone marrow, suppression of bone marrow by secondary infections or neoplasm causing ineffective hematopoiesis; additionally, nutritional deficiencies or drug side effects are also potential contributors.^{17,18} The well-known mechanism of CD4+T cell depletion in HIV patients is related to apoptosis in which the dying cells exceed the number of HIV-infected cells.. The Ethiopian guideline published in 2007 recommends use of AZT-based regimen as a first line treatment but for those children with Hgb <8.5 gm/dL, TDF- and ABC-based regimen was the preferred recommendation.²⁵ Each ARV drug is associated with specific adverse effects, among the ARV drugs, AZT remains to be the most widely used drug, resulting in myelosuppression.^{12–14} In the current study among children who were diagnosed to have anemia after ART, 85.7% of them received AZT-based regimen. The prevalence of anemia declined significantly after ART with increment of Hgb by 1.5 gm/dL. This is consistent with a study done in Jima, Ethiopia.²⁶ Other studies also showed significant improvement in Hgb and related hematological indices while on ART, even without specific additional treatment.²⁷ Thrombocytopenia was observed in 5.1% of the study patients, which is consistent with the study done in India, 7%,²⁴ in Uganda 8.3%,²³ and in Jima, Ethiopia, 7.8%.²⁶ Observation in other studies also identified thrombocytopenia in 10%–30% of HIV-infected patients and increased incidence was found to be associated with the progression of HIV disease.²⁸ Thrombocytopenia prevalence.²⁶ The mechanism of thrombocytopenia in HIV infection is mainly due to ineffective platelet production and increased platelet destruction by the spleen. In the current study, young age (<5 years), advanced stage and immunosuppression were independently associated with anemia which is consistent with other published studies.²⁹ Published literature on this area indicates that disease progression and severe immunosuppression are associated with cytokine-mediated myelosuppression resulting in multiple hematologic abnormalities, including anemia.³⁰ OIs are reported to attack the bone marrow in patients with HIV. These infections may cause marrow changes either directly by the organism itself or indirectly by causing reactive changes.³¹

Limitations- The current study has to be interpreted with few limitations. We did not identify the exact cause of anemia prior to ART.

Conclusion -We conclude that anemia was the top abnormality identified, followed by thrombocytopenia and leukopenia. After ART initiation, there was a significant improvement of the hematologic profile in the current study.

Acknowledgments We want to acknowledge SPHMMC and our colleagues who directly or indirectly helped us to finish this study.

8. Reference

1. Abebe M, Alemseged F. Hematologic abnormalities among children on Haart, in Jimma University Specialized Hospital, Southwestern ethiopia. *Ethiop J Health Sci.* 2011;19(2).
2. Beletew B, Mengesha A, Ahmed M, Fitwi A, Wudu M. Determinants of Anemia among HIV-Positive Children on Highly Active Antiretroviral Therapy Attending Hospitals of North Wollo Zone, Amhara Region, Ethiopia, 2019: A Case-Control Study. *Anemia.* 2020;2020.
3. Parinitha SS, Kulkarni MH. Haematological changes in HIV infection with correlation to CD4 cell count. *Australas Med J.* 2012;5(3):157–62.
4. EMOH 2010. Ethiopia Ministry of Health (EMOH) 2010. Health Sector Development Program IV 2010/11 – 2014/15. [Internet]. Vol. IV, Federal

- Democratic Republic of Ethiopia Ministry of Health. 2010. Available from: [http://phe-ethiopia.org/admin/uploads/attachment-721-HSDP IV Final Draft 11Octoberr 2010.pdf](http://phe-ethiopia.org/admin/uploads/attachment-721-HSDP_IV_Final_Draft_11Octoberr_2010.pdf)
5. UNAIDS. Global report: UNAIDS report on global AIDS epidemic 2016. UNAIDS, Geneva, Switz [Internet]. 2016; Available from: http://www.unaids.org/sites/default/files/media_asset/UNAIDS_FactSheet_en.pdf
 6. Joint United Nations Programme on HIV/AIDS (UNAIDS). UNAIDS data 2019 report. Vol. 268, Science. 2019. 350-350 p.
 7. Zheng J, Zhao D. Clinical, immunological, and virological outcomes of pediatric antiretroviral therapy in central China. BMC Res Notes. 2014;7(1).
 8. Musoke PM, Mudiope P, Barlow-Mosha LN, Ajuna P, Bagenda D, Mubiru MM, et al. Growth, immune and viral responses in HIV infected African children receiving highly active antiretroviral therapy: A prospective cohort study. BMC Pediatr. 2010;10.
 9. Debasu M, Menon M, Belayneh Y, Abebe W, Jerene D, Seifu D. Anti-retroviral Treatment Related Haematological Disorders among HIV- Infected Children Attending HIV Clinic at Yekatit 12 Hospital, Addis Ababa, Ethiopia. Int Blood Res Rev. 2015;4(2):1–18.
 10. Tsegay YG, Tadele A, Addis Z, Alemu A, Melku M. Magnitude of cytopenias among HIV-infected children in Bahir Dar, northwest Ethiopia: A comparison of HAART-naïve and HAART-experienced children. HIV/AIDS - Res Palliat Care. 2017;9:31–42.
 11. Geletaw T, Tadesse MZ, Demisse AG. Hematologic abnormalities and associated factors among HIV infected children pre- and postantiretroviral treatment, North West Ethiopia. J Blood Med. 2017;8:99–105.

12. Ebonyi AO, Oguche S, Ochoga MO, Agbaji OO, Anejo-Okopi JA, Abah IO, et al. Changes in the haematological parameters of HIV-1 infected children at 6 and 12 months of antiretroviral therapy in a large clinic cohort, North-Central Nigeria. *J Virus Erad.* 2017;3(4):208–11.
13. Ramaswamy S, Thandavarayan M, Thirumalaikumarasamy S, Sureshkumar A. A study on clinical profile of paediatric HIV infection in the age group of 18 months to 12 years and its correlation with CD4 count. *Int J Contemp Pediatr.* 2017;4(4):1232.
14. Moyle G, Sawyer W, Law M, Amin J, Hill A. Changes in the efficacy of thymidine analog-based HAART: a meta-analysis of six prospective, randomized, comparative studies. *Clin Ther.* 2004;26:1.
15. Aldeman H, Shekar M. Nutrition and health. In: Richard E. Behrman, editors. *Nelson Text Book of Pediatrics.* California: Elsevier; 2015:297–299.
16. Firnhaber C, Smeaton L, Saukila N, et al. Comparisons of anemia, thrombocytopenia, and neutropenia at initiation of HIV antiretroviral therapy in Africa, Asia, and the Americas. *Int J Infect Dis.* 2010;14(12):e1 088–e1092.
17. Zon LI, Groopman JE. Hematologic manifestations of the human immunodeficiency virus (HIV). *Semin Hematol* 1988;25:208–218.
18. Basu A, Ghosh K, Banerjee K. Bone marrow involvement in HIV infection: light, electron and immuno electron microscopic studies. *Indian J Hematol Blood Transf.* 1999;17(4):76–86.
19. Holm GH, Zhang C, Gorry PR, et al. Apoptosis of bystander T cells induced by human immunodeficiency virus type 1 with increased envelope/receptor affinity and coreceptor binding site exposure. *J Virol.* 2004;78:4541–4551.

20. Fevrier M, Dorgham K, Rebollo A. CD4+T cell depletion in human immunodeficiency virus (HIV) infection: role of apoptosis. *Viruses*. 2011;3(5):586–612.
21. Zheng J, Zhao D. Clinical, immunological, and virological outcomes of pediatric antiretroviral therapy in central China. *BMC Res Notes*. 2014;7:419.
22. De Santis GC, Brunetta DM, Vilar FC, et al. Hematological abnormalities in HIV-infected patients in University of São Paulo, Brazil. *Int J Infect Dis*. 2011;15:e808–e811.
23. Eunice N, Francis B, Julius K. Anemia in HIV-infected children: severity, types and effect on response to HAART in Rural Uganda. *BMC Pediatr*. 2012;12:170.
24. Dikshit B, Wanchu A, Sachdeva K, Sharma A, Das R. Profile of hematological abnormalities of Indian HIV infected individuals. *BMC Blood Disord*. 2009;9:5.
25. Federal Democratic Republic of Ethiopia Ministry of Health. Federal HIV/AIDS Prevention and Control Office. Guidelines for Pediatric HIV/AIDS Care and Treatment in Ethiopia. July 2007. Available from: http://www.ilo.org/wcmsp5/groups/public/---ed_protect/---protrav/---ilo_aids/documents/legaldocument/wcms_125387.pdf. Accessed June 15, 2017.
26. Muluneh A, Fessahaye A. Hematologic abnormalities among children on HAART in Jimma University Specialized Hospital
26. World Journal of Gastroenterology 2014 February 14;20(6):

Questionnaire

This is informed consent for a study to be conducted on Hematologic Abnormalities and Associated Factors Among HIV Infected Children at SPHMMC.

Good morning / good afternoon, My name is -----, I am currently a member of data collectors for a research which is conducted by Dr. Tigist Belete, a 3rd year pediatrics resident, on the study intended to determine the Hematologic Abnormalities and the Associated Factors. So I will ask you some questions related to the study. And you will give valuable information to identify factors associated. If you are willing to participate on this research, you need to understand and sign the agreement form. Your name or anything describing you and your child will not be mentioned to anyone. You have full right not to participate in this study but you will not loss any benefit from the result of the study and your participation is likely help us to meet the research objective. The study has approval and ethical clearance from the department as well as from hospital's ethical committee.. The interview will take only some minutes.

Do I have your permission to continue?

If, yes

Signature of the participant.....

Signature of interviewer.....

Date of interview

Part 1 Information on socio demographic characteristics of the care giver

1 Age yr

2 Sex 1.Male 2.female

3 Residence 1.Urban 2.Rural

4 Religion 1.Orthodox 2. Protestant 3 .Muslim 4. Catholic
5. Others

5 Marital status 1. Married 2. Single 3.Divorced 4.widowed

6 Level of education 1. Didn't read and write 2 .only read and write
3. Primary 4.secondary 5. College/university

7 Occupation 1.farmer 2.Government employee 3.house wife
4.merchant 5. private employee 6.Daily laborer 7.others

8 Monthly income Eth Birr

9 Family size

10 Relation with the child 1. Father 2. Mother 3. Grandparents
4.Relative (specify).... 5.Others

Part 2 Information on sociodemographic characteristics of the child.

- Age
 - <1.5yrs
 - 1.5-5 yrs
 - 5-10yrs
 - 10-18yr
- Sex
 - Male
 - Female
- Educational status
 - Not started
 - Kindergarten
 - Primary school(1-8)
 - Secondary school(9-12)
 - Others
- Birth order.....
- Address

Part 3 Information on clinical characteristics of the child

- 1 Age at diagnosis.....yrs
- 2 Duration of HAART.....yrs
- 3 ART regimen 6 mo.....
 12mo.....
 18 mo.....
- 4 Did the child take other medications than ART
 - Yes
 - No
- 5 If yes what medication
 - Bactrim
 - Anti TB
 - INH
 - Others (specify)
- 6 Who are responsible for medication of the child
 - Father
 - Mother
 - Siblings
 - Grand parents
 - Child him/her self
 - Other
- 7 Did the child lose any of his biologic parents
 - Yes
 - No
 - I don't know
 - If yes Mother only
 Father only
 Both
- 8 Does the child know about his illness Yes No
- 9 Weight 6 mo of ART..... KG

 12 mo of ART.....KG

 18 mo of ART.....KG
- 10 Height 6 mo of ART.....Cm
 12 mo of ART.....Cm
 18 mo of ART.....Cm
- 11 WHO clinical stage 6mo 12mo 18mo
 Stage 1 Stage 1 Stage 1
 Stage 2 Stage 2 Stage 2

		Stage 3 Stage 4	Stage 3 Stage 4	Stage 3 Stage 4
12	OI	6mo	12mo	18mo
	• TB • Persistent diarrhea • Pneumonia • PCP • Other OI's • No OI			
13	Anemia	6mo of ART	12mo of ART	18mo of ART
	Hgb	mg/dl	mg/dl	mg/dl
	MCV	fL	fL	fL
	MCHC	g/dl	g/dl	g/dl
	RDW	fL	fL	fL
14	Leukocyte	6mo of ART	12mo of ART	18mo of ART
	• Leukopenia • Leukocytosis • Normal			
15	Neutrophil count			
16	Lymphocyte count			
17	Thrombocyte count			