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Prevalence of anemia and associated factors among patients living with HIV/AIDS at Mizan-Tepi University Teaching Hospital, Southwest Ethiopia

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Abstract

Introduction: Patients living with human immunodeficiency virus (HIV) face serious health problems due to associated anemia, which increases the likelihood of infection progression to state of a disease. Therefore, determining the prevalence of anemia in this vulnerable group might help to develop strategies to reduce the incidence of related cases.

Material and methods: Institution-based cross-sectional study was conducted from May to October, 2021 among HIV-positive patients at Mizan-Tepi University Teaching Hospital. Study subjects were selected using a simple random sampling technique, and pre-tested structured questionnaires were applied to obtain socio-demographic and clinical data. Blood samples were collected from patients for hemoglobin determination by hematology analyzer and CD4+ T-cells count. Data were entered using Epi-data manager (version 4.0.2.101) and analyzed by SPSS version 25.0.

Results: A total of 244 patients participated in this study. Overall anemia prevalence was 39.8% (95% CI: 33.6-46.2%), in 33 (13.5%) males and 64 (26.2%) females. Sixty-two (25.4%) patients were newly introduced to antiretroviral therapy and 35 (14.3%) patients were experienced. CD4+ T-cell of < 200/mm^3 (AOR: 3.218; 95% CI: 1.401-7.387%), WHO clinical stage II (AOR: 9.060; 95% CI: 2.955-27.776%), female gender (AOR: 3.932, 95% CI: 1.878-8.233%), and body mass index of < 18.5 kg/m^2 (AOR: 5.849; 95% CI: 1.824-18.752%) were among variables, which showed significant association with anemia.

Conclusions: The prevalence of anemia in antiretroviral therapy-experienced patients was higher as compared to naïve individuals. This study determined that anemia remains a major health threat to HIV/AIDS patients.

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

Introduction

Anemia is a public health concern, with a global prevalence of about 24% [1]. It is a deficiency of oxygen-carrying hemoglobin in red blood cells. Anemia occurs when the hemoglobin level is significantly depressed up to hemoglobin or packed cell volume below 90% or 95% of normal reference range within the same age and sex group [2]. Human immune deficiency virus (HIV) infection is often associated with different abnormalities of hematologic sources, such as

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anemia. The etiology of anemia in HIV infection is multifactorial [3] and typically, anemia may result from low production of red blood cells (RBC), increased RBC destruction, or ineffective RBC production [4]. Anemia could be caused by chronic disease with low reticulocyte count, normocytic, normochromic RBCs with normal iron stores, and cytokine-mediated poor erythropoietin response [4]. HIV/AIDS infection can lead to anemia in many ways, including a change in cytokine production and the subsequent effect on hematopoietic concentration [5], and other mechanisms associated with direct HIV infection of bone marrow [6].

In HIV infection, lower hemoglobin levels have shown an association with decreasing cluster of differentiation 4+ cell counts [7]. Many studies have found that there is an association between anemia in established infection and a faster progression to AIDS and death [8]. It is possible that HIV/AIDS is a major causative factor in the development of anemia, and that anemia is an indication of the likely severity or procession of the disorder [9]. Developing countries shouldered majority of the disease burden of anemia, with the highest prevalence in Africa and Southeast Asia. It is as high as two-thirds among children under five years and nearly half among women. According to the World Health Organization (WHO), the prevalence of anemia in children is 40% [10]. The prevalence of HIV-1-related anemia increases as the disease progress. It ranges from 10% among asymptomatic cases to 80% in AIDS patients [11]. The prevalence is unrecognized, which poses high health burden and a threat to well-being of those diagnosed [11]. Anemia is associated with a more rapid progression of HIV to AIDS by decreasing the survival of CD4+ counts. The risk of death in anemia patients with acquired immune deficiency syndrome is up to 70% greater as compared with non-anemic counterpart [12].

Ethiopia is one of the countries that is severely affected by HIV and its' associated health and economic impact. The national HIV prevalence is estimated to be 1.14% in 2014. The number of people living with HIV is estimated to be 769,600, with 15,700 new HIV infections and 35,600 AIDS-related deaths [13]. Currently, 339,043 adults are receiving ART [13]. One of the complications of HIV infection is anemia, occurring in approximately 30% of patients with asymptomatic infection, and as many as 75-80% of those with AIDS [14]. Anemia in HIV-infected persons has been caused by multiple factors that make etiologic diagnosis challenging [15]. The virus itself, immune dysregulation, opportunistic infections, and medications result all in anemia [16].

Therefore, intervention to prevent anemia may improve the survival potential and overall health of HIV-infected individuals [17]. Several observational studies have also reported higher mortality of HIV-infected patients with low hemoglobin levels, even after adjusting for CD4+ cell count and viral load [17]. The most reliable procedure is laboratory method, which can detect anemia before the onset of symptoms. Determination of hemoglobin and packed cell volume (PCV) using a complete blood count (CBC) analyzer machine is the common laboratory method for the diagnosis of anemia. In addition, red cell morphology is used to identify the etiology of anemia [18].

Problems related to anemia in many resource-limited settings, such as the study area, worsen due to the characteristics of population, with undernutrition and prevalence of infectious diseases, i.e., tuberculosis and malaria, which may increase the burden of anemia direct effect on the RBC mass by altering the balance between production and destruction of the cells that lead to anemia.

Therefore, special attention and care should be given to HIV/AIDS patients to prevent further complications of the disease. The results of this study may provide baseline information on the problem, and may help to alert the concerned health departments and workers for the management and control of the disease.

Material and methods

Study area

The research was conducted in Mizan-Tepi University Teaching Hospital (MTUTH), which is located in Mizan-Aman town in Bench Sheko zone, Southwest Ethiopia. The hospital has gynecology, outpatient, inpatient (medical and surgical), emergency, psychiatry, antenatal care wards, a tuberculosis clinic, youth-friendly counseling wards, and the staff is composed of 57 general physicians, 10 specialists, 178 nurses, 44 midwifery, 35 pharmacists, 22 health officers, 8 anesthesia specialist, 1 dental, 32 laboratory, and 1 psychiatry specialists, 5 radiographers, and 443 total supportive staffs. This make up 861 (males: 411, females: 450) of total staff (obtained from the hospital official database).

Study period and design

A cross-sectional study was performed from May till October, 2021 at MTUTH among patients living with HIV/AIDS, in order to determine the prevalence of anemia and its' associated factors.

Source population

The source population included all sero-positive status patients living with HIV/AIDS, and visiting MTUTH for diagnostics and care.

Study population

The study population was all HIV/AIDS-positive patients aged ranging from one year and above, who were available during the study period.

Study unit

Patients who were available during the study period and showed a willingness to participate in the study were recruited based on eligibility criteria. Those, who were on

treatment for anemia for the last 3 months, taking iron supplementation, and who were not ready to voluntary participate were excluded.

Sample size and sampling technique

The single population proportion formula was used to calculate the sample size, and the following assumptions were considered: 95% confidence interval, and a previous anemia prevalence of 23.1% (p = 23.1%, according to a study by Gedefaw *et al.* from Southwest Ethiopia) [19]. Based on this considerations, the sample size was calculated using the following formula:

$$n = \frac{(Z\alpha/2)^2\, p\,(1 - P)}{d^2}$$

where n is sample size, $Z\alpha/2 = 1.96$ is the standard normal variation at 95% confidence level, d is the margin of error, of 0.05, p is of the prevalence of disease of 0.231, and q is the probability of failure, which is $1 - p = 0.769$.

Using the above-mentioned formula, we obtained:

$$n = \frac{(1.96)^2\,(0.231)\,(0.769)}{(0.05)^2} = 272.8 \approx 273$$

Our total population was less than 10,000; therefore, a correction factor was applied as follow: $n = n/1 + n/N$; $n = 273/1 + 273/1414$; n = 229.

Adding a 10% non-response rate, the final sample size was 251.9 ≈ 252.

Study participants were selected using a simple random sampling technique from ART clinic database. All patients were listed in the database, then each patient was assigned with their medical record number (MRN), and the assigned number was sorted. Medical record numbers of individuals were randomly selected. The first number was chosen by lottery method, and patients were selected randomly by their MRN, which was listed on the printout.

Demographic data and blood sample collection

A structured questionnaire prepared in English was used to collect data regarding socio-demographic, economic, and hematological characteristics, WHO disease stage, treatment history, and co-infection status. Health professionals from different departments participated in data collection. The 2011 World Health Organization (WHO) report on hemoglobin concentration to diagnose anemia was applied to describe the results. Based on that, Hgb concentration of < 13 g/dl (mild: 11.0-12.9 g/dl; moderate: 8.0-10.9 g/dl; severe: < 8.0 g/dl) in males, and Hb of < 12.0 (mild: 11.0-11.9 g/dl; moderate: 8.0-10.9 g/dl; severe: < 8.0 g/dl) in females for anemia specification were considered [20].

During the implementation of data collection, the study subject was asked for their willingness to participate in the study. This was done through verbal communication and the required information, such as previous history of diseases and co-infection were collected by structured questionnaires. After patient's identification and assembly of necessary materials, blood samples were collected according to standard operating procedures (SOPs).

Hemoglobin determination

A minimum of 2-5 ml of blood sample was collected into EDTA anti-coagulated tube for CBC determination by hematology analyzer (Cell Dyn 1,800). The automated machine counts the number and types of blood cells. The machine works by sucking the standard amount of blood through a tube, and within this tube, some sensors count the number of cells going through it and identify cell types.

Data analysis

Data were entered using Epi-data manager (v. 4.0.2.101), and analysis was done by SPSS version 25.0. Descriptive statistics (frequency and cross tabulation) and both bivariate and multivariable logistic regressions were performed to assess the existence of significant association between the risk factors and the outcome of variables.

Quality assurance

Questionnaires were pre-tested in randomly selected patients at Mizan-Aman Health Center. Also, a proper functioning of the machine and reagent were verified. Sample collection procedures and analysis were done according to SOPs.

Ethical consideration

Ethical clearance was obtained from the College of Health Science and Medicine of Mizan-Tepi University (Approval number: CHS/00955/2021). Before blood sample collection, the objectives of the study and procedure of sample collection were explained to study participants. Verbal consent was obtained from guardians or families if the patient was a child. All data collection, presentation, and consent to use the data for publication were based on keeping patients' confidentiality according to the Helsinki Declaration of 1975 revised in 2000.

Results

Socio-demographic characteristics of HIV/AIDS patients at MTUTH, 2021

A total of 252 HIV/AIDS patients were recruited for the study, out of which, only 244 provided blood samples for hemoglobin determination, with a response rate of 96.8% to

the interview. In this study, an overall anemia prevalence was recorded as 97 (39.8%). Based on the WHO criteria, hemoglobin value of < 11 g/dl is considered as anemic for children and pregnant women, and value of < 12 g/dl and < 13 g/dl for male and female adults, respectively [20]. A significant difference was observed between male and female study participants concerning anemia prevalence. The educational status of patients was assessed by interviewing adults and parents/caretakers of children. From a total of 244 patients, more than half of them could not read and write. The majority of patients included in the study were urban residents, which also contributes to the higher share of anemia prevalence relative to HIV-positive patients from rural areas. From this study, the economic capability of patients seemed to contribute to the high prevalence of anemia, as presented in Table 1.

Characteristics of HIV-infected patients related to antiretroviral therapy

The present study involved 244 HIV/AIDS patients, who visited MTUTH from May till October, 2021 for diagnostic and care services, of which almost two-thirds of them were females. The majority of the patients were on antiretroviral therapy. Patients within age category between 21 and 30 years accounted for most of the anemia cases, whereas those within age category from 1 to 10 years were classified as the least affected groups (Table 2).

Patient's previous history of some related diseases was assessed using a structured questionnaire prepared before the start of data collection, and accordingly, significant numbers of the study subjects reported having tuberculosis, in-

Table 1. Prevalence of anemia among HIV/AIDS patients concerning their socio-demographic characteristics at MTUTH, 2021 (*n* = 244)

Variables/Category	Anemic, *n* (%)	Non-anemic, *n* (%)	Total, *n* (%)
Sex			
Male	33 (13.5)	65 (26.6)	98 (40.2)
Female	64 (26.2)	82 (33.6)	146 (59.8)
Age (years)			
1-10	1 (0.4)	3 (1.2)	4 (1.6)
11-20	12 (4.9)	15 (6.1)	27 (11.0)
21-30	40 (16.4)	56 (23.0)	96 (39.3)
31-40	26 (10.7)	46 (18.9)	72 (29.6)
41-50	12 (4.9)	21 (8.6)	33 (13.5)
> 50	6 (2.5)	6 (2.5)	12 (5.0)
Educational status			
Cannot read and write	58 (23.8)	74 (30.3)	132 (54.1)
Can read and write	39 (16.0)	73 (29.9)	112 (45.9)
Occupational status			
Employed	20 (8.2)	20 (8.2)	40 (16.4)
Farmer	7 (2.9)	17 (7.0)	24 (9.8)
Merchant	11 (4.5)	10 (4.1)	21 (8.6)
Housewife	23 (9.4)	31 (12.7)	54 (22.1)
Daily laborer	2 (0.8)	6 (2.5)	8 (3.3)
Student	18 (7.4)	29 (11.9)	47 (19.3)
Other	16 (6.6)	34 (13.9)	50 (20.5)
Income			
Low	51 (20.9)	60 (24.6)	111 (45.5)
Middle	37 (15.2)	69 (28.3)	106 (43.4)
High	9 (3.7)	18 (7.4)	27 (11.1)
Residence			
Rural	27 (11.1)	43 (17.6)	70 (28.7)
Urban	70 (28.7)	104 (42.6)	174 (71.3)

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

Table 2. Characteristics of HIV-infected patients on and without highly active antiretroviral therapy at the start of the study (n = 244)

Characteristics/ Category	HIV-infected patients, *n* (%)	Patients not on antiretroviral therapy, *n* (%)	Patients on antiretroviral therapy, *n* (%)
Sex			
Male	98 (40.2)	27 (11.1)	71 (29.1)
Female	146 (59.8)	58(23.7)	88 (36.1)
Age in years			
1-10	4 (1.6)	3 (1.2)	1 (0.4)
11-20	27 (11.1)	15 (6.1)	12 (4.9)
21-30	96 (39.3)	37 (15.2)	59 (24.2)
31-40	72 (29.5)	18 (7.4)	54 (22.1)
41-50	33 (13.5)	11 (4.5)	22 (9.0)
> 50	12 (4.9)	1 (0.4)	11 (4.5)

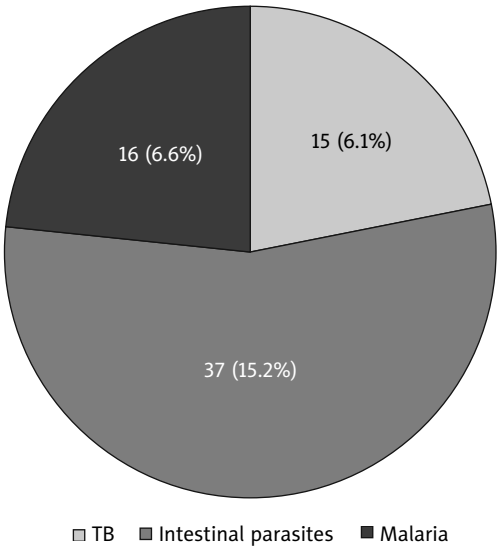
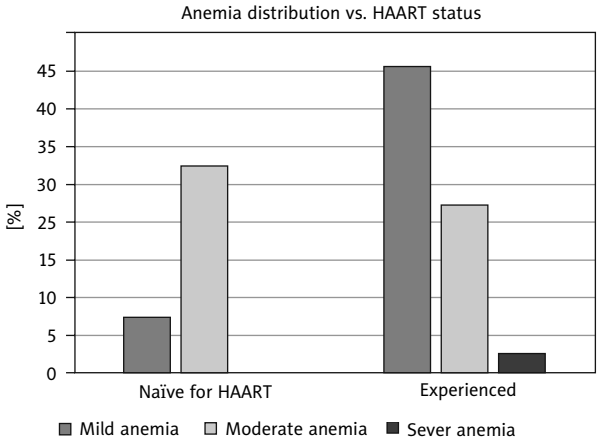


Figure 1. Previous history of some diseases among HIV/AIDS patients

testinal parasites, and malaria, which probably contributed to anemia prevalence (Figure 1).

The status of a patient regarding highly active antiretroviral therapy was assessed accordingly; more than one-third of the patients were new for highly active antiretroviral therapy and two-thirds were HAART-experienced. In this study, anemia was more prevalent in HAART-experienced patients than in naïve group. An adjusted odds ratio analysis in multivariable logistic regression showed that patients having CD4+ T-cells of < 200/mm^3, WHO clinical stage II, female participants, HAART status, patients with body mass index of < 18.5 kg/m^2, and those exposed to health education



HAART – highly active antiretroviral therapy

Figure 2. Anemia distribution concerning HAART status

presented statistically significant association with anemia (Table 3).

The World Health Organization classifies anemia as severe, moderate, and mild stages regardless of patients' sex, age, and status for a hemoglobin level of < 7 g/dl, 7-10 g/dl, and ≤ 11 g/dl, respectively [20]. In this study, anemia of different levels was found accordingly, and the following results were recorded: mild anemia: 26 patients (10.7%); moderate: 53 cases (21.7%); severe anemia: 18 patients (7.4%). The status of a HAART patient was assessed by interviewing patients, who could provide complete information as well as guardians/caregivers of children. Moderate type of anemia was found among both HAART-naïve and experienced patients. Mild anemia was the most common type of anemia among patients on HAART, and there was no severe anemia recorded for HAART-naïve patients (Figure 2).

Discussion

Globally, several million people are infected with HIV, and anemia is a common manifestation of HIV/AIDS; a large percentage of those infected with HIV can have anemia. In developing countries, HIV-infected individuals with anemia are most likely to experience devastating symptoms that may impair their functionality. The overall prevalence of anemia in this study among a total of two hundred forty-four study subjects (HIV/AIDS patients) was ninety-seven patients (39.8%; 95% CI: 33.6-46.2%). From the total anemic patients, mild, moderate, and severe anemia appeared in 26 (10.7%), 53 (21.7%), and 18 (7.4%) patients, respectively. The prevalence of anemia was high in the age group between 21 and 30 years of age, compared with other age categories. Out of one hundred forty-six female subjects participated in the study, sixty-four (26.2%) were anemic, and this was relatively lower compared with male participants (33 patients; 13.5%) from ninety-eight male study subjects. Study participants, who were HAART-naïve were more than four times more likely to develop anemia, as

Table 3. Bivariate and multivariable logistic regression analysis for possible risk factors of anemia among HIV/AIDS patients at MTUTH, 2021 (*n* = 244)

Risk factors/Category	Anemic, *n* (%)	Non-anemic, *n* (%)	Total, *n* (%)	OR (95% CI)	
				COR	AOR
Sex					
Male	33 (13.5)	65 (26.6)	98 (40.2)	Ref.	Ref.
Female	64 (26.2)	82 (33.6)	146 (59.8)	0.650 (0.382-1.107%)	3.932 (1.878-8.233%)**
HAART exposure status					
Naïve	62 (25.4)	69 (28.3)	131 (53.7)	0.499 (0.295-0.845%)**	5.378 (2.40-12.025%)**
Experienced	35 (14.3)	78 (32.0)	113 (46.3)	Ref.	Ref.
HAART regimen					
TDF/3TC/DTG	69 (28.3)	90 (36.9)	159 (65.2)	0.641 (0.370-1.111%)	0.923 (0.473-1.801%)
Not on treatment	28 (11.5)	57 (23.4)	85 (34.8)	Ref.	Ref.
WHO clinical stage					
I	14 (5.7)	66 (27.0)	80 (32.8)	Ref.	Ref.
II	17 (7.0)	44 (18.0)	61 (25.0)	0.549 (0.246-1.226%)	9.060 (2.955-27.776%)**
III	29 (11.9)	28 (11.5)	57 (23.4)	0.205 (0.094-0.445%)**	2.593 (0.798-8.422%)
IV	37 (15.2)	9 (3.7)	46 (18.9)	0.052 (0.020-0.131%)**	1.782 (0.609-5.216%)
CD4+ T-cell counts/mm^3					
< 200	46 (18.9)	50 (20.5)	96 (39.3)	0.425 (0.216-0.836%)**	3.218 (1.401-7.387%)**
200-500	33 (13.5)	51 (20.9)	84 (34.4)	0.605 (0.30-1.217%)	1.975 (0.894-4.364%)
> 500	18 (7.4)	46 (18.9)	64 (26.2)	Ref.	Ref.
Presence of co-infection					
Yes	15 (6.1)	10 (4.1)	25 (10.2)	Ref.	Ref.
No	82 (33.7)	137 (56.1)	219 (89.8)	0.399 (0.171-0.930)**	1.833 (0.638-5.270%)
Opportunistic infection					
Yes	12 (4.9)	18 (7.4)	30 (12.3)	Ref.	Ref.
No	85 (34.8)	129 (52.9)	214 (87.7)	0.988 (0.453-2.156%)	0.728 (0.245-2.162%)
History chronic disease					
Yes	26 (10.7)	31 (12.7)	57 (23.4)	Ref.	Ref.
No	71 (29.1)	116 (47.5)	187 (76.6)	0.730 (0.401-1.329%)	0.865 (0.381-1.965%)
Body mass index, kg/m^2					
< 18.5	32 (13.1)	12 (4.9)	44 (18.0)	1.213 (0.482-3.056%)	5.849 (1.824-18.752%)**
18.5-24.99	57 (23.4)	121 (49.6)	178 (73.0)	0.214 (0.072-0.639%)**	0.865 (0.330-2.261%)
> 24.99	8 (3.3)	14 (5.7)	22 (9.0)	Ref.	Ref.
Exposure to health education					
Yes	38 (15.6)	125 (51.2)	163 (66.8)	Ref.	Ref.
No	59 (24.2)	22 (9.0)	81 (33.2)	0.113 (0.062-0.209%)**	6.512 (2.681-15.818%)**

Ref. – reference category, HAART – highly active antiretroviral therapy
***Significance at p-value < 0.05*

compared with HAART-experienced patients (AOR: 5.378, 95% CI: 2.40-12.025%), and those not exposed to health education were more than five times more likely to become anemic (AOR: 6.512, 95% CI: 2.681-15.818%). Moreover, patients having CD4+ T-cell of < 200/mm^3, those with WHO clinical stage II, female participants, and study subjects having a body mass index of < 18.5 kg/m^2 were found to have statistically significant association with anemia. The result of this study was lower as compared with a study conducted in Cape Town, South-Africa (73%) [15]. Studies from seven sub-Saharan countries, such as Burundi, Democratic Republic of Congo, Ghana, Gambia, Mali, Senegal, and Togo, showed anemia prevalence of 62.5% (95% CI: 25.9-89.8%) [21]. Additionally, the finding of this study was lower

compared with a study done in Gondar University Hospital, Northwest Ethiopia among HAART-naïve HIV-positive individuals that showed the prevalence of anemia of 35%, and majority of patients had mild to moderate anemia and severe anemia. That study also indicated that female HAART-naïve HIV-positive patients had a significantly higher prevalence compared with males (62% vs. 38%) [22].

The prevalence of anemia observed in the current study is higher when compared with a study conducted at Jimma Specialized Hospital. The results had shown that from the total of 234 HIV-positive participants, the prevalence of anemia was fifty-four (23.1%) [19], which was lower than the finding of the current study (38.5). Unlike the study conducted at Jimma Specialized Hospital that showed insignificant differences in the prevalence of anemia among 19 HAART-experienced patients (16.2%) and 35 (29.9%) HAART-naïve participants, anemia prevalence in this study was much higher among HAART-experienced study subjects with 71 cases (31%), and ??? (34.8%) for HAART-naïve study subjects.

Studies from different countries consider anemia a common problem for HIV/AIDS patients, making their life miserable: India (51.9%, 164/316) [23], China (55.15%, 255/462) [24], Indonesia with HAART-naïve and patients on HAART as 60.8% and 40.3%, respectively [25], Nepal (66.7%, 140/210) [26], and Uganda (67.38%, 95/141) [27]. In the above-mentioned studies, the rates of prevalence were much higher as compared with the finding of the present study, and other research showed relative lower findings, even though the number of patients included in the respective studies differed: Nigeria (36.6%, 128/350) [28], Northwest Ethiopia (16.2%, 43/265) [29], South Ethiopia (36.5%, 150/411) [30], United States (10.3%, 1,551/15,126) [31], and Ethiopia (31.0%, 2,504/8,079) [32]. The above differences in anemia prevalence might be due variations in nutritional status of patients, their family histories, diseases caused by a genetic disorder, the presence of current co-infections caused by either parasites or other diseases that can contribute to the occurrence of anemia.

Conclusions

The prevalence of anemia in this study among HIV/AIDS patients was high. Age group between 21 and 30 years, patients on HAART, and female patients were the major indicators for the prevalence. Early diagnosis of anemia, regular follow-up of HIV/AIDS-positive patients' health status, and enhancing their nutritional practices are important.

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Conflict of interest

The authors declare no conflict of interest.

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