

# Anemia and associated factors among HIV/AIDS patients treated with antiretroviral therapy at Mizan-Tepi University Teaching Hospital, Southwest Ethiopia

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## Abstract

**Introduction:** Human immunodeficiency virus (HIV) and treatments given to HIV patients to reduce complications and fast disease progression, cause a series of hematological abnormalities. Anemia is among hematologic manifestations commonly observed in HIV-positive persons on treatments, initiated by multiple factors. This study aimed to determine the prevalence of anemia and associated factors among patients on highly active antiretroviral therapy (HAART) at Mizan-Tepi University Teaching Hospital from June to September 2021.

**Material and methods:** A hospital-based cross-sectional study was conducted from June to September 2021 among HIV-positive patients on treatment at Mizan-Tepi University Teaching Hospital. Participants were selected with a convenient sampling technique, and pre-tested structured questionnaires were used for gathering important both socio-demographic and clinical data. Blood samples were collected for hemoglobin determination and CD4+ cell count. Data were entered using Epi-data manager and analyzed using a statistical package for social sciences.

**Results:** A total of 159 HIV/AIDS patients were included in the study. The overall prevalence of anemia was observed in 51 (32.1%) patients, out of which 20 (12.6% %) were males and 31 (19.5%) were females. Moreover, female subjects (AOR = 7.379; 95% CI: 2.369-22.985%), patients on HAART for ≤ 6 months (AOR = 6.065; 95% CI: 2.425-15.170%), and those with body mass index of < 18.5 kg/m<sup>2</sup> (AOR = 5.283; 95% CI: 1.312-21.267%) were factors showing statistically significant association with anemia.

**Conclusions:** A high prevalence of anemia was observed among patients on antiretroviral treatment. Routine screening and strict follow-up of patients on treatment are needed.

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**Key words:** anemia, prevalence, HIV/AIDS, HAART, Southwest Ethiopia.

## Introduction

Human immunodeficiency virus (HIV) infection is one of the major causes of anemia observed more with the disease progression [1]. Anemia causes impaired physical functioning, psychological distress, and poor quality of life as

well as reduces life expectancy in HIV-positive patients [2]. HIV and its therapy are the reason for a variety of hematological abnormalities, which are known as the most common causes of morbidity and mortality in HIV-positive patients, involving different factors [3, 4]. HIV infection results

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in different bone marrow abnormalities, which affect blood cell production both in terms of number and function [1, 5, 6]. The rate of progression and mortality in this subgroup of patients is high compared with non-anemic patients. In sub-Saharan Africa (SSA), with the advancement of antiretroviral therapy, the magnitude of anemia is not well-known [7]. It is among common hematological abnormalities in people living with HIV/acquired immunodeficiency syndrome (AIDS), and is a determining factor for disease progression and death.

Of the countries in SSA, Ethiopia is among the most HIV-affected nations [8]. Anemia may result from low production of red blood cells (RBC), increased RBC destruction, or ineffective RBC production [9]. The major cause of anemia is malnutrition associated with iron deficiency, folate deficiency, and infections, such as malaria, HIV, and helminthiasis [10].

HIV/AIDS can lead to anemia in many ways, such as a change in cytokine production and subsequent effect on hematopoietic concentration [11], administrations of therapeutic agents [12], and other mechanisms associated with HIV direct infection of bone marrow [13]. Diagnosis of anemia includes clinical laboratory methods, out of which the most reliable is the one that can detect anemia before the onset of symptoms by determining hemoglobin concentration. Anemia prevalence can be unrecognized; its health burden is high, being a threat to quality of life of those diagnosed [14]. Moreover, anemia is associated with more rapid disease progression from HIV to AIDS by decreasing the survival of CD4+ T cells. The risk of death in AIDS patients is up to 70% of anemia patients as compared with non-anemic individuals [15].

The burden of anemia in SSA is extensively high, accompanied by HIV infection and additional contribution of food insecurity that is common among persons with HIV who start receiving antiretroviral therapy. It makes anemia a major clinical case resulting in many illnesses and deaths [16].

In Ethiopia, despite the availability of highly active antiretroviral therapy (HAART) for more than 15 years, there is still insufficient data on the prevalence of anemia and its associated factors in HIV-positive adults [8].

The problem of anemia in many resource-limited settings, such as the study area, is even worse by the fact that population characteristics (e.g., endemic hereditary disorders) and prevalence of infectious diseases, such as malaria, tuberculosis, and intestinal parasitosis, may all add to the burden of anemia directly affecting the blood and its components (RBC) by altering the balance between production and destruction, hence leading to anemia. Although reports showed that Ethiopia has a large number of patients living with both HIV/AIDS and anemia, the magnitude of these cases among patients receiving HAART is not well-assessed in the frames of the study area.

Therefore, HIV/AIDS patients on antiretroviral therapy need strict follow-up for compliance with HAART protocol and care, which contributes to relatively low anemia

prevalence among individuals on antiretroviral therapy compared with naïve patients, to prevent further health complications.

## Material and methods

### Study area

The research was conducted at Mizan-Tepi University Teaching Hospital (MTUTH), located in the Bench Sheko Zone, Southwest Ethiopia, with a latitude and longitude of 7° 0' N 35° 35' E and an elevation of 1,451 meters. The hospital has different departments, including gynecology, outpatient, inpatient (medical and surgical), emergency, psychiatry, antenatal care, tuberculosis clinic, and youth-friendly and counseling wards. There are 57 general physicians, 10 specialists, 178 nurses, 44 midwiferies, 35 pharmacists, 22 health officers, 8 anesthetists, 1 dentist, 32 laboratories (technologists and technicians), 1 psychiatrist, 5 radiographers, 443 of total supportive staff, which add up to 861 (411 males and 450 females) of the total staff (data obtained from the hospital's official database).

### Study period and design, source and study population

A hospital-based cross-sectional study was conducted from June to September 2021 at MTUTH. The source population were HIV/AIDS-positive patients who attended MTUTH for therapeutic care or services, and included all HIV/AIDS-positive patients on HAART who were available during the study period and fulfilled eligibility criteria.

### Inclusion criteria

Study participants of age  $\geq 1$  year who were available during the study period and showed a willingness to participate in the study were recruited.

### Exclusion criteria

Patients who were on treatment for anemia for the last 3 months, who were taking iron supplementation, and HAART-naïve cases were excluded.

### Sample size determination and sampling technique

A single population proportion formula was used to calculate the sample size considering a 95% confidence interval and previous anemia prevalence for patients on HAART from Southwest Ethiopia (16.2%) (Gedefaw *et al.*) [17]. Based on these considerations, the sample size was calculated with the following formula:

$$= \frac{(Z_{\alpha/2})^2 \times p(1-p)}{d^2}$$

where  $n$  is the sample size,  $Z_{\alpha/2} = 1.96$  is the standard normal distribution at 95% confidence level,  $d = 0.05$  is the margin of error,  $p = 0.162$  is the prevalence of disease [17], and  $q$  is the probability of failure, which is  $1 - p = 0.838$ .

Using the above formula, we had:

$$= \frac{(1.96)^2 \times 0.162 (1 - 0.162)}{0.05^2}$$

Since our total population was less than 10,000, we used correction factor as follows:

$$n = n/1 + n/N$$

$$n = 209/1 + 209/922$$

$$n = 209.2$$

After adding a 10% non-response rate, the final sample size was  $230.12 \approx 230$ .

Study participants were recruited using a convenient sampling technique that employs selecting study subjects or participants who were available and easy to access/reach.

### Demographic data and blood sample collection

Data related to socio-demographic and economic characteristics were collected from the study subjects using pre-tested and structured questionnaires. The questionnaires were prepared in English and translated into local language to obtain information, such as hematological characteristics, stage of disease, treatment history, and co-morbidity status of related characteristics. Health professionals from different departments, including ART nurses as data collectors, and public health officers as supervisors participated in data gathering. World Health Organization 2011 report on the level of hemoglobin (Hgb) concentration to diagnose anemia was applied. Therefore, in males, anemia was defined as Hgb concentration of  $< 13$  g/dl (mild anemia: 11.0-12.9 g/dl; moderate anemia: 8.0-10.9 g/dl; and severe anemia:  $< 8.0$  g/dl), whereas in females, Hgb concentration was defined as Hgb  $< 12.0$  (mild anemia: 11.0-11.9 g/dl; moderate anemia: 8.0-10.9 g/dl; and severe anemia:  $< 8.0$  g/dl) [18]. Before data collection, patients were asked about their willingness to participate in the study, and the required information were collected with structured questionnaires, which were pre-tested at a similar facility 50 km away from the actual study site of Mizan-Tepi University Teaching Hospital.

### Sample processing

An average of 50  $\mu$ l of blood was collected into a tube containing EDTA anticoagulant for determination of hemoglobin level. Hematology analyzer (Horiba ABX Micros 60) unit, with a sensitivity of (94.6 to 99.8%) and specificity of (25.5 to 43.7%) at a 95% confidence interval was utilized for hemoglobin measurements after diluting the blood specimen with a reagent containing potassium ferricyanide. Oxidation of the ferrous ion of hemoglobin by potassium ferricyanide into the ferric ion of methemoglobin was performed, and then converted into stable cyanmethemoglobin by po-

tassium cyanide; its absorbance was measured at 550 nm wavelength for quantitation of the hemoglobin.

### Data analysis

A total of 230 patients were participating in the study, from which 71 patients (19 patients who were not willing to provide responses for the interview and 52 patients who refused to provide blood sample) were excluded from the analysis. Therefore, data of 159 patients were included in the analysis. Data entry and analysis were performed using Epi-data manager version 4.0.1.102 and SPSS version 25.0. Bivariate and multivariable logistic regression analyses (i.e., crude odds ratio and adjusted odds ratio) were done to assess the association between related factors and outcome variables. Descriptive assessment (i.e., cross-tabulation and frequency of each variable) was calculated.

### Quality assurance

To ensure the reliability and validity of the data, the following activities were applied before, during, and after the actual laboratory tests performed. The questionnaire was pre-tested in randomly selected HIV/AIDS patients at Mizan-Tepi General Hospital. Proper functioning of the fully automated device (Horiba ABX Micros 60) was checked with reagents (diluent: ABX Minidil LMG, 10 liters; cleaner: ABX Miniclean, 1 liter; and lyse: ABX Minilyse, 1 liter). Moreover, questionnaires and specimens were retained for re-checking.

### Ethical approval

Ethical clearance was obtained from the Research Committee of the College of Health Science and Medicine of Mizan-Tepi University. Before blood sample collection, the objectives of the study and procedure of sample collection were described to the study participants. Written informed consent was obtained from all study subjects (guardian or family member gave the consent if the patient was a minor).

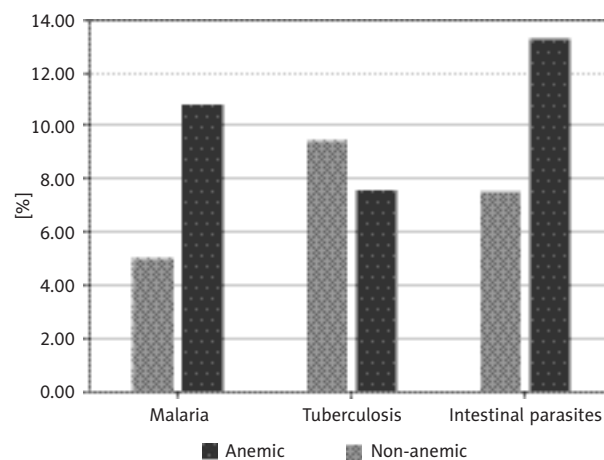
### Results

The study involved 159 HIV/AIDS-positive patients who were on HAART and attended MTUTH for care and services from June to September 2021, of which almost two-thirds were females. Anemia prevalence was higher among urban residents who accounted for two-thirds of the study subjects. The overall anemia prevalence in HIV/AIDS patients was 51 (32.1%), and a significant difference was observed between male and female study participants (Table 1). The patient's previous history of some related diseases was assessed using a structured questionnaire. The questionnaire was prepared before the start of data collection, and significant numbers of the study subjects reported having tuberculosis, intestinal parasites, and malaria, which probably influenced anemia prevalence among pa-

**Table 1.** Anemia prevalence among HIV/AIDS patients at MTUTH, and their socio-economic and demographic characteristics, 2021 ( $n = 159$ )

Variables/Category	Anemic, $n$ (%)	Non-anemic, $n$ (%)	Total, $n$ (%)
<b>Sex</b>			
Male	13 (8.2)	47 (29.6)	60 (37.7)
Female	38 (23.9)	61 (38.4)	99 (62.3)
<b>Age (years)</b>			
1-10	1 (0.6)	1 (0.6)	2 (1.3)
11-20	3 (1.9)	10 (6.3)	13 (8.2)
21-30	17 (10.7)	48 (30.2)	65 (40.9)
31-40	14 (8.8)	33 (20.8)	47 (29.6)
41-50	10 (6.3)	12 (7.5)	22 (13.8)
> 50	6 (3.8)	4 (2.5)	10 (6.3)
<b>Educational status</b>			
Cannot read and write	29 (18.2)	77 (48.4)	106 (66.7)
Can read and write	22 (13.8)	31 (19.5)	53 (33.3)
<b>Occupational status</b>			
Employed	11 (6.9)	19 (11.9)	30 (18.9)
Farmer	5 (3.1)	9 (5.7)	14 (8.8)
Merchant	7 (4.4)	8 (5.0)	15 (9.4)
Housewife	10 (6.3)	24 (15.1)	34 (21.4)
Daily laborer	1 (0.6)	3 (1.9)	4 (2.5)
Student	7 (4.4)	21 (13.2)	28 (17.6)
Others	10 (6.3)	24 (15.1)	34 (21.4)
<b>Income</b>			
Low	27 (17.0)	65 (40.9)	92 (57.9)
Middle	20 (12.6)	32 (20.1)	52 (32.7)
High	4 (2.5)	11 (6.9)	15 (9.4)
<b>Residence</b>			
Rural	15 (9.4)	30 (18.9)	45 (28.3)
Urban	36 (22.6)	78 (49.1)	114 (71.7)

Numbers may not add up to 100% because multiple variables are computed together.

**Figure 1.** Prevalence of anemia among patients with a previous history of diseases

tients with a previous history of a disease, with 8 (5.0%), 15 (9.4%), and 12 (7.5%), respectively (Figure 1).

The majority of the study participants who were found to be anemic in this study had a history of past opportunistic infections and co-infections. Sex (female), educational status (cannot read and write), duration on HAART ( $\leq 6$  months),

WHO clinical stage (III and IV), body mass index ( $< 18.5 \text{ kg/m}^2$ ), and exposure to health education showed significant association with the prevalence of anemia (Table 2). Accordingly, a total of 51 HIV/AIDS patients on antiretroviral therapy were found to have anemia on a certain level, i.e., mild anemia, moderate anemia, and severe anemia.

**Table 2.** Bivariate and multivariable logistic regression analysis of anemia and associated factors among HIV/AIDS patients on highly active antiretroviral therapy at MTUTH, 2021 ( $n = 159$ )

Variables/Category	Anemic, n (%)	Non-anemic, n (%)	Total, n (%)	OR (95% CI)	
				COR	AOR
<b>Sex</b>					
Male	13 (8.2)	47 (29.6)	60 (37.7)	Ref.	Ref.
Female	38 (23.9)	61 (38.4)	99 (62.3)	0.444 (0.213-0.927%)**	7.379 (2.369-22.985%)**
<b>Educationalstatus</b>					
Cannot read and write	29 (18.2)	54 (34.0)	83 (52.2)	0.759 (0.388-1.483%)	2.329 (1.013-5.355%)**
Can read and write	22 (13.8)	54 (34.0)	76 (47.8)	Ref	Ref
<b>Duration on HAART</b>					
$\leq 6$ months	38 (23.9)	46 (28.9)	84 (52.8)	0.254 (0.122-0.530%)**	6.065 (2.425-15.170%)**
$> 6$ months	13 (8.2)	62 (39.0)	75 (47.2)	Ref.	Ref .
<b>WHO clinical stage</b>					
I	4 (2.5)	50 (31.4)	54 (34.0)	0.827 (0.173-3.944%)	1.053 (0.363-3.054%)
II	3 (1.9)	31 (19.5)	34 (21.4)	Ref.	Ref.
III	16 (10.1)	9 (5.7)	25 (15.7)	0.045 (0.012-0.166%)**	0.066 (0.017-0.255%)**
IV	28 (17.6)	18 (11.3)	46 (28.9)	0.051 (0.016-0.167%)**	0.056 (0.017-0.188%)**
<b>CD4+ T cells/mm<sup>3</sup></b>					
$< 200$	33 (20.8)	45 (28.3)	78 (49.1)	0.620 (0.259-1.483%)	0.960 (0.311-2.968%)
200-500	8 (5.0)	41 (25.8)	49 (30.8)	Ref.	Ref .
$> 500$	10 (6.3)	22 (13.8)	32 (20.1)	2.330 (0.804-6.753%)	0.472 (0.126-1.766%)
<b>Presence ofco-infection</b>					
Yes	6 (3.8)	11 (6.9)	17 (10.7)	Ref.	Ref.
No	45 (28.3)	97 (61.0)	142 (89.3)	0.903 (0.307-2.653%)	0.840 (0.185-3.812%)
<b>Past opportunistic infections</b>					
Yes	2 (1.3)	5 (3.1)	7 (4.4)	Ref.	Ref.
No	49 (30.8)	103 (64.8)	152 (95.6)	1.153 (0.212-6.273%)	0.120 (0.010-1.458%)
<b>History of chronic disease</b>					
Yes	16 (10.1)	25 (15.7)	41 (25.8)	Ref.	Ref.
No	35 (22.0)	83 (52.2)	118 (74.2)	0.667 (0.315-1.411%)	1.606 (0.483-5.346%)
<b>Body mass index</b>					
$< 18.5$	26 (16.4)	70 (44.0)	96 (60.4)	0.595 (0.207-1.711%)	5.283 (1.312-21.267%)**
18.5-24.99	17 (10.7)	24 (15.1)	41 (25.8)	0.653 (0.181-2.360%)	0.515 (0.152-1.748%)
$> 24.99$	8 (5.0)	14 (8.8)	22 (13.8)	Ref.	Ref.
<b>Exposure to health education</b>					
Yes	16 (10.1)	89 (56.0)	105 (66.0)	Ref.	Ref.
No	35 (22.0)	19 (11.9)	54 (34.0)	0.039 (0.013-0.119%)**	13.981 (3.847-50.809%)**

Ref. – reference category. \*\*Significance with  $p$ -value  $< 0.05$ .

## Discussion

A total of 230 subjects were selected to participate in the study, of which 19 were not willing to respond to the interview and 52 refused to provide a blood sample for hemoglobin level determination. The majority of the study participants were females, with the highest share of anemia prevalence of 33 (23.9%).

The overall anemia prevalence recorded in this study was 51 (32.1%; 95% CI: 24.9-39.9%) among a total of 159 HIV/AIDS patients. Anemia prevalence of 23.9% and 8.2% were found among HIV-positive patients on treatment at  $\leq 6$  months and above 6 months, respectively. Bivariate and multivariable logistic analysis of the associated factors revealed that female patients on ART were more than 7 times more likely to be anemic compared with male subjects, and patients on HAART for  $\leq 6$  months were more than 6 times more likely to develop anemia than those who were on treatments for more than 6 months. Moreover, patients with body mass index  $< 18.5$  kg/m<sup>2</sup> were more than 5 times more likely to be anemic compared with those having body mass index  $> 18.5$  kg/m<sup>2</sup>.

Of the total anemic patients, mild anemia, moderate anemia, and severe anemia accounted for 13.8%, 10.7%, and 7.6%, respectively, and the prevalence of anemia was high in the age group between 21 and 30 years, followed by 31-40 years compared with other age categories. More than two-third of the study participants were urban residents, and patients having low and medium incomes were found to have relatively higher anemia prevalence as compared with patients with high income, which might indicate the fact that persons having high incomes can purchase nutritious food items, which directly contribute to the low anemia prevalence in this group. The finding of this study was lower as compared with other studies done in various parts of the world revealing the following anemia prevalence among HIV/AIDS patients receiving antiretroviral treatment: China (39.2%; 3,384/8,632) [19], Northwestern Tanzania (40.46%; 100/346) [7], Lagos, Nigeria (54.2%; 89/164) [20], and South Ethiopia (80.5%; 309/384) [21] (38.8%; 99/256) [22]. The result of this study was comparable to the related research on similar segments of the population, specifically on HAART-experienced patients in different parts of the country: Tertiary Hospitals in Addis Ababa, Ethiopia (33%; 201/616) [23], Ayder Specialized Hospital, Tigray Region (33.5%; 71/212) [24], Gedeo Zone, SNNPR (34.8%; 147/422) [25], Debere Tabor Hospital, Northwest Ethiopia (34.0%; 124/365) [26], and another report from Ethiopia showing anemia prevalence of 34.6% [27] among patients on antiretroviral therapy. The prevalence of anemia observed in the current study was higher compared with studies conducted in South Africa (25.8%; 2,647/10,259) [28], Northeast Nigeria (24.3%; 45/185) [29], Jimma Specialized Hospital, Ethiopia (16.2%) [17], Southern Ethiopia (26.2%; 105/401) [2], Northwest Ethiopia (18.9%; 42/222) [30], Debre Berhan Re-

ferral Hospital, Ethiopia (26.2%; 62/237) [8], Debre Tabor Comprehensive Specialized Hospital, North Central Ethiopia (17.4%; 58/334) [31], Hawassa Comprehensive Specialized Hospital, Southern Ethiopia (11.4%; 31/273) [3], Black Lion Specialized Hospital, Ethiopia (11.4%; 29/255) [32], Northwest Ethiopia (11.5%; 40/114) [33], and Northern Ethiopia (7%; 16/241) [34]. Another related study from Zewditu Memorial Hospital, Ethiopia showed anemia prevalence of 20.9% and 14.3% [35] for patients at 6 months and 12 months on antiretroviral treatment, respectively, which was lower than the values found for patients on HAART for less than 6 months (23.9%). The result we found for patients on treatment for more than 6 months was 8.2%, and a systematic review study in Ethiopia showed an overall anemia prevalence of 22.3% [36].

## Limitations of the study

This study did not incorporate the nutritional status of patients, their family history, menstrual disorder in females, diseases caused by a genetic disorder, and the presence of current co-infections either by important parasites or other diseases, which can contribute to the occurrence of anemia. Also, diet preferences were not assessed.

## Conclusions

The overall prevalence of anemia in this study was 51 (32.1%), with the higher prevalence seen in the age group between 21 to 30 years. Additionally, a relatively higher prevalence was recorded in patients on HAART for 6 months or less. It is also understood that the prevalence of anemia was higher in females compared with male study participants.

There should be an established protocol for timely and continuous screening of anemia, strict follow-up management, and uninterrupted care services for HIV/AIDS-positive patients to improve their quality of life and life expectancy.

## Disclosures

1. Institutional review board statement: Ethical clearance was obtained from the Research Committee of the College of Health Science and Medicine of Mizan-Tepi University, with approval number: CHS/00964/21.
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