2020-07

Incidence and Predictors Of Anemia Among Adults On Human Immunodeficiency Virus Care at Debre Ta Bor General Hospital Art Clinic, From 2015 To 2019; Northwest Ethiopia.

Agimasie, Tigabu

BAHIR DAR UNIVERSITY

COLLEGE OF MEDICINE AND HEALTH SCIENCES

SCHOOL OF HEALTH SCIENCE DEPARTMENT OF ADULT HEALTH NURSING

INCIDENCE AND PREDICTORS OF ANEMIA AMONG ADULTS ON HUMAN IMMUNODEFICIENCY VIRUS CARE AT DEBRE TA-BOR GENERAL HOSPITAL ART CLINIC, FROM 2015 TO 2019; NORTHWEST ETHIOPIA.

BY: AGIMASIE TIGABU (BScN.)

A THESIS SUBMITTED TO THE DEPARTMENT OF ADULT HEALTH NURSING, SCHOOL OF HEALTH SCIENCE, COLLEGE OF MEDICINE AND HEALTH SCIENCE IN PARTIAL FULFILLMENT OF THE REQUIREMENTS FOR THE DEGREE OF MASTERS OF SCIENCE IN ADULT HEALTH NURS-ING.

JULY, 2020

BAHIRDAR, ETHIOPIA

Bahir Dar University

College of Medicine and Health Sciences

School of Health Science Department of Adult Health Nursing

A Thesis Report submitted to the Department of Adult Health Nursing, School of Health Science, College of Medicine and Health Science in Partial Fulfillment of the Requirements for the Degree of Masters of Science in Adult Health Nursing.

Full name of investigator	Agimasie Tigabu Demelash Cell phone: +251-0923525306 E-mail: ethiomom23@gmail.com
Name of advisors	Sr. Yeshwork Beyene (BSc, Assistant professor in Adult Health Nursing) Cell phone: +251-09 11 90 56 74 E-mail: Dagmawit2005natnael@gmail.com
	Mr. Getnet Dessie (BSc, MSc) Cell phone: +251-09 23 52 27 12 E-mail: ayalew.d16@gmail.com
Title of the research project	Incidence and predictors of anemia among adults on HIV care at Debre Tabor General Hospital ART clinic, Northwest Ethiopia.
Project area and period	Debre Tabor General Hospital from January 1, 2015 to December 30, 2019.

July, 2020

Bahir Dar, Ethiopia

Bahir Dar University

College of Medicine and Health Sciences

School of Health Science Department of Adult Health Nursing

This is to certify that the thesis prepared by Agimase Tigabu, entitled "**Incidence and Predictors of Anemia among adults on HIV care at Debre Tabor General Hospital from 2015 to 2019; Northwest Ethiopia"** and submitted in partial fulfillment of the requirements for the degree of "Degree of Master of Science in Adult Health Nursing" complies with the regulation of the university and meets the accepted standards with respect to originality and quality.

Name of candidate: Agimasie Tigabu Signature_____Date_____

Name of advisors

- Sr. Yeshiwork Beyene (BSc, Assistant Professor in Adult Health Nursing)
  - ✓ Signature_____
  - ✓ Date_____
- Getnet Dessie (BSc, MSc in Adult Health Nursing)
  - ✓ Signature_____
  - ✓ Date_____

Signature of Board of examiners (BoE)

External examiner_____ signature_____date_____

Internal examiner_____signature_____date_____

Chair person's name _____Signature _____Date_____

Acknowledgment

First, I would like to thank my advisors Sr. Yeshwork Beyene and Mr. Getnet Dessie for their meticulous advice and constructive comments from a selection of the topic to the overall process of the thesis preparation.

Secondly, I would like to thank Bahir Dar University, College of Medicine and Health Sciences, school of health science, department of adult health nursing for giving a chance to conduct this research project.

My deepest gratitude also goes to card room workers, data collectors, supervisor, and anti-retroviral therapy focal person and administers of Debre Tabor General Hospital for their valuable contribution to the realization of this study.

Abstract

Background: Anemia is a major public health problem that affects an estimated 1.62 billion people worldwide which equivalent to 24.8% the population. Few cross-sectional studies have been conducted on anemia and human immuno-deficiency virus. However, it cannot address the incidence and predictors of anemia among human immuno-deficiency virus [HIV] infected adults.

Objective: To assess incidence and predictors of anemia among adults on human immuno-deficiency virus care at Debre Tabor General Hospital ART clinic, 2020.

Methods: An institution-based retrospective cohort study was conducted among 434 HIV positive adults that have follow up from the 1st of January 2015 to the 30th of December 2019 at Debre Tabor General hospital. Computer-generated simple random sampling technique was employed to select the study participants. Ethical clearance was obtained from Institutional Review Board College of Medicine and Health Science, Bahir Dar University and also, I got permission letter from the concerned bodies in the hospital. Data were entered using Epi-data version 3.1, and analyzed by using STATA version 14.0. A Kaplan Meier survival curve and log rank test were used. Bivariable and Multivariable Cox proportional hazards model were fitted.

Results: The overall incidence density rate of anemia during study period was 6.27 (95% CI: 0.051, 0.077) per 100-person year. clinical stage III/IV (AHR=1.04; 95% CI=1.02, 1.06), Body Mass Index less than 18.5 kg/m2 (AHR=3.11; 95% CI= 1.56, 6.22), serum creatinine greater than 1.1 IU/L(AHR=2.07; 95% CI= 1.12, 3.81), fair/poor level of adherence(AHR=1.05; 95% CI= 1.03, 1.07) and anti-tuberculosis treatment (AHR=2.47; 95% CI= 1.10, 5.54) were statistically significant predictors of anemia while increased anti-retroviral treatment duration (AHR= 0.98; 95% CI= 0.97, 0.99) decrease the risk of anemia at 95 % confidence level.

Conclusion and recommendation: The overall incidence density rate of anemia was high. So that, prevention measures should be taken beside with HIV care especially, within 6-months ART initiation. Patients with clinical stage III/IV, under nutrition, serum creatinine greater than 1.1 IU/L, fair/poor level of adherence and taking anti TB treatment had significant predictors of anemia while increased anti-retroviral treatment duration decrease the risk of anemia.

Key word: Incidence, anemia, adults with HIV; antiretroviral therapy; Debre Tabor, 2020

Acronyms and abbreviations

AIDS	Acquired Immunodeficiency Syndrome
AHR	Adjusted Hazard Ratio
ALT	Alanine Amino Transferase
ART	Antiretroviral Therapy
AZT	Zidovudine
BMI	Body Mass Index
CD4	Cluster of differentiation 4
CPT	Cotrimoxazole Prophylactic Therapy
DTG	Dolutegravir
DTGH	Debre Tabor General Hospital
FMOH	Federal Ministry of Health
FDC	Fixed-Dose Combination
HAART	Highly Active Antiretroviral Therapy
HIV	Human Immunodeficiency Virus
HGB	Hemoglobin
OI	Opportunistic Infection
PLWHA	People Living With HIV/AIDS
PY	Person per year
RBC	Red Blood Cell
TB	Tuberculosis
WHO	World Health Organization

Table of Contents

List of tables

List of figures

1. Introduction

1.1. Background

Anemia is a hematological disorder results from low number or abnormal size of red blood cells. Consequently, hemoglobin concentration falls below the cut-off value, that can impair the capacity of the blood to transport oxygen to tissue (**1–3**).

World Health Organization [WHO] (**2**) definition, the level of hemoglobin concentration < 12 g/dl for non-pregnant women ≥15 years old and <13 g/dl for men ≥15 years old with smoking and altitude adjustment.

For human immuno-deficiency virus [HIV] infected nonpregnant women and men whose age ≥15 years old, anemia defined as; the level of hemoglobin concentration < 11 g/dl and morphological basis according to the size of erythrocytes; it is classified as Microcytic [mean corpuscular volume(MCV) <80 femtoliter (FL)], Normocytic (MCV 80-100 FL) and Macrocytic (MCV >100 FL) (**2,4,5**).

The major hypothesis that stated about the mechanism of anemia among HIV infected people is a disruption of bone marrow cytokine homeostasis that leads to hemopoietic progenitor cells inadequate to respond for anemia (**6,7**). In addition in HIV positive individuals, there is an obvious low red blood cell [RBC] production, high RBC destruction, and ineffective RBC production (**8**). This may be associated with neoplastic disease (e.g., Kaposi's sarcoma in the gastrointestinal tract) or gastrointestinal lesions that accompany opportunistic cytomegalovirus infection (**9,10**).

Anemia is a major public health problem that affects an estimated 1.62 billion people worldwide which equivalent to 24.8% the population (**11,12**), in which, one of the sufferers are HIV infected individuals. The prevalence of anemia among HIV positive adults, ranges between 23% and 51.9% globally(**11,13–17**), ranges between 16.2% and 69% in Africa (**18–25**) and between 11.4% and 42.9% in Ethiopia (**17, 21, 25–29**).

1.2. Statement of the problem

Anemia is a global public health problem, affecting both developing and developed countries which have an impact on the health and socio-economic development of nations (**3,11**). In low and mid income countries like Sub-Saharan Africa including Ethiopia, both human immunodefi-

ciency virus acquired immunodeficiency syndrome [HIV/AIDS] and anemia have considerable public health problems and continues to be a major co-morbidity among adult HIV patients (**18**).

The causes of HIV-related anemia include impaired hematopoiesis due to increased cytokine production, decreased endogenous erythropoietin production, blood loss, hemolysis that may result from RBC autoantibodies, infiltration of the bone marrow by neoplasm or HIV infection itself, opportunistic infections with Mycobacterium avium complex or parvovirus B-19 and drugs such as zidovudine or cotrimoxazole (**9,31**).

The comorbidity is high in these individuals who take antiretroviral treatment (ART) and those who are ART-naïve (**18,32**). Aside that from the total diseases occurrence patients with symptomatic HIV infection accounts for 75–80% of co morbidity (**27**). Regarding severity of the diseases, it increases with a decrease in Cluster of differentiation 4 [CD4] cell counts and advancement of HIV infection (**5,15,33**).

Anemia has increased the risk of acquired immunodeficiency syndrome (AIDS) related death more than double. This comorbid related high level of death can be explained by shorter time to immunologic disease progression, greater need for transfusions and poor quality of life (**10,34,35**). The presence of blood transfusion also has no role in minimizing mortality due to transfusion-related immunosuppression that finally increase diseases progression (**34**). Aside of physical impact anemia HIV co morbidity significantly decrease patients functional level which final leads to poor quality of life (**36**).

Hematological manifestations due to HIV infection often respond to combination antiretroviral therapy, However, zidovudine (AZT) is a commonly used part of antiretroviral therapy in resource-limited settings associated with myelotoxicity and risk of myelosuppression (**15,16**). AZT-induced anemia often occurs soon after initiating treatment and its hematological toxicity is thought to be dose-dependent with increase the risk of anemia with high dose (**10,37**). In particular, the probability of high intensity of adverse outcomes including early death increases in the first year of antiretroviral therapy (**25**).

Anemia leads to Poor physical functioning, psychological distress, poor quality of life, accelerated disease progression and shorter life expectancy (**18**) and suffer from fatigue, weakness, dyspnea, pallor, lethargy, depression, and impaired cognitive function (**5,10,38**). The Potential factors for HIV patients at risk for developing anemia were female sex, patients with low CD4 cell count

< 200 cells per mm3 and patients with advanced disease stage III / IV (**16,39,40**) and may result from genetic disorders, chronic diseases, and nutritional deficiencies (**9,38**).

Since test and treat programs launched in 2013, it has achieved remarkable improvements in the prevention of HIV related opportunistic infections [OIs] (**41–43**). Ethiopia is one of the countries, which adopted and implemented this program for HIV positive adults since June 2017 (taken from Amhara health bureau).

Optimization of current antiretroviral drug regimens is a critical component to support country efforts to achieve the 90/90/90 treatment targets and the goal of end of acquired immunodeficiency syndrome [AIDS] pandemic as a public health threat by 2030 (**44**). Following this, More than 50 low- and middle-income countries (LMICs) are including or planning to include dolutegravir (DTG) containing regimens in their national protocols, as the preferred first-line option, particularly the fixed-dose combination (FDC) tenofovir/lamivudine/dolutegravir at the end of 2017(**45**). Even though Ethiopia is one of the countries which adopted and implemented this new HIV drug in 2018, its impact on anemia is not understood.

Given the importance of knowing the incidence of anemia and its predictors in low-income settings is critical for improving health of HIV positive patients. However, research on incidence of anemia in low-income countries is relatively sparse.

Few available cross-sectional studies cannot address the incidence and predictors of anemia after the new regimen have been started especially, the study area. To address this gap in the literature, this study aims to assess the incidence and predictors of anemia among HIV-infected adults at Debre Tabor general hospital.

1.3. Significance of the study

Conducting this study among adults on HIV care will important to prevent, manage and reduce complications related to anemia for improving their health.

This finding will provide valuable information to health care providers, health care service and policymakers.

For health professionals: - to give emphasize anemia screening and management along with HIV care,

For health care service: - it can encourage linkage of ART care with health education, nutritional screening service, and anemia management strategies, and also;

For policymakers: - it may enhance decision making and planning of appropriate interventional strategies to prevent this comorbidity.

It will be also used as a baseline for prospective study by including variables that will not be assessed by this study, like dietary diversity assessment variables, income status and serum ferritin.

2. Literature review

The incidence rate of anemia among adults on ART

The incidence of anemia among HIV-infected patients on combination antiretroviral therapy (cART) throughout the world ranges from 6.6 to 22.9 per 100 person-years in African, Asian and America regions (**16**). The magnitude of anemia among HIV-infected patients in china was 51.9%. Of which 32.4%, 17.0%, and 2.5% were mild anemia, moderate anemia and severe anemia respectively (**13**).

Ikunaiye NY et al found that individuals on AZT containing regimen significantly increase the incidence of anemia in Nigeria among HIV-infected adults and adolescents who took AZT containing regimen have an incidence of 73.3 per 100 person-years at 6 months, and 60.5 per 100 person-years at 12 months, with an overall incidence of 22.3% (38.2 incidences per 100 person-years). The majority (75%) of the AZT-related anemia has occurred early with estimated time-to-event occurring within the first 3.8 months (**15**).

The evidence in South Africa showed that the incidence rate of anemia among HIV positive adults whose age ≥ 18 years was 3.1/1000 person-years (PY). It was highest in the first 3 months after ART initiation at a rate of 34.7/1000PY and decreased to 16.7/1000 PY between 3 and 6 months on treatment and then fairly stable over the remaining 18 months of follow-up, between7.7 and 8.4/1000PY and the magnitude of anemia at ART initiation was 25.8% (**46**)

Another evidence in Tanzania; revealed that the average incidence of anemia in HIV-infected adults who were in a care and treatment program was 60% (**10**) and among 346 adult patients on highly Active Anti-Retroviral Therapy were enrolled, of whom 100(40.46%) had moderate to severe anemia (**40**). Similarly in Congo among adult study subjects whose age ≥ 15 years showed that the incidence of anemia was 69% (**25**).

Ethiopia is also one of the countries that affected most with anemia. The Incidence was higher in patients who were taking Zidovudine containing regimen which is 44.5 per 100 person-years as compared to those patients who were taking non-Zidovudine containing regimen which is 26.01 per 100 person-years with overall incidence of 35.3 per 100 person years. Regarding time, the highest incidence was observed after 3 years of follow up in both categories (**39**). This significant level of anemia in Ethiopia was also indicated in another study with an incidence rate of 27

per 100 person years of observation from northwest Ethiopia. Of which, the highest incidence was at 6 month follow-up period (**47**). The magnitude of anemia has also reported in different part of the country. Anemia in the cohort of HIV-infected adults in northwest Ethiopia was found in 25% (**48**). In the capital city of Ethiopia, the magnitude of anemia among HIV positive patients was 42.9% (**30**) and another study also found that, it was 34.6% among HIV positive adults on ART while about 5%, 15.6%, and 14% of the patients had severe, moderate, and mild prevalence of anemia, respectively (**28**) and Prevalence of anemia before and after ART initiation was 41.9 and 11.4% respectively (**49**). In Wolaita Sodo University Teaching Referral Hospital, Prevalence of anemia among HIV positive patients was 36.5% (**22**). Similarly, In Hawassa, 13% of anemia was found among HIV positive patients. Majority of cases had mild anemia 58.5%, while 19.0%, and 22.5% of the patients had moderate and severe anemia respectively (**24**). In North Gondar, magnitude of anemia was found 11.7% and 29.7% among HIV positive patients who are on HAART and HAART naïve patients respectively (**29**). Similar evidence at Debre Tabor showed that, magnitude of anemia among HIV positive adults who are on ART was 23% (**18**) and 34% (**3**) at different study period.

Predictors of anemia

Various predictors contribute to the occurrence of anemia in HIV positive adults who are on ART which are discussed and showed different works of literature, mainly predictors of anemia are; socio-demographic characters, clinical characters, and treatment-related characters.

Socio-demographic variables

The available Literatures showed that, female and age ≥ 50 years have high risk of anemia (**10,23**). On the other hand, being married was reported as a protective factor when compared with being single (**10**). Different literatures in Africa showed that, the presence of significant relationship between being female sex increased risk of anemia (**3,10,23,46**). Single study from Malawian indicated that, the presence of relatively high risk of anemia among urban dwellers than rural (**23**).

Low literacy level, being Unemployed were also another socio demographic factors that significantly increased the risk of anemia among HIV positive patients on ART in low income countries including Ethiopia (**3,23,50**).

Clinical-related characteristics

In African countries, decreased BMI, decreasing CD4 T-cell count < 50 cells/μl, increased ALT$> 120 mmol/L$, and WHO clinical stage III/IV were some of the clinical factors which increase the risk of anemia among HIV positive patients on ART (**3,10,15,18,46**). The evidence showed that in Tanzania, The risk of being anemic were strongly predicted by low baseline CD4 count (< 200 cells/μl) and HIV stage 3&4 at enrollment and Most of the anemic patients had mean corpuscular volume of >100fl (**40**). There are also evidences from Ethiopia which reported the presence of significant high anemia among HIV positive patients with CD4 cell count <350 cells/μL and being bed ridden (**22,39**).

Treatment-related characteristics

In Tanzania; The risk of being anemic were strongly predicted by Zidovudine containing regimen (**10,40**), absence of cotrimoxazole prophylaxis and currently being treated for TB were significantly associated with an increased risk of anemia. Whereas, those who have retained on ART had low risk to develop anemia (**10**). Contrary to this, evidence from Nigeria indicated that the presence of high level of anemia among HIV positive adults who took Cotrimoxazole prophylaxis (**15**).

3. Conceptual framework

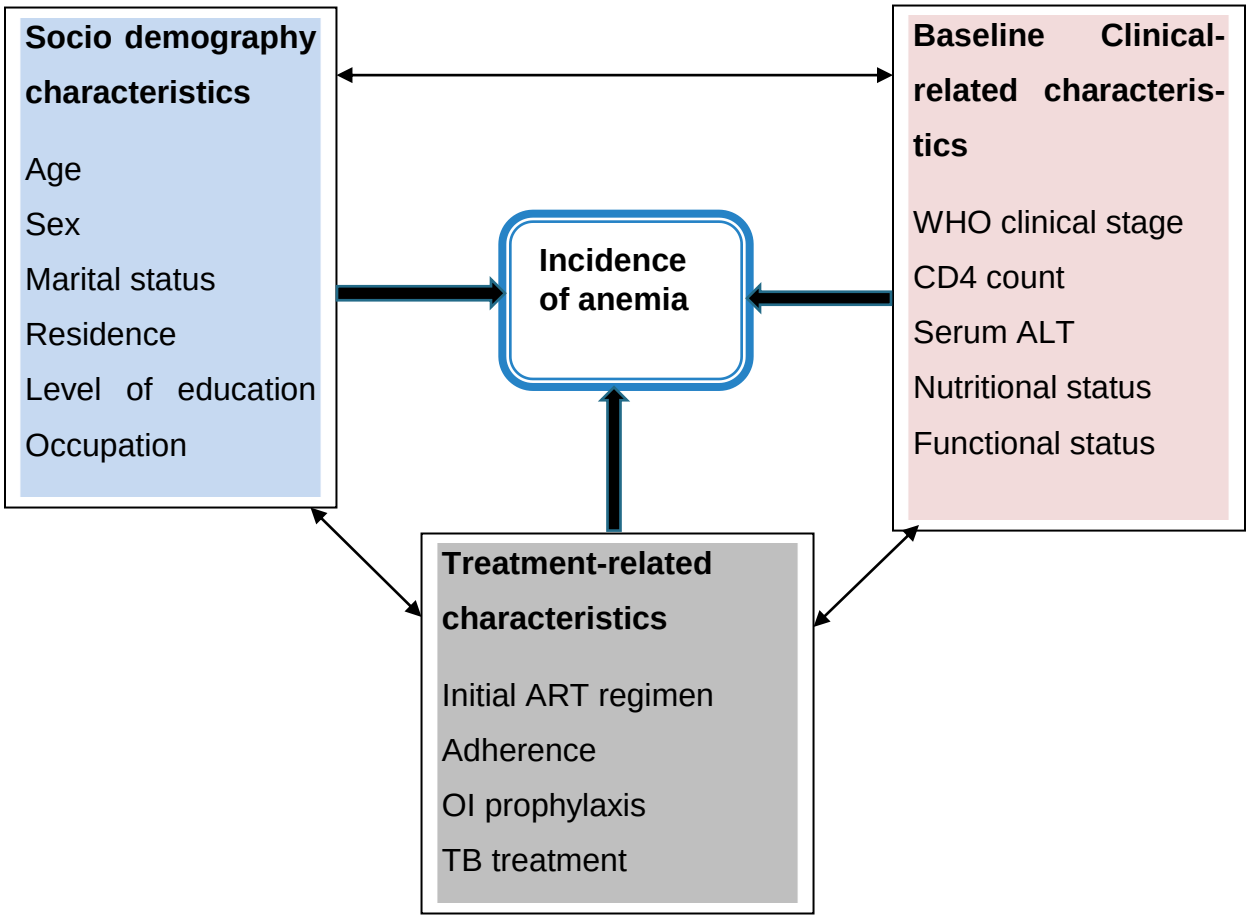

Figure 1: Conceptual framework of Anemia and its predictors among HIV infected adults who are on ART, adapted from various literature, 2019/2020 (3,10,15,18,23,28).

4. Objectives

4.1. General objective

- To assess incidence and predictors of anemia among adults on human immuno-deficiency virus care at Debre Tabor General Hospital ART clinic, from 2015 to 2019, Debre Tabor, Northwest Ethiopia.

4.2. Specific objectives

1. To determine the incidence of anemia among adults on human immuno-deficiency virus care at Debre Tabor General Hospital.
2. To identify predictors of anemia incidence among adults on human immuno-deficiency virus care at Debre Tabor General Hospital.

5. Methods and Materials

5.1. Study design

An institutional-based retrospective cohort study was conducted.

5.2. Study area and period

The study was conducted at Debre Tabor General Hospital which is found in Debre Tabor town ("Mount Tabor"). Debre Tabor is the capital town of the south Gondar zone. It is located 667 kilometers northwest of Addis Ababa, which is the capital city of Ethiopia and about 99 kilometers northeast of Bahir Dar, the capital city of the Amhara region and 50 kilometers east of Lake Tana.

The Hospital is the only general hospital in South Gondar Zone which was established in 1923 E.C. It serves a population of approximately 2.3 million people, including 55,596 residents living in the town of Debre Tabor, of whom 27,644 are men and 27,952 women. It started giving ART service in 1997 E.C and the case-team comprised trained physician, nurses, pharmacists, laboratory technicians, data clerks, and ART education adherence counselors. At the beginning, there were 3450 HIV positive patients enrolled at the ART clinic; now, there are 2210 patients on ART. Of them 2157 were adults (taken from ART data base from the hospital). The study was conducted from January 1, 2015, to December 30, 2019 Gregorian colander [GC].

5.3. Source population

All HIV positive adults ever started ART at DTGH ART clinic who had follow up.

5.4. Study population

All HIV positive adults ever started ART at DTGH ART clinic who have follow up and whose card available at the time of data collection.

5.5. Eligibility criteria

5.5.1. Inclusion criteria

Men and non-pregnant women HIV-infected adults (i.e. aged ≥15 years) who are on ART.

5.5.2. Exclusion criteria

Adults who had anemia at the beginning of the follow-up and incomplete baseline data for all listed important variables [age, sex, Hgb, BMI, baseline CD4 cell count, initial ART regimen and date of ART initiation] were excluded from the study.

5.6. Study Variables

5.6.1. Dependent variable;
Incidence of Anemia

5.6.2. Independent variables;
Socio demographic characters: (age, sex, residence, marital status, disclosure status, occupation, level of education).

Clinical characteristics: (WHO clinical stage, CD4 cell count, HIV viral load, previous TB history, functional status, serum creatinine level, serum alanine aminotransferase (ALT) and nutritional status).

Treatment-related: [initial ART regimen, level of adherence, treatment duration, Opportunistic infections (OIs) prophylaxis, TB treatment].

5.7. Operational definitions

Survival status: This is the outcome of adults on HIV care; either anemic or censored that ascertained by patient document review.

Event: The occurrence of anemia for HIV-positive adults after ART initiation until the end of the study that ascertained by patient document review.

Censored: Adults did not develop anemia (transfer out to other services, switch off antiretroviral therapy, Death, drop out, and still on ART in the Hospital) that ascertained by patient document review.

Time-to-event (anemia): Defined as the midpoint of the time interval between being case free and becoming a case.

The incidence rate of anemia: the occurrence of anemia dividing by the number of adult person-time at risk of the follow-up period and adjusted per 100 person-year.

Drop out: Defined as patients who missed visits to the same health facility for more than 3 months after the last scheduled visit (taken from ART follow up form).

Functional status: described as working, ambulatory, bedridden. (taken from ART follow up form).

Working: - able to perform normal activities.

Ambulatory: - able to perform activities of daily living, (like dressing, toileting).

Bedridden: - not able to perform activities of daily living.

Nutritional status: described as Well nourished, mild malnourished, moderately malnourished and severely malnourished (**51**).

Well nourished: - study participants, who have body mass index (BMI) ≥18.5 <25 Kg/m^2

Mild malnourished: - study participants, who have BMI ≥17 < 18.5 Kg/m^2

Moderately malnourished: - study participants, who have BMI ≥16 <17 Kg/m^2

Severely malnourished: - study participants, who have BMI < 16 Kg/m^2.

Over nourished: - study participants ≥ 25 Kg/m^2.

5.8. Sample size determination and sampling procedures

The sample size was determined by using a two-sample comparison of survival functions Log-rank test via Stata version 14.0 by using significant predictors for incidence of anemia in the previous studies in Ethiopia.

R: the ratio of non-exposed to exposed 1:1

P1= percent outcome in the exposed group,

P2=percent outcome in the unexposed group,

Z **α**/2=normal standard deviate at 0.05 **α** -level, the corresponding value of z is 1.96

Zβ = normal standard deviate at 80% power, the corresponding value of z is 0.84

Table 1: sample size determination by using predictors of previous study via Stata version 14.0 for incidence and predictors of anemia among adults on HIV care.

Associated predictors		P1 and p2	Adjusted Hazard ratio (95% CI)	Final sample size with 10% incomplete data
Nutritional status	BMI≥16 <17 Kg/m^2	P1=0.64	1.49(1.03-2.16)	434 (**47**)
	BMI≥18.5<25 Kg/m^2	P2=0.5		
Past pulmonary	Yes	P1=0.8	2.98(1.61-5.51)	190 (**47**)

TB	No	P2=0.6		
Sex	Female	P1=0.78	2.94(2.15-4.0)	44 (**47**)
	Male	P2=0.3		

According to the sample size calculation, we use the largest of all. So that, the determined final sample size was 434.

Computer-generated simple random sampling technique was employed to select Chart of the study participants and the selected charts were retrieved based on their medical registration number system. The way how to select charts of the study participants was already predetermined randomly going from up to down ward after locating the first medical registration number of the study participant from the available Excel data of HIV positive adults in the hospital.

5.9. Data collection tools and procedures

The data extraction checklist was adapted from the Federal Ministry of Health ART follow-up forms and the validity of the extracted checklist was evaluated by experts. Data were collected by using this validated and reliable checklist. By using patient charts socio-demographic variables, Clinical and treatment-related variables of HIV infected adults were extracted. Charts were retrieved by two card room workers based on their medical registration number. Data were collected by three BSc Nurses working at HIV care clinic that had comprehensive HIV care training. Additional one health care provider who has ART training certificate has participated as a supervisor. Once data extraction from patient charts has been completed, code was given for each chart to avoid duplication.

5.10. Data quality control

A pretest was conducted among 44 medical records to check the consistency of the abstraction tool; two-day training was provided for data collectors and supervisor about how to review the documents based on the inclusion criteria, how to calculate the charts of study participant follow up time, extract data from medical records for data collectors and about the entire data collection process. The filled formats were checked for completeness by the data collectors, supervisor and at last by principal investigator on daily bases.

5.11. Data processing and analysis

Data were entered using EPI-data Version 3.1, and analyzed using STATA Version 14 statistical software after clear and completed. Descriptive statistics were summarized using percentage and median, and presented using tables and figures. At the end of study, the outcome of each study participant was dichotomized into censored or event. Assumption of Cox proportional hazard regression model was checked using Schoenfeld residual and Log-Log plot tests. In addition, the model goodness of fit was assessed using Cox-Snell residual test. The Kaplan Meier survival curve was used to estimate the anemia free survival time of HIV-positive adults on ART. Log rank test was used to compare the survival curves of different categorical explanatory variables. Bi-variable Cox-proportional hazard regression model was used to select variables for the final model. Variables having *p*-value ≤ 0.25 in the bi-variable analysis were fitted into the multivariable Cox-proportional hazard regression model. Finally, adjusted hazard ratio with its corresponding 95% confidence interval was conveyed to declare the presence of significant association between the explanatory and outcome variables.

5.12. Ethical Considerations

Ethical clearance was obtained from Ethical Review Board of College of Medicine and Health science, Bahir Dar University. Permission letter was obtained from concerned bodies of Debre Tabor General Hospital. Names and unique ART numbers of patients was not included in the checklist. Moreover, data collectors and the supervisor were health professionals who have work experience in the ART clinic. Information retrieved was used only for the study purpose.

6. Results

6.1. Socio-demographic characteristics of adults on ART

A total of 434 charts were reviewed. In which, 411 HIV positive patient's medical records were included in the analysis with completeness rate of 94.7%. The median age of the entire cohort was 34 years (IQR; 12). More than half (52.1%) of people living with HIV [PLHIV] were females and 323(78.6%) were Orthodox Christian followed by Muslim 60(14.6%) and protestant 28(6.8%) follower. Majority, 245 (59.6%), of the patients came from urban areas. A total of 382 (92.9%) patients had disclosed their HIV status to either their husband/wife or other family members. Majority 251(61.1%) of them were unemployed. Regarding educational status only less than half (45.7%) of participants attained secondary and above 188(45.7%) (**Table 2**).

Table 2: Baseline socio demographic characteristics of HIV positive adults on ART at Debre Tabor General Hospital January 1, 2015 to December 30, 2019

Characteristics	Number[n=411]	Percent (%)
Age		
15 to <30	134	32.6
30 to <34	163	39.7
40 to <50	88	21.4
≥50 years	26	6.3
Marital Status		
Married	210	51.1
Never married	72	17.5
divorced	81	19.7
Widowed	48	19.7
Level of Educational status		
No education	123	29.9
Primary	100	24.3
Secondary	115	28
Tertiary and above	73	17.8
Occupation		
Employed	160	38.9
Unemployed	251	61.1
Residence		
Urban	245	59.6
Rural	166	40.4

6.2. Clinical and treatment related characteristics of HIV positive adults on ART

More than half of 245 (59.6%) the study participants had a normal nutritional status followed by mild acute malnutrition 57(13.9%), severe malnutrition 53(12.9) and moderate malnutrition 35(8.5%). A total of 186 (45.3%) of adults were WHO clinical stage one and more than half of 224(54.5%) adults had baseline CD4 count between 50 to 200 cell/ul.

Most of the study participants had normal baseline serum creatinine and serum alanine aminotransferase (ALT) 340(82.7%) and 354(86.1%) respectively. A total of 298(72.5%) adults were functional status of working at baseline.

The predominant regiments initially prescribed were a combination of TDF, 3TC and EFV (1e) 212(51.6%) followed by AZT, 3TC and NVP (1c) 76(18.5%). Two hundred six (60.1%) patients had changed their initial regimen during the follow-up period. From the total participants, 26(12.6%) patients switched to second line HAART. The reason for changing the initial regimen was due to new drugs available 99(48%) and due to drug side effects 80(40.2%). However, the remaining reason for changing the initial regimen was not recorded.

The present finding also showed that 331(80.5%) of the participants has good level of ART drug adherence and the mean of ART duration was 86.56 months (95% CI= 81.51, 91.61) (**Table 3**).

Table 3: Baseline Clinical and treatment related characteristics of HIV positive adults on ART at Debre Tabor General Hospital January 1, 2015 to December 30, 2019.

Variables	Frequency(n=411)	Percent (%)
Baseline WHO clinical stage		
Stage I	186	45.3
Stage II	80	19.5
Stage III	89	21.7
Stage IV	56	13.6
Baseline CD4 count		
>=200 cells/ul	139	33.8
50 to<200 cell/ul	224	54.5
<50 cell/ul	48	11.7
ART adherence		
Good	331	80.5
fair	58	14.1
poor	22	5.4
Functional status		
Working	298	72.5
Ambulatory	102	24.8
Bedridden	11	2.7

Past TB history		
No	342	83.2
Yes	69	16.9
Anti TB treatment		
No	317	77.1
Yes	94	22.9
Cotrimoxazole prophylaxis		
No	25	6.1
Yes	386	93.9
Isoniazid prophylaxis		
No	82	20
Yes	329	80
Initial regimen		
1j	9	2.2
1e	212	51.6
1a	50	12.2
ELSE*	64	15.6
1c	76	18.5
Changed Regimen		
No	205	49.9
Yes	206	60.1
Changed regimen type		
1j	99	48
1e	30	14.6
2f and 2h	26	12.6
ELSE**	26	12.6
1c	25	12.14
Recent viral load		
not detected	384	93.4
<150 cells/ul	15	3.6
150 to <1000	5	1.2
>=1000	7	1.7

ELSE*=[1b(d4t-3TC-EFV), 1d(AZT-3TC-EFV), 1f(TDF+3TC-NVP), 1g(ABC+3TC-EFV) and 1h(ABC-3TC-NVP)], **ELSE**=[**1a(d4t-3TC-NVP), 1b(d4t-3TC-EFV), 1d(AZT-3TC-EFV), 1f(TDF+3TC-NVP), 1g(ABC+3TC-EFV) and 1h(ABC-3TC-NVP)], 1j=(TDF-3TC-DTG), 2f=(AZT-3TC-ATV/r), 2h=(TDF-3TC-ATV/r).

6.3. Incidence of anemia during follow-up period

Four hundred eleven (411) study participants were followed for five years. which gave us 1419.63 person years of observation (PYO). During the follow-up period, 89 new anemia cases were observed. Hence, the overall anemia incidence density rate (IDR) in the cohort was 6.27 (95% CI:0.051, 0.077) per 100 person Years of observation and cumulative incidence was 21.65% while 322 (78.35%) were censored. Of the censored patients, 262 (81.4%) didn't develop anemia until the end of the study, 31 (9.6%) were transferred out, 18 (5.59%) were dropped out, 4 (1.24%) were lost to follow up and 7 (2.17%) were died.

Study participants were followed for a minimum of 0.67 and a maximum of 60.63 months. The median follow-up period was 49.03(IQR; 35.3) months.

The highest anemia incidence density rate of adults living with HIV after enrolling HIV care was 74.58(95% CI=0.24, 2.30) per 100 PYO (person Years of observation) in 6-months follow-up period and decreased to 25.5 (95% CI=0.11, 0.61), 33 (95% CI=0.23, 0.47), 18 (95% CI=0.12, 0.27) and 2.7 per 100 PYO (95% CI=0.02, 0.038) in the subsequent months of follow up (i.e. in 12-months, 24 months, 36 months and > 36 months) respectively.

Anemia incidence density rate stratified by different predictors; the highest Incidence density rate of anemia among HIV-positive adults who have higher baseline serum creatinine level was 26.69/100 PYO whereas, patients who have taken dolutegravir containing regimen (1j) did not develop anemia **(Table 4)**.

Table 4: Anemia incidence density rate stratified by socio-demographic, clinical and treatment related predictors among HIV positive adults on ART

Predictors	Frequency	PY	Anemia	Anemia IDR/100 PYO
Age category				
15 to <30	134	485.17	28	5.77
30 to <34	163	564.85	23	4.07
40 to <50	88	290.97	23	7.9
≥50 years	26	78.64	15	19.07
Sex				
Male	197	660.41	31	4.69
Female	214	759.22	58	7.64
Marital Status				
Married	210	757.42	30	3.96
Single	201	662.21	59	8.91
Level of Education				
No educated	123	402.05	42	10.45
Primary	100	351.29	25	7.12
Secondary and above	188	666.29	22	3.3
Occupation				
Employed	160	576.89	18	3.12
Unemployed	251	842.74	71	8.42
Residence				
Urban	245	888.82	31	3.49
Rural	166	530.81	58	10.93
Disclosure status				
Disclosed	382	1350.33	74	5.48
Not Disclosed	29	69.3	15	21.65
Baseline WHO clinical stage				
Stage I/II	266	948.33	21	2.21
Stage III/IV	145	471.3	68	14.43
Baseline CD4 count				
>=200 cells/ul	139	480.69	18	3.74
50 to<200 cell/ul	224	772.27	51	6.6
<50 cell/ul	48	166.67	20	12
BMI category				
Normal	245	899.89	14	1.56
over nutrition	21	79.12	2	2.53
under nutrition	145	440.62	73	16.57
Serum creatinine				
<= 1.1 IU/L	340	1221.06	36	2.95
>1.1 IU/L	71	198.57	53	26.69
ART adherence				

Good	331	1187.18	37	3.12
fair/poor	80	232.45	52	22.37
Functional status				
Working	298	1056.24	26	2.46
Ambulatory	102	333.06	55	16.51
Bedridden	11	30.33	8	26.38
Anti TB treatment				
No	317	1132.2	48	4.24
Yes	94	287.43	41	14.26
Cotrimoxazole prophylaxis				
No	25	87.73	9	10.25
Yes	386	1331.9	80	6
Isoniazid prophylaxis				
No	82	241.3	38	15.75
Yes	329	1178.33	51	4.33
Initial regimen				
1j	9	20	0	0
1e	212	417	40	9.59
1a	50	103	9	8.74
1c	76	164	**22**	13.41
ELSE*	64	124	18	14.52

ELSE*=[1b(d4t-3TC-EFV), 1d(AZT-3TC-EFV), 1f(TDF-3TC-NVP), 1g(ABC-3TC-EFV) and 1h(ABC-3TC-NVP)].

The cumulative probability of anemia free survival of adults on HIV care at the median follow up period (4.09 year) was 79% (95% CI= 0.74, 0.83) and at the end of fifth year was 71% (95% CI=.0.66, 0.76) **(figure 2).**

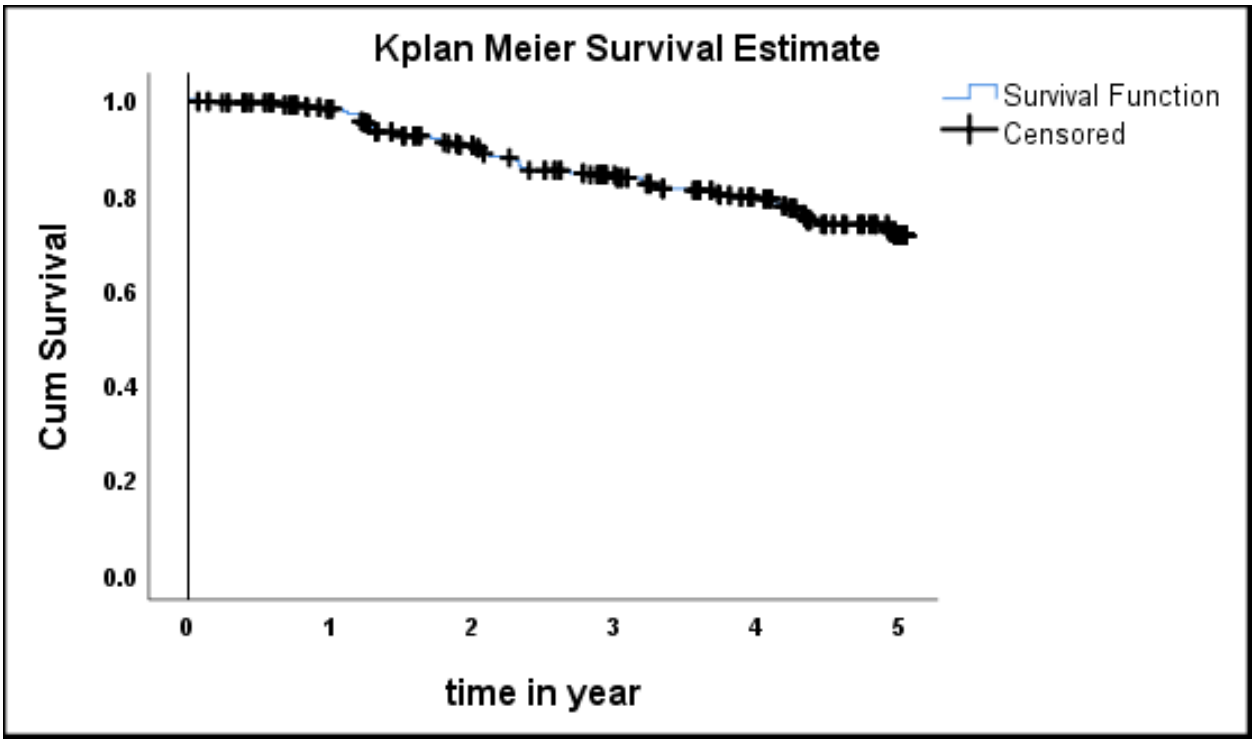

Figure 2: Kaplan-Meier curve of anemia-free survival probability among adults on HIV care at Debre Tabor Hospital, January 1, 2015 to December 30, 2019.

Log rank (Mantel-Cox) test of equality of survival for the different categories of explanatory variables (like, WHO clinical staging, Serum creatinine and TB treatment) had showed statistical difference of survival curves among the groups (**Table 5**).

Table 5: Log-rank test for equality of survivor distributions for the different levels of WHO clinical staging, TB treatment and serum creatinine

Categorical explanatory variables		Medians for survival time				Log rank test	
		Median estimate	Standard error	95% confidence interval		X^2	Sig.
				Lowe bound	Upper bound		
WHO clinical staging	Stage I/II	-----	-----	------	-----		
	Stage III/IV	53.33	3.923	45.641	61.02	76.56	0.000
Serum creatinine	≤1.1 IU/L	----	-----	-----	-----		
	>1.1 IU/L	38.23	5.27	27.91	48.55	168	0.000
TB treatment	No	---	----	----	----		
	Yes	50.83	4.8	41.39	60.27	39	0.000

Median Estimation is limited to the largest survival time

The median survival time of anemia free for patients with clinical stage III/IV was 53.33 months. Patients with stage I/II survive better and the difference was statistically significant between survival curves among the groups (p-value=0.000) **(Table 5, Figure 3).**

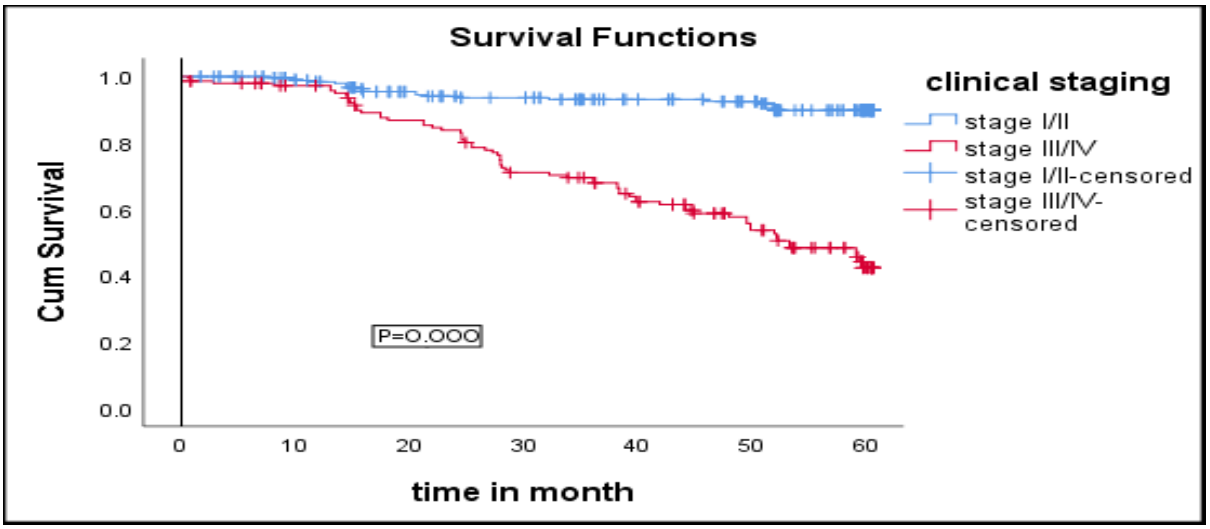

Figure 3: Kaplan-Meier survival curve of anemia -free survival proportion based on WHO clinical staging among adults on HIV care at Debre Tabor Hospital from 2015 to 2019.

The median survival time of anemia free for patients who have serum creatinine level > 1.1 IU/L was 38.23 months. Patients who have serum creatinine level ≤ 1.1 IU/L survive better and the difference was statistically significant between survival curves among the groups (p-value=0.000) **(Table 5, Figure 4).**

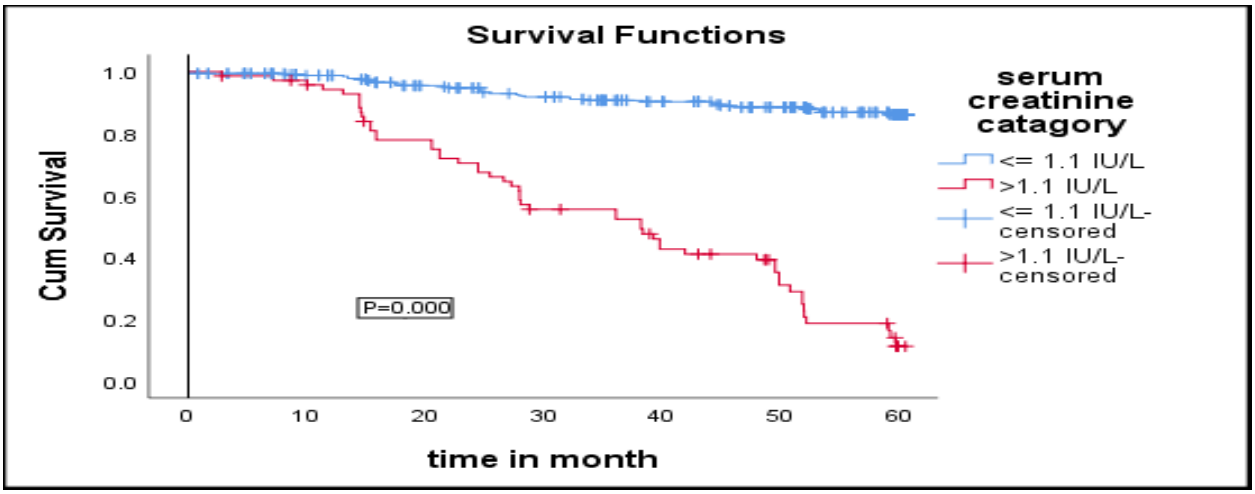

Figure 4: Kaplan-Meier survival curve of anemia -free survival proportion based on serum creatinine among adults on HIV care at Debre Tabor Hospital from 2015 to 2019.

The median survival time of anemia free for patients who are on anti TB treatment was 50.83 months. Patients who are not on anti TB treatment survive better and the difference was statistically significant between survival curves among the groups (p-value=0.000) **(Table 5, Figure 5).**

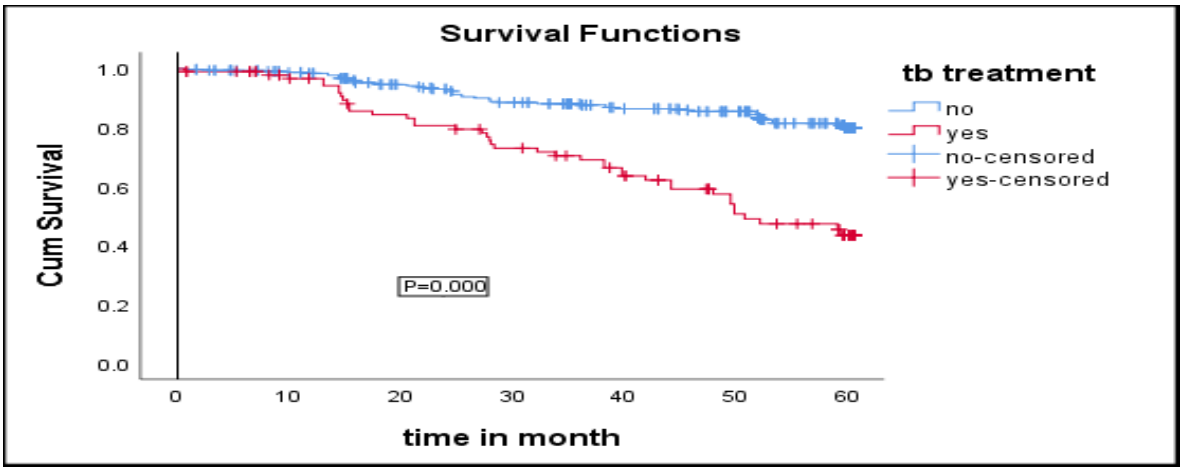

Figure 5: Kaplan-Meier survival curve of anemia -free survival proportion based on TB treatment among adults on HIV care at Debre Tabor Hospital from 2015 to 2019.

6.4. Cox-regression analysis

Age category, sex, marital status, residence, educational status, occupation, disclosure status, Baseline WHO clinical stage, baseline CD4 cell count, functional status at enrolment, level of adherence, undernutrition, serum creatinine, serum ALT, past TB history, TB treatment, cotrimoxazole prophylaxis, isoniazid prophylaxis and recent viral load were eligible for multivariable analysis. WHO clinical staging III/IV, undernutrition, increased serum creatinine, fair/poor adherence and TB treatment remained statistically significant predictors of anemia in multivariable Cox-regression analysis. On the other hand, increased ART duration decreased the risk of anemia.

The current finding showed that, the hazard of anemia among patients with WHO clinical stage III/IV was 1.04 times (AHR=1.04; 95% CI=1.02, 1.06) as compared to patients with WHO clinical stage I/II at any time. Similarly, the hazard of anemia among patients who were undernutrition was 3.11 times (AHR=3.11; 95% CI= 1.56, 6.22) as compared to those who were well-nourished at any time.

The present finding was also showed that, the hazard of anemia among patients who have baseline serum creatinine level greater than 1.1 IU/L was 2.07 times (AHR=2.07; 95% CI= 1.12, 3.81) as compared to those who have baseline serum creatinine less than or equal to 1.1 IU/L at any time. Similarly, the hazard of anemia among patients who have fair/poor adherence was 1.05 times (AHR=1.05; 95% CI= 1.03, 1.07) as compared to those who have good adherence. Additionally, the hazard of anemia among patients who were on anti TB treatment was 2.47 times

(AHR=2.47; 95% CI= 1.10, 5.54) as compared to those who were not on TB treatment. On the other hand, this study showed that, as ART duration increased by one month, the hazard of anemia was decreased by 2% times (AHR= 0.98; 95% CI= 0.97, 0.99) (**Table 6**).

Table 6: Bivariable and Multivariable analysis for predictors of anemia among HIV positive adults on ART at Debre Tabor General Hospital from January 1, 2015 to December 30, 2019.

Variables		Censored (n=322)	Anemia (n=89)	Crude HR (95% CI)	Adjusted HR (95% CI)	P-value
Age category_tvc	15 to <30 years	106	28		1	
	30 to <40 years	140	23	0.7 (0.41, 1.22)	1.0(0.98, 1.02)	0.729
	40 to <50 years	65	23	1.37(0.79, 2.38)	1.02(1.00, 1.04)	0.063
	>=50 years	11	15	3.37(1.8, 6.33)	1.01(0.99, 1.03)	0.434
Sex	Male	166	31		1	
	Female	156	58	1.61(1.04, 2.49)	1.16(0.67, 2.02)	0.593
Marital status	Married	180	30		1	
	Single	142	59	2.27(1.46, 3.52)	1.53(0.9, 2.62)	0.120
Residence	Urban	214	31		1	
	Rural	108	58	3.23(2.1, 5)	0.9(0.51, 1.75)	0.852
Occupation	employed	142	18		1	
	unemployed	180	71	2.76(1.64, 4.63)	0.74(0.26, 2.13)	0.582
Educational status	secondary and above	166	22		1	
	Primary	75	25	2.17(1.22, 3.85)	2.37(0.87, 6.42)	0.090
	not educated	81	42	3.24(1.93, 5.43)	1.84(0.68, 4.98)	0.230
Disclosure status	disclosed	308	74		1	
	not disclose	14	15	4.21(2.4, 7.37)	1.46(0.71, 3.02)	0.303
Clinical staging_tvc	stage I/II	245	21		1	
	stage III/IV	77	68	6.6(4.08, 10.87)	1.04(1.02, 1.06)	0.001 *
cd4 category	>=200 cells/ul	121	18		1	
	50 to <200 cells/ul	173	51	1.74(1.02, 2.98)	1.19(0.6, 2.34)	0.618
	<50 cells/ul	28	20	3.23(1.71, 6.11)	1.47(0.68, 3.15)	0.326
BMI category	Normal	231	14		1	
	Over nutrition	19	2	1.55(0.35, 6.83)	1.7(0.32, 9)	0.535

	Undernutrition	72	73	11.2(6.33,19.93)	3.11(1.56, 6.22)	0.001*
Serum creatinine category	<= 1.1 IU/L	304	36		1	
	>1.1 IU/L	18	53	10.2(6.65,15.76)	2.07(1.12, 3.81)	0.020 *
Serum ALT category	<=50 IU/L	302	52		1	
	>50 IU/L	20	37	6.31(4.12, 9.67)	1.49(0.85, 2.59)	0.164
Adherence category_tvc	Good	294	37		1	
	fair/poor	28	52	8.11(5.23, 12.47)	1.05(1.03, 1.07)	0.000*
Functional status	Working	272	26		1	
	ambulatory	47	55	6.88(4.31, 10.98)	1.04(0.51, 2.12)	0.918
	Bedridden	3	8	11.8(5.33, 26.13	0.45(0.13, 1.55)	0.206
Past TB history	No	286	56		1	
	Yes	36	33	3.62(2.36, 5.58)	1.02(0.51, 2.03)	0.953
TB treatment	No	269	48		1	
	Yes	53	41	3.48 (2.29, 5.29)	2.47(1.10, 5.54)	0.028*
Cotrimoxazole prophylaxis	No	16	9		1	
	Yes	306	80	0.59(0.3,1.17)	0.63(0.24, 1.66)	0.355
Isoniazid prophylaxis	No	44	38		1	
	Yes	278	51	0.27(0.17, 0.40)	1.56(0.69, 3.52)	0.289
Recent viral load	not detected	307	77		1	
	<150 cells/ul	8	7	2.71(1.25, 5.88)	1.38(0.57, 3.35)	0.471
	>=150<1000	2	3	3.02(0.95, 9.57)	0.29(0.07, 1.23)	0.092
	>=1000	5	2	1.57(0.39, 6.4)	2.02(0.43, 9.5)	0.373
ART duration	…..	….	…	0.99(0.98, 0.99)	0.98(0.97, 0.99)	0.000*

tvc= time vary covariates; Variables in tvc equation interacted with time; Marital status: Single includes Unmarried, widowed and divorced; BMI=body mass index; ALT=alanine aminotransferase; ART= anti-retroviral therapy; IU/L=international unit per liter; Statistical significance at 95% CI, $P < 0.05$; ∗reference statistically significant.

6.5. Assumptions check and model fitness

On the graphical presentations, some categorical predictors are not fulfilling parallel line assumption. This indicates the presence of time dependent variables which are identified by correlation matrix partial residual test and those significant time dependent predictors are age, level of adherence and clinical staging. However, in global test, the model shows that the model is fit for cox proportional hazard. Because a p value of 0.083 indicates that we fail to reject null hypothesis that indicates the presence of model fitness. The goodness of fit test for Cox-proportional hazard regression model was done by Cox-Snell residual test in which the hazard curve was close to the reafline. This can assure from **figure 6**.

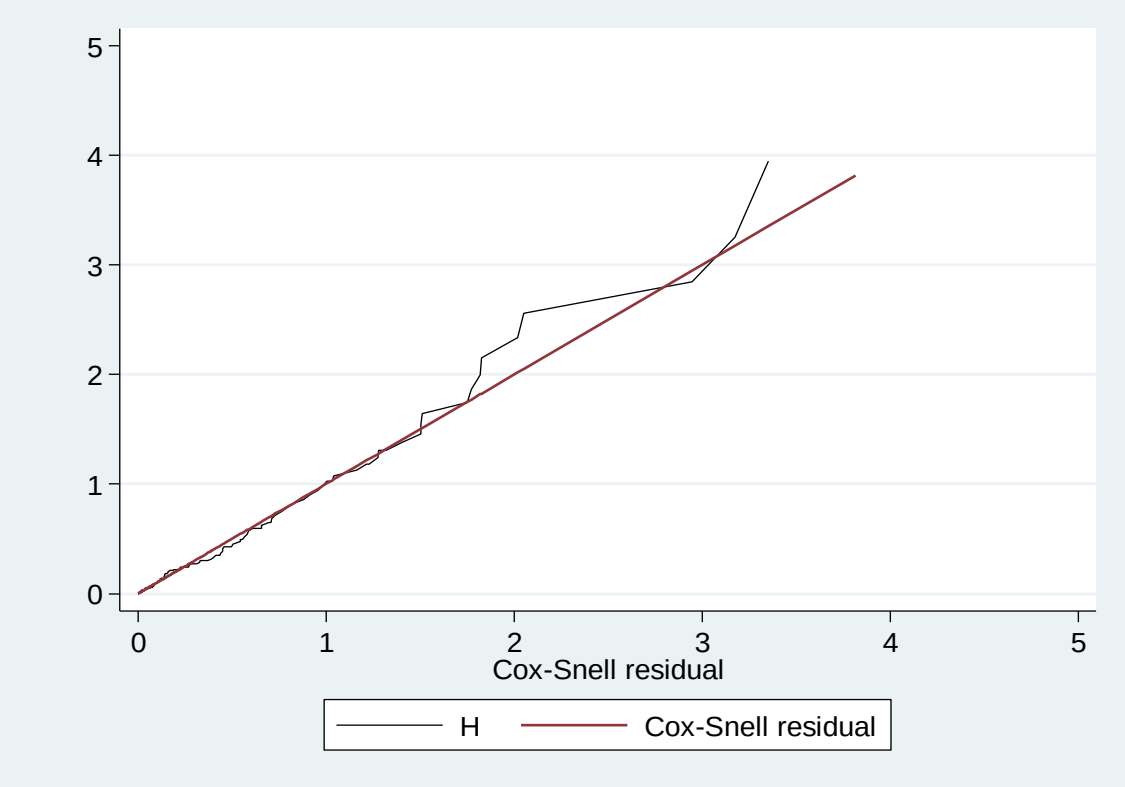

Figure 6: goodness of fit of cox proportional hazard regression model checked by cox Snell residual test

7. Discussion

This is a study of HIV positive adults whose ages greater than or equal to 15 years old under DTGH HIV care in the South Gondar zone, Amhara Regional State, northwest Ethiopia, to determine the incidence of anemia and identify its predictors.

Almost one fifth (21.6%) of the study participants develop anemia giving an incidence rate of 6.27(95% CI: 0.051, 0.077) per 100 person-years of observation (PYO). The overall incidence rate was lower than studies conducted in northwest Ethiopia 27/100 PYO (**47**) and in capital city of Ethiopia which accounted for 35.3/100 PYO (**39**). This noticeable discrepancy might be related to early initiation of ART for participants in the current study irrespective of CD4 count and WHO clinical staging (**41**) and availability of new drug regimen (dolutegravir containing regimen). This drug is associated with a more rapid viral suppression and higher genetic resistance barrier when compared with nonnucleoside reverse transcriptase inhibitors (**45**).

Similarly, the current finding is also lower than study conducted in Nigeria which was 38.2/100 PYO (**15**). This variation might be related with the utilization of zidovudine containing regimen in the previous study while this regimen has come down in the current study.

In this study, adults living with HIV who were clinical stage III/IV at baseline have a higher risk to develop anemia at any time as compared to those with WHO clinical stage I/II. This is supported by other evidence from Ethiopia(**28**), Tanzania(**10**), and South Africa (**46**). This is due to the fact that, having advanced WHO clinical staging compromise immunity which leads to viral duplication and higher loads of opportunistic infections which results in anemia via increased cytokine-mediated myelosuppression(**52**). The current study suggests the need for anemia preventive measures along with HIV care for those patients who have advanced disease stage. Additionally, early initiation of ART drugs and good adherence should be encouraged to prevent the progression of the advanced disease stage.

The current finding showed that, those HIV positive adult patients who were undernutrition at baseline have a higher risk to develop anemia at any time than those who were well nourished. This finding is similar with the studies conducted from northwest Ethiopia(**47**)**,** Tanzania(**10**) and South Africa (**46**). This is due to the fact that, patients who were undernutrition will have micronutrient deficiencies. The most common nutritional deficiencies are iron, folic acid, or vitamin B12(**38,53**). Nutritional deficiencies play a significant role in causing anemia in these pa-

tients(**54**). This finding suggests that improving nutritional status of people living with HIV/AIDS taking ART drugs through enhancing awareness of the benefit of consuming a balanced diet and micronutrient supplementation during treatment follow-up can be decreased anemia. Consuming balanced diet helps the body in producing and proliferating enough amounts of red blood cells (**55**).

This finding also showed that, A patient who has baseline serum creatinine level greater than 1.1 IU/L were more likely to develop anemia at any time as compared to those who have baseline serum creatinine less than or equal to 1.1 IU/L. Increased serum creatinine related to decrement of renal function to filter it which can result in blunt erythropoietin production in response to lower hemoglobin concentration(**56**). This finding suggests that, the need of erythropoietin treatment besides with regular monitoring of hemoglobin concentration for patients who have elevated serum creatinine.

The present finding also showed that, a patient who has fair/poor adherence was more likely to develop anemia at any time as compared to those who have good adherence. To the best of our understanding, patients who have missed their ART drug could be exposed to opportunistic infectious disease and increased the disease progression which leads to anemia via increased cytokine-mediated myelosuppression(**52,57**). This finding suggests that, more motivation, encouragement, and advice for HIV patients to adhere their ART drug therapy consistently so they can gain optimal therapeutic effect.

Additionally, patients who have taken anti tuberculosis treatment were more likely to develop anemia at any time as compared to those who did not take tuberculosis treatment. This is similar to the study conducted in northwest Ethiopia(**18**) and Tanzania(**10**). The Noticeable side effects of anti-tuberculosis drugs can account for a significant level of anemia among TB/HIV patients. The currently available TB drugs (i.e. Isoniazid and rifampicin) may directly cause hemolytic anemia and long term exposure to anti TB medications increased the risk of hypo- regenerative bone marrow disorder characterized by a reduction in the amount of hemopoietic production which leads to the reduction of red blood cell production(**58,59**). This finding suggests that, the need of more interventions, continuous monitoring and evaluation of TB patients for anemia during tuberculosis treatment.

On the other hand, this study showed that, as ART duration increased, the hazard of anemia was decreased by 2% times. It is in line with the study conducted at Black Lion Specialized Hospital,

Addis Ababa, Ethiopia(**49**) and in Tanzania(**10,25**). Once ART has been initiated for HIV patients, there is quite a suppression of viral load. That finally prevent and reverse anemia (18,35,55,60) and as the duration of its utilization increased, the patients have sufficient time to recover from advanced disease progression(**10**). Therefore, this finding suggested that need of more Interventions to promote adherence to ART and continuous patient counseling.

8. Limitation of the study

Data were collected from routine medical care records and there were limited data on possible predictors of anemia, such as socio-demographic like family size, disclosure status and clinical characteristics like baseline viral loads.

Some important variables like food diversity, serum ferritin level and income status can't be assessed.

Over or under estimation of anemia is expected due to excluded incomplete charts.

9. Conclusions

One out of five adult individuals develop anemia with high overall incidence rate.

WHO clinical stage III/IV, BMI less than 18.5 Kg/m2, serum creatinine greater than 1.1 IU/L, anti TB treatment and fair/poor level of adherence were Statistically significant predictors of anemia while increased ART duration decrease the risk of anemia.

10. Recommendations

Even if the overall incidence rate of anemia was lower as compared to previous studies in Ethiopia, still the incidence of anemia was high. So, prevention measures should be taken beside with HIV care especially within 6-months ART initiation.

- **To governmental and non-governmental organization**

Early initiation of ART drug and good adherence level should be encouraged to prevent advanced disease stage.

Well-integrated nutritional and HIV care system should be preserved to control the negative effect of under nutrition.

Anemia intervention measures for patients who are on anti TB treatment and elevating serum creatinine along with HIV care are highly suggested.

- **To health care providers**

Give emphasize adherence counseling and nutritional screening and its management along with HIV care.

Screening renal function test and its management should be preserved along with HIV care.

Special monitoring of serum hemoglobin concentration has to be given for those patients who are on anti TB treatment.

- **To researchers**

Prospective study should be conducted to include dietary diversity assessment variables, income status and serum ferritin.

11. References

1. Rachel Kyeyune1,2*, Elmar Saathoff4,5, Amara E Ezeamama6 , Thomas Löscher4 , Wafaie Fawzi7 and David Guwatudde3;Prevalence and correlates of cytopenias in HIV-infected adults initiating highly active antiretroviral therapy in Uganda;Kyeyune et al. BMC Infectious Diseases 2014, 14:496 http://www.biomedcentral.com/1471-2334/14/496.

2. Hemoglobin concentrations for the diagnosis of anaemia and assessment of severity VMNIS | Vitamin and Mineral Nutrition Information System; WHO/NMH/NHD/MNM/2011.

3. Zerihun KW, Bikis GA, Muhammad EA. Prevalence and associated factors of anemia among adult human immune deficiency virus positive patients on anti-retroviral therapy at Debre tabor Hospital, Northwest Ethiopia. BMC Res Notes. 2019 Dec;12(1):168.

4. Ministry of Public Health state of Quatar; Anaemia - assessment and classification; 2019 PDF.

5. Ajay Panwar, SC Sharma, Sanjeev Kumar1, Arti Sharm; A study of anemia in human immunodeficiency virus patients: Estimating the prevalence, analyzing the causative effect of nutritional deficiencies, and correlating the degree of severity with CD4 cell counts;[Downloaded free from http://www.mjdrdypu.org on Monday, November 25, 2019, IP: 196.190.96.7].

6. Sat_Arifa_Parker Anaemia.pdf [Internet]. [cited 2019 Dec 21]. Available from: https://sahivsoc.org/Files/Sat_Arifa_Parker%20Anaemia.pdf

7. OPIE, Jessica. Haematological complications of HIV Infection. South African Medical Journal, p. 465-468, mar. 2012.

8. Volberding PA, Levine AM, Dieterich D, Mildvan D, Mitsuyasu R, Saag M. Anemia in HIV infection: clinical impact and evidence-based management strategies. Clin Infect Dis. https://academic.oup.com/cid/article-abstract/38/10/1454/347195 by guest on 15 November 2019.

9. Mata-Marín JA, Gaytán-Martínez JE, Martínez-Martínez RE, Arroyo-Anduiza CI, Fuentes-Allen JL, Casarrubias-Ramirez M. Risk factors and correlates for anemia in HIV treatment-naïve infected patients: a cross-sectional analytical study. BMC Res Notes. 2010 Dec;3(1):230.

10. Hertzmark E, Petraro P, Sando D, Makubi A, Duggan C, Aboud S, et al. Determinants of Anemia Among Human Immunodeficiency Virus-Positive Adults at Care and Treatment Clinics in Dar es Salaam, Tanzania. The American Journal of Tropical Medicine and Hygiene. 2016 Feb 3;94(2):384–92.

11. Worldwide prevalence of anaemia 1993–2005 : WHO global database on anaemia / Edited by Bruno de Benoist, Erin McLean, Ines Egli and Mary Cogswell.

12. Kassebaum NJ, Jasrasaria R, Naghavi M, Wulf SK, Johns N, Lozano R, et al. A systematic analysis of global anemia burden from 1990 to 2010. Blood. 2014 Jan 30;123(5):615–24.

13. Shen Y, Wang Z, Lu H, Wang J, Chen J, Liu L, et al. Prevalence of Anemia among Adults with Newly Diagnosed HIV/AIDS in China. PLOS ONE. 2013 Sep 18;8(9):e73807.

14. Harris RJ, Sterne JA, Abgrall S, Dabis F, Reiss P, Saag M, et al. Prognostic importance of anaemia in HIV-1 infected patients starting antiretroviral therapy: collaborative analysis of prospective cohort studies in industrialized countries. Antivir Ther. 2008;13(8):959–67.

15. Ikunaiye NY, Denue BA, Aina BA, Aderemi-Williams R, Rawizza he. incidence of anaemia among HIV-infected patients treated with zidovudine-containing antiretroviral therapy in northeastern Nigeria. Ann Ib Postgrad Med. 2018 Dec;16(2):115–24.

16. Zhou J, Jaquet A, Bissagnéné E, Musick B, Wools-Kaloustian K, Maxwell N, et al. Short-term risk of anaemia following initiation of combination antiretroviral treatment in HIV-infected patients in countries in sub-Saharan Africa, Asia-Pacific, and central and South America. In: Journal of the International AIDS Society. 2012.

17. Semba RD, Shah N, Klein RS, Mayer KH, Schuman P, Vlahov D. Prevalence and Cumulative Incidence of and Risk Factors for Anemia in a Multicenter Cohort Study of Human Immunodeficiency Virus–Infected and –Uninfected Women. Clin Infect Dis. 2002 Jan 15;34(2):260–6.

18. Melese H, Wassie MM, Woldie H, Tadesse A, Mesfin N. Anemia among adult HIV patients in Ethiopia: hospital-based cross-sectional study. HIV AIDS (Auckl). 2017 Feb 14;9:25–30.

19. Denue BA, Kida IM, Hammagabdo A, Dayar A, Sahabi MA. Prevalence of anemia and immunological markers in HIV-infected patients on highly active antiretroviral therapy in Northeastern Nigeria. Infect Dis (Aucki). 2013;6:25–33.

20. Bhattad D, Kulkarni V, Bhave A, Balasubramanian M, Upase DP, Khude S. Refractory anaemia in an immunocompromised patient– J Assoc Physicians India. 2013;61(9):673–675.

21. Gebreweld A, Tsegaye A. Prevalence and Factors Associated with Anemia among Pregnant Women Attending Antenatal Clinic at St. Paul's Hospital Millennium Medical College, Addis Ababa, Ethiopia [Internet]. Advances in Hematology. 2018 [cited 2019 Dec 6].

22. Ageru TA, Koyra MM, Gidebo KD, Abiso TL. Anemia and its associated factors among adult people living with human immunodeficiency virus at Wolaita Sodo University teaching referral hospital. PLOS ONE. 2019 Oct 9;14(10):e0221853.

23. Adamu AL, Crampin A, Kayuni N, Amberbir A, Koole O, Phiri A, et al. Prevalence and risk factors for anemia severity and type in Malawian men and women: urban and rural differences. Popul Health Metrics. 2017 Dec;15(1):12.

24. Mengesha MB, Dadi GB. Prevalence of anemia among adults at Hawassa University referral hospital, Southern Ethiopia. BMC Hematol. 2019 Dec;19(1):1.

25. Akilimali PZ, Kashala-Abotnes E, Musumari PM, Kayembe PK, Tylleskar T, Mapatano MA. Predictors of Persistent Anaemia in the First Year of Antiretroviral Therapy: A Retrospective Cohort Study from Goma, the Democratic Republic of Congo. PLoS One [Internet]. 2015 Oct 16 [cited 2019 Nov 15];10(10).

26. Tamir Z, Alemu J, Tsegaye A. Anemia among HIV infected individuals taking art with and without zidovudine at Addis Ababa, Ethiopia. Ethiop J Health Sci. 2018 Jan 10;28(1):73.

27. Tesfaye, Yesuf, Oumer, Abdu, Muhie, Habtewold, Shibru; Prevalence and predictors of anemia among adult HIV infected patients at the University of Gondar Hospital, Northwest Ethiopia; HIV/AIDS - Research and Palliative Care 2019:11 211–217.

28. Gebremedhin KB, Haye TB. Factors Associated with Anemia among People Living with HIV/AIDS Taking ART in Ethiopia [Internet]. Advances in Hematology. 2019 [cited 2019 Nov 16]. Available from: https://www.hindawi.com/journals/ah/2019/9614205/

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

30. Assefa M, Abegaz WE, Shewamare A, Medhin G, Belay M. Prevalence and correlates of anemia among HIV infected patients on highly active anti-retroviral therapy at Zewditu Memorial Hospital, Ethiopia. BMC Hematology [Internet]. 2015 [cited 2019 Nov 20];15. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4455710/

31. Ssali F, Stöhr W, Munderi P, Reid A, Walker AS, Gibb DM, et al. Prevalence, incidence and predictors of severe anaemia with zidovudine-containing regimens in African adults with HIV infection within the DART trial. 2006 [cited 2019 Nov 25];

32. Martin C, Poudel-Tandukar K, Poudel KC. HIV Symptom Burden and Anemia among HIV-Positive Individuals: Cross-Sectional Results of a Community-Based Positive Living with HIV (POLH) Study in Nepal. PLOS ONE. 2014 Dec 31;9(12):e116263.

33. Negesse A, Getaneh T, Temesgen H, Taddege T, Jara D, Abebaw Z. Prevalence of anemia and its associated factors in human immuno deficiency virus infected adult individuals in Ethiopia. A systematic review and meta-analysis. BMC Hematology. 2018 Nov 12;18(1):32.

34. Dr. Patrick Sullivan, Fred Hutchinson,Associations of Anemia, Treatments for Anemia, and Survival in Patients with Human Immunodeficiency Virus Infection,The Journal of Infectious Diseases 2002;185(Suppl 2):S138–42.

35. Johannessen A, Naman E, Gundersen S, Bruun J. Antiretroviral treatment reverses HIV-associated anemia in rural Tanzania. BMC infectious diseases. 2011 Jul 11;11:190.

36. Habtamu Milkias Wolde, et al. (2014) Incidence and Risk Factors of Anemia among HIV/AIDS Patients Taking Anti-Retroviral Therapy at Tertiary Hospitals in Addis Ababa, Ethiopia: A Retrospective Cohort Study. J HIV AIDS Infect Dis2: 1-06.

37. World Health Organisation (WHO), 2016. Antiretroviral medicines in low- and middle-income countries: forecasts of global and regional demand for 2015–2020, Geneva. (http://www. who.int/hiv/pub/amds/2013forecast_report/en, accessed 28 March 2018).

38. Brentlinger PE, Silva WP, Vermund SH, Valverde E, Buene M, Moon TD. Practical Management of HIV-Associated Anemia in Resource-Limited Settings: Prospective Observational Evaluation of a New Mozambican Guideline. AIDS Res Hum Retroviruses. 2016 Jan 1;32(1):12–25.

39. Milkias H. Incidence and Risk Factors of Anemia among HIV/AIDS Patients Taking Anti-Retroviral Therapy at Tertiary Hospitals in Addis Ababa, Ethiopia: A Retrospective Cohort Study. Journal of HIV/AIDS and Infectious Diseases [Internet]. 2013 Aug 22 [cited 2019 Nov 15];

40. Gunda DW, Kilonzo SB, Mpondo BC. Magnitude and correlates of moderate to severe anemia among adult HIV patients receiving first line HAART in Northwestern Tanzania: a cross sectional clinic-based study. Pan African Medical Journal [Internet]. 2016 04 [cited 2019 Nov 20];23.

41. WHO, Revised Guideline on When To Start Antiretroviral Therapy And On Pre-exposure Prophylaxis For Hiv September, 2016.

42. NATIONAL GUIDELINES FOR COMPREHENSIVE HIV PREVENTION, CARE AND TREATMENT; FEDERAL MINSTRY OF HEALTH; Feb, 2017.

43. Consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection; CLINICAL GUIDELINES: ANTIRETROVIRAL THERAPY.

44. GLOBAL HEALTH SECTOR STRATEGY ON HIV 2016–2021.pdf.

45. DTG-TLD-arv_briefing_2018.pdf [Internet]. [cited 2019 Nov 28]. Available from: https://www.who.int/hiv/pub/arv/DTG-TLD-arv_briefing_2018.pdf?ua=1

46. Takuva S, Maskew M, Brennan AT, Sanne I, MacPhail AP, Fox MP. Anemia among HIV-Infected Patients Initiating Antiretroviral Therapy in South Africa: Improvement in Hemoglobin regardless of Degree of Immunosuppression and the Initiating ART Regimen [Internet]. Journal of Tropical Medicine. 2013 [cited 2019 Nov 16].

47. Manaye Y, Asrat A, Mengesha EW. Time to Development of Anemia and Predictors among HIV-Infected Patients Initiating ART at Felege Hiwot Referral Hospital, Northwest Ethiopia: A Retrospective Follow-Up Study. BioMed Research International. 2020 Mar 10; 2020:1–7.

48. Deressa T, Damtie D, Workineh M, Genetu M, Melku M. Anemia and thrombocytopenia in the cohort of HIV-infected adults in northwest Ethiopia: a facility-based cross-sectional study. EJIFCC. 2018 Apr;29(1):36.

49. Woldeamanuel GG, Wondimu DH. Prevalence of anemia before and after initiation of antiretroviral therapy among HIV infected patients at Black Lion Specialized Hospital, Addis Ababa, Ethiopia: a cross sectional study. BMC Hematology. 2018 Dec;18(1):7.

50. Gebremedhin KB, Haye TB. Factors Associated with Anemia among People Living with HIV/AIDS Taking ART in Ethiopia. Advances in Hematology. 2019 Mar 3;2019:1–8.

51. NACS-Users-Guide-Module2-May2016.pdf.

52. Gibellini D. Effects of human immunodeficiency virus on the erythrocyte and megakaryocyte lineages. World J Virol 2013;2(2):91-101. https://doi.org/10.5501/wjv.v2.i2.91.

53. Ajay Panwar, SC Sharma, Sanjeev Kumar1, Arti Sharma; A study of anemia in human immunodeficiency virus patients: Estimating the prevalence, analyzing the causative effect of nutritional deficiencies, and correlating the degree of severity with CD4 cell counts; January 22, 2020, IP: 197.156.97.148].

54. Panwar A, Sharma SC, Kumar S, Sharma A. A study of anemia in human immunodeficiency virus patients: Estimating the prevalence, analyzing the causative effect of nutritional deficiencies, and correlating the degree of severity with CD4 cell counts. Medical Journal of Dr DY Patil University. 2016 May 1;9(3):312.

55. Gebremedhin KB, Haye TB. Factors Associated with Anemia among People Living with HIV/AIDS Taking ART in Ethiopia. Adv Hematol [Internet]. 2019 Mar 3 [cited 2020 May 7];2019. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6421011/

56. McClellan WM, Jurkovitz C, Abramson J. The epidemiology and control of anaemia among pre-ESRD patients with chronic kidney disease. Europ J Clin Invest 2005;35(supp 3):58-65.

57. Tadesse S, et al., J Trop Dis 2014, 2:2 ; Adherence to Antiretroviral Treatment and Associated Factors among People Living with HIV/AIDS in Northwest Ethiopia; Journal of Tropical Diseases.

58. Kassa E, Enawgaw B, Gelaw A, Gelaw B. Effect of anti-tuberculosis drugs on hematological profiles of tuberculosis patients attending at University of Gondar Hospital, Northwest Ethiopia. BMC Hematol [Internet]. 2016 Jan 8 [cited 2020 May 7];16.

59. Ethiopia-National-guideline-for-TB-Leprosy-and-DR_TB-6th-ed-Aug-2018.pdf.

60. HAART improves anemia; a r i f a p a r k e r m i t c h e l ' s p l a i n h o s p i t a l / t y g e r b e r g h o s p i t a l; Johannessen et al. BMC Infectious Diseases 2011 11:190.

12. Annex

Annex 1: Information sheet form

Title of the Research Project: Incidence and predictors of anemia among HIV infected adults attending HIV care at Debre Tabor General Hospital from 2015 to 2019: A retrospective follow up study, Northwest Ethiopia.

Name of Investigator: Agimasie Tigabu (BSc in nursing)

Name of the Organization: Bahir Dar University, College of Medicine and Health Sciences, School of Health Science, Department of Adult Health Nursing.

Introduction: This information sheet is prepared for Debre Tabor General Hospital administration and Hospital HIV care clinic coordinating office. This form aims to make the above-concerned office clear about the purpose of research, data collection procedures and get permission to conduct the research.

Purpose of the Research Project: To assess the incidence and Predictors of anemia among adults on human immuno-deficiency virus care at Debre Tabor General Hospital ART clinic.

Procedure: To achieve the above objective, the information will be taken from HIV care medical record follow up forms which are necessary for the study.

Risk and /or Discomfort: Since the study will be conducted by taking appropriate information from the medical chart, it will not inflict any harm to the patients. The name or any other identifying information will not be recorded on the checklist and all information taken from the chart will be kept strictly confidential and in a safe place. The information retrieved will only be used for the study purpose.

Benefits: the research has no direct benefit for one whose document/ record is included in this research. But the indirect benefit of the research for the participant and other clients in the program is clear. This is because if program planners are preparing a predicted plan there is a benefit for clients in the program of getting appropriate care and treatment services. Of all, the research work has a paramount direct benefit for health care planners and managers.

Confidentiality: to reassure confidentiality the data on the chart will be collected by those individuals who are working on the HIV care clinic in the facility and information will be collected

without the name of the clients. The information collected from this research project will be kept confidential and will be stored in a file. Besides, it will not be revealed to anyone except the investigator and it will be kept in a key and locked system with a computer pass ward.

Person to contact: This research project will be reviewed and approved by the institutional review board of the College of Medicine and Health Science, Bahir Dar University. If you want to know more information, you can contact the committee through the address below. If you have any question you can contact any of the following individuals (Investigator and Advisors) and you may ask at any time you want.

1. **Agimasie Tigabu**: Bahir Dar University, College of Medicine and Health Science, School of Health Science, Department of Adult Health Nursing: principal investigator

   Cell phone: +251- 09 23 52 53 06

   E-mail: ethiomom23@gmail.com

2. **Sr. Yeshwork Beyene**: Bahir Dar University, College of Medicine and Health Science, School of Health Science, Department of Adult Health Nursing: Advisor

   Cell phone: +251-09 11 90 56 74

   E-mail: Dagmawit2005natnael@gmail.com

3. **Mr. Getnet Dessie**: Bahir Dar University, College of Medicine and Health Science, School of Health Science, Department of Adult Health Nursing: Advisor

   Cell phone: +251-09 23 52 27 12

   E-mail: ayalew.d16@gmail.com

Thank you for your cooperation:

Annex 2: Data extraction tool

The checklist is prepared for the collection of socio-demographic, clinical and treatment-related information on the patients ART follow up forms and patients' chart to assess incidence and Predictors of anemia among HIV infected adults who are attending HIV care at Debre Tabor General Hospital, Amhara Regional State, Northwest Ethiopia from 2015 to 2019.

Data collection date----------month----------Year----------

Name of the Hospital ----------

Name of data collector---------- signature----------

Name of supervisor----------signature----------

Code No._____

Part I: Socio demographic characteristics			**Remark**
101	Date of enrollment to HIV care	----------/---------/-------- DD/MM/YY	
102	Age at enrollment	----------Year	
	Current age	----------year	
103	Sex	1. Male 2. Female	
104	Marital status	1. Married 2. Never married 3. Divorced 4. Windowed	
105	Residence	1. Urban 2. Rural.	
106	Occupation	1. Employed 2. Not employed	
107	Educational status	1. Tertiary and above 2. Secondary 3. Primary 4. No education	
108	Religion	1. Orthodox, 2. Muslim 3. Protestant 4. Other	
109	Disclosure status	1. Disclosed 2. Not disclosed	
110	If yes for question No 109, for whom the participant discloses?	1. Wife/husband 2. Family members 3. Neighbors 4. Friends 5. Others(specify)-------	
111	Family size	---------	
112	Does the study participant use	1. No	If no-go to

	any of the substance?	2. Yes	question No 201
113	If yes to question No 112, which of the stated substance used?	1. Alcohol 2. Cigarette 3. Chat 4. Others(specify)----------	
Part II: clinical related characteristics: You can choose more than one, in the multiple-choice.			
201	WHO clinical staging at baseline	1. Stage I 2. Stage II 3. Stage III 4. Stage IV	
202	CD4 count at base line	--------- cells/µl	
203	Viral load at baseline	----------copies/mL	
204	Serum Hemoglobin at baseline	---------- g/dl	
205	Weight	(-------) kg	
206	Height	(--------) m	
207	BMI in kg/m^2	--------	
208	MUAC in cm	----------	
209	Serum creatinine	----------mmol/L	
210	Serum ALT	----------U/L	
211	Serum AST	----------	
212	Hepatitis B surface antigen	1. Positive 2. Negative	
213	Hepatitis C surface antigen	1. Positive 2. Negative	
214	Functional status	1. Working 2. Ambulatory 3. Bedridden	
215	Past TB history	1. Yes 2. No	
216	If yes to question No 215, what types of TB did the study participant have?	1. Pulmonary TB 2. Extrapulmonary TB 3 disseminated TB	
217	did the study participant have past TB Treatment?	1. Yes 2. No	
218	Does the study participant have comorbid cases	1. Yes 2. No	
219	If yes to Question No 218, what	1. Intestinal parasite	

	type of comorbidity did the study participant have?	2. Malaria 3. Asthma 4. COPD 5. allergic diseases 6. Other (specify)-------	
220	Opportunistic infection	1. Yes 2. No	
221	If yes, what type of infection	✓ TB ✓ CMV ✓ PCP ✓ Herpes simplex ✓ Kaposi sarcoma ✓ Toxoplasmosis ✓ Encephalopathy ✓ Wasting syndrome ✓ Herpes zoster ✓ PGL ✓ PML ✓ Candidiasis ✓ Diarrhea ✓ Pneumonia ✓ Other (specify)-------	
222	If yes for question no 220, When those OIs did occur	----dd----mm------yy, ----dd----mm------yy, ----dd------mm--------yy, ----dd-----mm---------yy, ---------- ----respectively	
Part III; treatment-related characteristics			
301	If yes for question No 215, what types of anti-TB treatment regimen had taken	……..	
302	If the study participant is on anti-TB currently, what types of regimen has taken?	----------	
303	Date confirmed HIV positive	DD------MM------YY-----	
304	Date ART started	DD------MM------YY-----	
305	Initial Regimen type	------	
306	Was the Regimen changed?	1. Yes 2. No	

307	If yes, when it was changed?	DD------MM------YY-----	
308	What is the new (changed) regimen?	----------	
309	Reason for switch	1. Adverse effects 2. Due to new TB 3. New drug available 4. Clinical failure 5. Immunologic failure 6. Virologic failure 7. Others (specify)----------	
310	Duration of treatment	----------	
311	Level of Adherence	1. Poor 2. Fair 3. Good	
312	If poor or fair Adherence for Question No 312, In why column note the reason?	1.drug side effect 2. share with others 3. forgot 4. felt better 5. too ill 6. stigma, the discloser 7. drug stock out 8. Lost/ran out of pills 9. Delivery/travel problems 10. Alcohol 11. Depression 12. Other(specify)-------	
313	Is the study participant have stopped follow-up	1. Yes 2. No	
314	If yes for Question No 314, For how long stopped the follow-up?	----------	
315	If stop, in why column, note reason	1. Toxicity 2. Treatment failure 3. Poor adherence 4. Illness (hospitalization) 5. Drugs out of stock 6. Other (specify)	
316	was OI prophylaxis given?	1. not given 2. Cotrimoxazole 3. INH 4. Other (specify)--------	

317	Multivitamin supplement	1.yes 2. No	

Part IV HIV Care/ART follow up form

Follow-up date (DD/MM/YY)										
Months on ART										
Nutritional assessment	Wt. (kg)									
	MUAC									
	BMI									
	N, UN/OW									
	Nutritional supplementation (Y/N)									
Functional status (W, A, B)										
WHO stage (I-IV)										
TB screen (P/N)										
TB prophylaxis/Rx										
OIs										
CD4 count /mm^3										
Recent Viral load										
Hemoglobin (Hgb)										
Serum creatinine										
Alanine aminotransferase (ALT)										
Aspartate aminotransferase (AST)										
Cotrimoxazole	ADH (G, F, P)									
	Dispense dose									
Other medication dispensed										
ARV drug	ADH (G, F, P)									
	Why									
	Dispense (dose/code)									
	Side effect									
	Reason for change									
The client set HIV prevention plan										
Next visit date (dd/mm/yy)										

401	Follow up frequency	1. Weekly 2. Monthly to 3 months 3. > 3 months	
	Did the patient develop anemia during follow up	1. Yes, 2. No	
402	When was it developed?	/ / D D/MM/YY	
403	Follow up conclusion	1. On follow up 2. Transferred out 3. Loss to follow up 4. Drop out 5. Dead 6. Other(specify)	
404	Last visit date	DD____MM____YY_____	

Name of data collector ----------sign ----------date ----------
Approved by ----------sign ----------date ----------

Annex 3: WHO HIV clinical staging and level of Adherence criteria

WHO Clinical stage 1: a person with confirmed HIV infection who is asymptomatic or persistent generalized lymphadenopathy (PGL)?

WHO Clinical stage 2: A person with confirmed HIV infection and having:

- Moderate unexplained weight loss (<10% of presumed or measured body weight)
- Recurrent respiratory tract infections (RTIs, sinusitis, bronchitis, otitis media, pharyngitis)
- Herpes zoster
- Angular cheilitis
- Recurrent oral ulcerations
- Papular pruritic eruptions
- Seborrheic dermatitis

- Fungal nail infections of fingers

WHO Clinical stage 3: Conditions where a presumptive diagnosis can be made based on clinical signs or simple investigations:

- Severe weight loss (>10% of presumed or measured body weight) Unexplained chronic diarrhea for longer than one month
- Unexplained persistent fever (intermittent or constant for longer than one month)
- Oral candidiasis
- Oral hairy leukoplakia
- Pulmonary tuberculosis (TB) diagnosed in the last two years
- Severe presumed bacterial infections (e.g. pneumonia, empyema, pyomyositis, bone or joint infection, meningitis, bacteremia)
- Acute necrotizing ulcerative stomatitis, gingivitis or periodontitis

WHO Clinical stage 4: Conditions where a presumptive diagnosis can be made based on clinical signs or simple investigations:

- HIV wasting syndrome
- Pneumocystis Carinii Pneumonia
- Recurrent severe or radiological bacterial pneumonia
- Chronic herpes simplex infection (orolabial, genital or anorectal of more than one month's duration)
- Esophageal candidiasis
- Extrapulmonary TB
- Kaposi's sarcoma
- Central nervous system (CNS) toxoplasmosis
- HIV encephalopathy

level of Adherence:

Estimate adherence using the table below. Adherence percent missed doses.

Level of adherence	**Percent (%)**	**(of 30 doses)**	**(of 60 doses)**
G(good)	$> 95\ \%$	$< 2\ doses$	$< 3\ doses$

F(fair)	85-94 %	2-5 doses	3-9 doses
P(poor)	$< 85\%$	$\geq 6\ doses$	$> 9\ doses$

Annex 4: Declaration

I, the undersigned, MSc Student declare that this thesis is my original work in partial fulfillment of the requirement for the degree of Master of Science in Adult Health Nursing.

Student's Name: Agimasie Tigabu

Signature: _____

Place of submission: department of Adult Health Nursing, school of health science, college of medicine and health science, Bahir Dar University.

Date of Submission: _____

This thesis work has been submitted for examination with my approval as university advisor(s).

Advisors, Name Date Signature

1. Sr. Yeshwork Beyene (BSc, MSc, Assistant professor) _____ _____
2. Mr. Getnet Dessie (BSc, MSc in AHN) _____ _____