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PREVALENCE OF ANEMIA AND ITS ASSOCIATED FACTORS AT THE TIME OF ART INITIATION AMONG HIV-INFECTED ADULTS AT DEBRE-MARKOS REFERRAL HOSPITAL, NORTHWEST ETHIOPIA: A RETROSPECTIVE CROSS-SECTIONAL STUDY

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ABSTRACT

Objective: The aim of this study was to assess the prevalence of anemia and its associated factors at the time of Antiretroviral Therapy (ART) initiation among HIV-infected adults at Debre-Markos Referral Hospital.

Methods: an institution-based retrospective cross-sectional study was conducted among 473 patients' charts enrolled from 2014 to 2018 at Debre-Markos Referral Hospital. Patients' chart numbers were selected from the computer using a simple random sampling technique. Data were entered using EPI INFO version 7.2.2.6 and analyzed with Stata 14.0. Anemia prevalence at the time of ART initiation was computed and described using frequency tables. Both bivariate and multivariate logistic regression models were fitted to identify factors of anemia prevalence. Model fitness was checked by using the Hosmer-Lemeshow goodness of fit test.

Results: from 473 patients' charts, 468 charts were included in the analysis, and a total of 164 anemia cases were recorded. The overall prevalence of anemia among HIV-infected adults at the time of ART initiation was 35.04%. After multivariate analysis, an increased risk of anemia was seen among males (Adjusted odds ratio (AOR)=2.45; 95% Confidence interval (CI): 1.51-3.98); had no formal education (AOR=2.38; 95% CI: 1.12-5.05); baseline CD4 count \leq 200 cells/mm³ (AOR=4.67; 95% CI: 2.78-7.85); Body mass index (BMI) <18.5 kg/m² (AOR=2.43; 95% CI: 1.42-4.16); and ambulatory/bedridden baseline functional status (AOR=2.69; 95% CI: 1.41-5.12).

Conclusion: The current study showed that still anemia is a problem among HIV patients at the time of ART initiation. Giving special attention to patients with no formal education and for males is crucial to reduce anemia.

Keywords: Anemia; ART; Ethiopia; HIV/AIDS

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STRENGTHS AND LIMITATIONS OF THIS STUDY

- This study provided baseline information about Anemia status before starting ART.
- To make a representative sample, reviewed charts were selected randomly.
- Since it was based on chart review, this study lacks some variables like, smoking, alcohol consumption, chat chewing, etc.

INTRODUCTION

Anemia is described as a reduction in the proportion of the red blood cells or the hemoglobin concentration within them. This lower concentration of normal hemoglobin leads to an insufficient oxygen-carrying capacity of red blood cells. It is an important health indicator of both poor nutrition and poor health. Anemia might have a negative effect on the quality of life and also it adversely impacts the social and economic development of a patient with HIV and the country at large [1-6].

Anemia is a serious global public health problem that affects all age groups of the population. It affects up to one-third of the global population and if it is undiagnosed or left untreated for a prolonged period of time, it can lead to multi-organ failure and can even death [6, 7].

Anemia is the most common hematologic abnormality associated with HIV infection, especially among patients with advanced HIV disease [8]. In addition to weakening of the immune system, HIV infection has a negative impact on the hematopoietic system of infected individuals which results in a decreased concentration of hemoglobin in the blood. On the other hand, Anemia contributes to the progression of HIV infection to the Acquired Immunodeficiency Syndrome (AIDS) stage and this, in turn, accelerates progression to mortality [9-13].

Globally in 2019, a total of 1.74 billion anemia cases with an overall prevalence of 22.8% were reported [14]. The burden of anemia is more in developing countries, especially in sub-Saharan Africa, which accounts for more than 89% of the overall Anemia [15, 16]. This anemia prevalence increased more among HIV-infected patients who didn't start ART [8]. In different study settings, the prevalence of anemia at the time of ART initiation among HIV-infected patients was estimated and it was about 55.8%, 51.9%, and 25.8% in Nepal, China, and Johannesburg in South Africa [13, 17, 18], respectively.

Ethiopia is one of the most seriously affected countries by HIV and Anemia is a known predictor of disease progression and death among HIV-infected patients [5, 19]. Studies conducted in Ethiopia showed that the prevalence of anemia at the time of ART initiation among HIV-infected patients was estimated to be between 21.2% and 52.6% [19-25].

Identifying risk factors of anemia prevalence is crucial for developing effective interventions and for monitoring anemia control programs among HIV-infected patients. A cross-sectional survey conducted in China showed that age, low CD4 count, and ethnicity were significant factors of Anemia at the time of ART initiation [13]. Studies conducted in Ethiopia showed that sex, World Health Organization (WHO) clinical stage, TB/HIV co-infection, CD4 cell counts, opportunistic infection (OI), and history of Tuberculosis (TB) were independent predictors of Anemia occurrence at baseline [19-24].

Ethiopia is strongly committed to promote health and wellbeing among HIV-infected patients and the community at large, and anemia control is among its priorities. However, the relative contribution of different risk factors of anemia among HIV-infected patients in Ethiopia still varies from one setting to another. So, knowing of factors at local levels is important to intervene BMJ Open: first published as 10.1136/bmjopen-2021-057235 on 20 June 2022. Downloaded from http://bmjopen.bmj.com/ on June 7, 2025 at Agence Bibliographique de l Enseignement Superieur (ABES) . Protected by copyright, including for uses related to text and data mining, Al training, and similar technologies.

accordingly. Therefore, this study aimed to assess the prevalence of anemia at the time of ART initiation and its associated factors among HIV-infected patients at Debre-Markos referral hospital.

METHOD AND MATERIALS

Study design, setting and period

An institution-based retrospective cross-sectional study was conducted at Debre Markos Referral Hospital from January 1, 2014, to December 31, 2018, among HIV-infected adults. Patients' charts were reviewed to collect the data from randomly selected charts. Debre-Markos Referral Hospital is found at Debre Markos town in East Gojjam Zone of Amhara Nation Regional State (ANRS). It is situated 299 km from Addis Ababa, the capital city of Ethiopia, and 265 km from Bahir Dar, the capital city of ANRS [26]. The study was conducted by reviewing patients' chart from January 1, 2014, to December 31, 2018.

Source and Study Population

Source Population: All adult people living with HIV aged 15 years old and above attending ART Clinic at Debre-Markos Referral Hospital, Northwest Ethiopia.

Study population: randomly selected HIV-positive adults age 15 years old and above who were newly enrolled in ART Clinic at Debre-Markos Referral Hospital from January 1, 2014, to December 31, 2018, Northwest Ethiopia.

Inclusion and exclusion criteria

Adults, age 15 years and above who were newly enrolled in ART Clinic at Debre-Markos Referral Hospital at the time of the study were included in this study. Patients' charts with transferred in record information were excluded because these charts may lack baseline information.

Sample size and sampling procedure

The Sample size was determined by using a formula to estimate single population proportion with the assumption of 95% level of confidence, 23.4% proportion [22], 4% marginal error, and Power 80%.

$$n_1 = \frac{(za/2)^2 \cdot p(1-p)}{w^2}$$

Where, $n_1 =$ Initial sample size, a = Precision level or level of significance, P = population Proportion of Anemia, w= Marginal error, and $Z_{a/2}$ = the value under the standard normal table. Finally, the sample size was calculated using EPI INFO statistical package version 7.2.2.6 and with consideration of 10% expected incomplete records the final sample size was 473. During the study period, a total of 1264 patients were newly enrolled in Debre-Markos ART Clinic. Of these, 1117 patients' charts fulfill the inclusion criteria. Then by generating a random number on the computer, a total of 473 patients' charts were selected through a simple random sampling technique, and data were collected from them.

Operational definition

Anemia in this study was defined as anemic or non-anemic based on WHO criteria: Hemoglobin concentration < 13 g/dl for males and < 12 g/dl for females [1].

Functional status was classified based on WHO criteria as, Working(W) = capable of going out of home and do routine activities including the daily work; Ambulatory (A) = capable of self-care and going to the toilet unsupported; Bed-ridden (B) = can't go even to the toilet unsupported [27].

Baseline WHO Clinical stages: taken from chart record at enrolment to ART based on WHO classification criteria, labeled as stage I to IV.

Body mass index (BMI): Defined as the weight of the individual in kilograms divided by height in meter square.

Data collection tools and procedures

First, an extraction tool was developed from HIV/AIDS care monitoring and evaluation tools. Forms used for laboratory request and ART intake were also incorporated into the development of the extraction tool. The tool contains socio-demographic and related baseline clinical variables. Prior to data collection, training was given for three nurses regarding the tool and the way they extract the data from the chart. With the help of medical record number (MRN), patients' charts were selected by computer-generated simple random sampling technique. Patient charts were picked up from the chart room using MRN and then data were extracted from the patient's medical charts by using the tool. Common code was given for each selected chart after data was extracted so that there was no chance of recollection of data from a similar chart. In this way, all selected patients' charts which fulfill the inclusion criteria were reviewed and data extraction was completed.

Data quality assurance

Pretested data extraction tool was used to maintain data quality. Quality also maintained by extracting data using trained nurses and close monitoring of the procedure by the supervisor. Data clerks were involved in the selection of patients' charts from the computer as well as from the chart room. Before returning of the chart to the shelf, completeness of data extraction tool was checked and a necessary correction was made.

Data processing and analysis

After the data were extracted from the chart, it was first checked for consistency and completeness. After that it was coded and entered to EPI INFO version 7.2.2.6 and exported to STATA version 14.0 for analysis. A frequency table was used to describe socio-demographic and clinical variables of the study. The prevalence of Anemia at the time of ART initiation was estimated. Model fitness was checked by using the *Hosmer-Lemeshow goodness of fit test (p-value = 0.6106)* and the model was fitted well. Bivariate analysis was executed for each variable and those variables with p-value < 0.2 were entered into multivariate binary logistic regression to identify factors associated with anemia prevalence at the time of ART initiation. Odds ratio with 95% CI was computed and variables having p-value < 0.05 in the multivariate logistic regression was considered as statistically independent factors for Anemia at ART initiation.

Patient and public involvement

Since the study was based on chart review without active involvement of patients, no patient was involved.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

Ethical clearance was obtained from the Institutional Review Board (IRB) of the University of Gondar (Ref. No.:-S/N/1600/06/2011). Upon the ethical clearance, a letter of cooperation was obtained from the school of nursing to collect data. Permission was also obtained from Debre Markos Hospital Medical director and ART focal person. Confidentiality was maintained by avoiding the registration of personal identifiers like names to the extraction tool, or it was fully anonymized. Also, no raw data was given for anyone other than the investigator and it was fully anonymized.

RESULT

Socio-demographic characteristics of HIV infected adults

Out of all patients enrolled in the ART Clinic from January 1, 2014, to December 31, 2018, a total of 473 charts were selected and reviewed based on the inclusion criteria. From these reviewed charts, 468 charts were included in the analysis and only five charts were excluded due to data incompleteness. Of all patients' charts included in the analysis, 281 (60.04%) were females and about 40.60% of participants were grouped under the category of age 25 to 34 years (**Table 1**).

Table 1: Prevalence of Anemia at the time of ART initiation stratified by socio demographiccharacteristics of HIV infected adults at Debre-Markos Referral Hospital from January 1, 2014 toDecember 31, 2018 (n = 468).

Characteristics	Frequency (%)	An	Anemia status		
		Anemic (%)	Not Anemic (%)		
Sex					
Male	187 (39.96)	86 (45.99)	101 (54.01)		
Female	281 (60.04)	77 (27.40)	204 (72.60)		
Age in years					
15-24	51 (10.90)	11 (21.57)	40 (78.43)		
25-34	190 (40.60)	65 (34.21)	125 (65.79)		
35-44	157 (33.55)	61 (38.85)	96 (61.15)		
≥45	70 (14.96)	27 (38.57)	43 (61.43)		
Religion					
Orthodox	447 (95.51)	158 (35.35)	289 (64.65)		
Muslim	20 (4.27)	6 (30.00)	14 (70.00)		
Protestant	1 (0.21)	0	1 (100.00)		
Marital status					
Single	56 (11.97)	18 (32.14)	38 (67.86)		
Married	251 (53.63)	85 (33.86)	166 (66.14)		
Divorced/separated	125 (26.71)	47 (37.60)	78 (62.40)		
Widowed	36 (7.69)	14 (38.89)	22 (61.11)		
Educational level					
No education	171 (36.54)	62 (36.26)	109 (63.74)		
Primary	109 (23.29)	38 (34.86)	71 (65.14)		
Secondary	113 (24.15)	44 (38.94)	69 (61.06)		
College +	75 (16.03)	20 (26.67)	55 (73.33)		
Residence	· · · · · · · · · · · · · · · · · · ·	X			
Rural	101 (21.58)	45 (44.54)	56 (55.45)		
Urban	367 (78.42)	119 (32.43)	248 (67.57)		

Occupation				
Employed	153 (32.69)	50 (32.68)	103 (67.32)	
Unemployed	315 (67.31)	114 (36.19)	201 (63.81)	
Family size				
< 2 person	187 (39.96)	55 (29.41)	132 (70.59)	
3-4 person	213 (45.51)	82 (38.50)	131 (61.50)	
>4 person	68 (14.53)	27 (39.71)	41 (60.29)	
HIV disclosure status				
Disclosed	426 (91.03)	149 (34.98)	277 (65.02)	
Not disclosed	42 (8.97)	15 (35.71)	27 (64.29)	

Clinical and Immunological related characteristics of HIV infected adults

Of all study participants included in the analysis, around 29.06% had started ART six months and above after HIV status has confirmed and only 16.67% of study subjects had past OIs. From the group, about 25.85% and 6.20% of patients were grouped under baseline WHO clinical staging of three and four, respectively. One-third of patients included in the analysis had a baseline CD4 count of less than 200 cells/µl and 28.63% of patients were grouped under the category of BMI of less than 18.5kg/m². Regarding the functional status of HIV-infected patients in this study, around 20.84% had ambulatory or bedridden functional status at enrolment to Highly Active Antiretroviral Therapy (HAART) **(Table 2).**

Table 2: Prevalence of Anemia at the time of ART initiation stratified by clinical and immunologicrelated characteristics of HIV infected adults at Debre-Markos Referral Hospital from January 1,2014 to December 31, 2018 (n = 468)

Characteristics	Frequency (%)	Anemia status		
		Anemic (%)	Not Anemic (%)	
Pre-ART duration				
< 6 month	332 (70.94)	122 (36.75)	210 (63.25)	
\geq 6 month	136 (29.06)	42 (30.88)	94 (69.12)	
Past OI				
Yes	78 (16.67)	34 (43.59)	44 (56.41)	
No	390 (83.33)	130 (33.33)	260 (66.67)	
Past CPT treatment				
Yes	93 (19.87)	32 (34.41)	61 (65.59)	
No	375 (80.13)	132 (35.02)	243 (64.80)	
Past INH prophylaxis				

Yes	15 (3.21)	3 (20.00)	12 (80.00)
No	453 (96.79)	161 (35.54)	292 (64.46)
Past TB treatment history			
Yes	14 (2.99)	8 (57.14)	6 (42.86)
No	454 (97.01)	156 (34.36)	298 (65.64)
Baseline clinical staging			
Ι	197 (42.09)	43 (21.83)	154 (78.17)
II	121 (25.85)	35 (28.93)	86 (71.07)
III	121 (25.85)	63 (52.07)	58 (47.93)
IV	29 (6.20)	23 (79.31)	6 (20.69)
Baseline CD4 count (cells/µl)			
<100	89 (19.02)	62 (69.66)	27 (30.34)
100 - 199	74 (15.81)	41 (55.41)	33 (44.59)
200 - 349	124 (26.50)	34 (27.42)	90 (72.58)
≥ 350	181 (38.68)	27 (14.92)	154 (85.08)
Baseline BMI			
< 18.5	134 (28.63)	78 (58.21)	56 (41.79)
18.5-24.9	286 (61.11)	76 (26.57)	210 (73.43)
>24.9	48 (10.26)	10 (20.83)	38 (79.17)
Baseline functional status			
Working	370 (79.06)	93 (25.14)	277 (74.86)
Ambulatory	90 (19.23)	65 (72.22)	25 (27.78)
Bedridden	8 (1.71)	6 (75.00)	2 (25.00)

ART=Antiretroviral Therapy; OI=Opportunistic Infection; CPT=Cotrimoxazole preventive therapy; INH=Isoniazid; TB=Tuberculosis; CD4=Cluster of Differentiation four; BMI=Body Mass Index

Prevalence of Anemia at the time of ART initiation among HIV infected adults

The overall prevalence of Anemia at the time of ART initiation in this study was 35.04% (95% CI: 30.84 - 39.49). Of this, around 39.63%, 45.12 %, and 15.24% were grouped under the category of mild, moderate, and severe anemia levels, respectively (Figure 1).

Factors that determine Anemia prevalence at the time of ART initiation

After applying bivariate logistic regression, variables with a p-value of 0.2 or less were taken to multivariate logistic regression. Variables included in multivariate analysis were sex, age at enrolment, level of education, residence, family size, pre-ART duration, past OIs, CD4 count at enrollment, Body Mass Index, WHO clinical stage, and functional status at enrollment. After

multivariate logistic regression, five variables including sex, level of education, CD4 count, BMI, and functional status at enrollment were found to be statistically independent predictors of anemia prevalence at the time of ART initiation at a p-value of less than 0.5.

The current study revealed that the odds of being anemic at the time of ART initiation among males was 2.45 times that of females (AOR = 2.45; 95% CI: 1.51 - 3.98). Similarly, the odds of developing anemia among patients with no formal education was 2.38 times that of college and above educational level (AOR = 2.38; 95% CI: 1.12 - 5.05). CD4 count was also another significant factor of anemia at the time of ART initiation. The likely hood of developing anemia at the time of ART initiation among patients with CD4 count less than 200 cells/µl was 4.67 times that of 200 cells/µl or more (AOR = 4.67; 95% CI: 2.78 - 7.85). In the same manner, the odds of being anemic at enrolment to ART was 2.43 times among patients with a BMI of less than 18.5 kg/m² than patients with normal BMI (AOR = 2.43; 95% CI: 1.42 - 4.16). Lastly, the odds of being anemic among ambulatory and/or bedridden patients was 2.69 times that of working functional status at the time of ART initiation (AOR = 2.69; 95% CI: 1.41 - 5.12) (**Table 3**).

Table 3: Bivariate and multivariable logistic regression analysis of factors associated with Anemiaat the time of ART initiation among HIV infected adults at Debre-Markos Referral Hospital fromJanuary 1, 2014 to December 31, 2018 (n = 468)

Characteristics	Frequency		COR (95% CI)	AOR (95% CI)	P-Value
	Anemic	Not anemic			
Sex of the patient					
Male	86	101	2.30 (1.56, 3.40)	2.45 (1.51, 3.98)	<0.001*
Female	77	204	1.00	1.00	
Age at enrolment (in year	r)				
15-24	11	40	1.00	1.00	
25-34	65	125	1.89 (0.91, 3.93)	1.96 (0.79, 4.85)	0.145
35-44	60	97	2.31 (1.10, 4.85)	1.65 (0.65, 4.22)	0.295
45+	27	43	2.28 (1.003, 5.19)	1.65 (0.58, 4.67)	0.346
Level of education					
No education	62	109	1.57 (0.88, 2.82)	2.38 (1.12, 5.05)	0.024*
Primary	37	72	1.32 (0.70, 2.51)	1.69 (0.76, 3.77)	0.195

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Secondary	44	69	1 87 (1 01 3 45)	1 88 (0 87 4 04)	0.107	
College+ 20 55		1.00	1.00 (0.07, 1.01)	0.107		
Patient's residence						
Rural	118	249	1.67 (1.07, 2.62)	1.58 (0.91, 2.75)	0.105	
Urban	45	56	1.00	1.00		
Family size		I	l		1	
$\leq 2 \text{ person}$	55	132	1.00	1.00		
3–4 person	81	132	1.50 (0.99, 2.28)	1.30 (0.76, 2.22)	0.333	
\geq 5 person	27	41	1.58 (0.89, 2.82)	1.41 (0.68, 2.94)	0.352	
Pre-ART duration						
< 6 months	122	210	1.00	1.00		
\geq 6 months	42	94	0.77 (0.50, 1.17)	0.93 (0.55, 1.60)	0.807	
Presence of past OI						
Yes	34	44	1.55 (0.94, 2.53)	0.88 (0.46, 1.69)	0.708	
No	130	260				
CD4 count at enrolment ((cells/µl)	-	-	_	_	
< 200	103	60	6.86 (4.49, 10.49)	4.67 (2.78, 7.85)	<0.001*	
\geq 200	61	244	1.00	1.00		
Body Mass Index (kg/m ²))	0				
<18.5	78	56	3.85 (2.49, 5.93)	2.43 (1.42, 4.16)	0.001*	
18.5 - 24.9	76	210	1.00	1.00		
> 24.9	10	38	0.73 (0.35, 1.53)	1.26 (0.54, 2.93)	0.593	
WHO Clinical staging	42	1.50	1.00	1.00		
Stage I	43	158	1.00	1.00	0.050	
Stage II	35	86	1.49 (0.89, 2.51)	0.94 (0.51, 1.73)	0.850	
Stage III/IV	86	60	5.27 (3.29, 8.44)	1.78 (0.96, 3.30)	0.068	
Functional status at enrol	ment	0.55		1.00	1	
Working	93	277		1.00		
Ambulatory/bedridden	71	27	7.83 (4.74, 12.93)	2.69 (1.41, 5.12)	0.003*	
*significance at a p-val	ue <0.05					

AOR=Adjusted Odds Ratio; ART=Antiretroviral therapy; CD4=Cluster of Differentiation; COR=Crude Odds Ratio; OI=Opportunistic Infection; WHO=World Health Organization

DISCUSSION

There are varieties of hematologic abnormalities associated with HIV infection, of which anemia remains a public health challenge in HIV-positive patients around the world, particularly in Sub-Saharan African, including Ethiopia. It is a known complication of HIV infection that is associated with an increased risk of morbidity and mortality for patients with HIV.

The overall prevalence of anemia at the time of ART initiation in the current study was 35.04% (95% CI: 30.84 - 39.49). This is higher than studies conducted in Ethiopia, particularly in Hawassa University Referral Hospital, South Ethiopia (23.4%) [22], and University of Gondar Referral Hospital, Northwest Ethiopia (21.2%) [23]. It is also higher than a study done in Johannesburg, South Africa, with a prevalence of 25.8% [18]. However, anemia prevalence in the current study is lower than studies from Addis Ababa, Ethiopia; namely Black Lion Specialized Hospital (41.9%), Zewditu Memorial Hospital (42.9%), Minilik II Hospital (52.6%) [19, 20, 24], Similarly, the prevalence of anemia at the time of ART initiation is lower than the study conducted at Arba Minch Town, Southern Ethiopia which is 52.3% [21]. Anemia at the time of ART initiation in the current study is also lower than studies conducted from China and Nepal with the prevalence of 51.9% [13] and 55.8% [17], respectively. This lower prevalence of anemia in the current study could be related to differences in socio-demographic characteristics, or it could be due to differences in the time period by which better interventions to reduce anemia were applied recently than in previous times. Additionally, the majority of patients (72.3%) from china had CD4 count less than 200 cells/mm3 [13] compared to the current study, which is about 34.83%. This may be an important biological implication of the current finding in that the lower CD4 count was associated with an increased risk of anemia [11, 28].

In this study, the male sex was found to be an independent predictor of anemia at the time of ART initiation. The odd of being anemic at the time of ART initiation among males is 2.45 times that of females (95% CI: 1.51 - 3.98). This is in line with studies conducted in Zewditu memorial hospital and Arba minchi town, Ethiopia [19, 21]. More alcohol consumption among males than females might contribute to this difference between males and females. As males consume more alcohol, the rate of Vitamin B12 absorption to the circulatory system becomes lower and may

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result in pernicious or megaloblastic anemia. In contrast to the current study, the odds of being anemic at the time of ART initiation at Hawassa University referral hospital was higher in females than males [22]. This might be due to the fact that the presence of menstrual blood loss and in the drains on iron stores that occur with pregnancy and delivery might contribute to the development of anemia in women [19]. In addition, in the previous study, more than two-third of the subjects were females which might contribute to the female sex be significant factor.

Similarly, the current study showed that the odds being anemic among patients with no formal education was 2.38 times that of college and above educational status (AOR = 2.38; 95% CI: 1.12 - 5.05). This is supported by a retrospective cross-sectional study from Mizan-Aman General Hospital, Ethiopia [29]. This may be explained by patients with no formal education are less aware of better nutrition and better health care. When HIV infection is observed among those with no formal education, the risk of poor nutrition and occurrence of anemia will be double burdened. Additionally, non-educated patients are not fully aware of anemia symptoms so that they will come to the hospital quite late with high anemic grades.

The current study revealed that the odds of being anemic among patients with CD4 count less than 200 cells/ mm³ was 4.67 times that of CD4 count greater than 200 cells/ mm³ (95% CI: 2.78, 7.85). This is congruent with studies from the University of Gondar referral hospital, Arba minchi town, and Black Lion specialized hospital [21, 23, 24]. It could be due to the fact that bone marrow abnormalities are found at all stages of HIV disease and increases in frequency and severity as the disease advanced more. So, the risk of anemia occurrence increases with progressive immunologic deterioration, and a CD4 cell count of less than 200 cells/mm3 is related to the development of anemia [30].

Body mass index was another variable found to be a significant factor for the occurrence of anemia at the time of ART initiation. The likelihood of developing anemia among patients with a BMI less than 18.5 kg/m² was 2.43 times that of patients with normal BMI (95% CI: 1.42 - 4.16). This is congruent with a study from Wolaita Sodo University teaching referral hospital, Ethiopia [31]. This might be as a result of deficiencies of micronutrients such as iron, folate, and vitamin B12 in patients with undernutrition. This deficiency of micronutrients directly contributes to the development of anemia among those with a BMI of less than 18.5 kg/m².

Lastly, the likelihood of developing anemia among HIV patients was statistically associated with baseline functional status. The odds being anemic at the time of ART initiation among HIV patients with Ambulatory and/bedridden functional status were 2.69 times that of patients with working functional status (AOR=2.69; 95% CI: 1.41 - 5.12). Being in ambulatory or bedridden functional status could be an indicator of HIV infection advancement and the occurrence of other opportunistic infections. Patients in ambulatory or bedridden functional status may also be at risk for loss of appetite which may expose them to malnutrition and result in anemia.

CONCLUSION

The current study showed that still anemia was a problem among HIV patients at the time of ART initiation. Being male sex, having no formal education, CD4 count of less than 200 cells/mm³, undernutrition (BMI < 18.5Kg/m²), and being on ambulatory or bedridden functional status at the time of ART initiation were found to be independent predictors of Anemia. Hence, giving special attention to patients with no formal education and for those males is crucial to reduce anemia. If possible, initiation of ART sooner after status confirmed is crucial especially for those patients who are more at risk of developing low immunity.

ABBREVIATIONS

AIDS: Acquired Immunodeficiency Syndrome; AOR: Adjusted Odds Ratio; ART: Antiretroviral Therapy; BMI: Body Mass Index; CD4: Cluster of Differentiation Four; CI: Confidence Interval; COR: Crude Odds Ratio; CPT: Cotrimoxazole Prophylactic Therapy; HAART: Highly Active Antiretroviral Therapy; HIV: Human Immunodeficiency Virus; INH: Isoniazid; MRN: Medical Record Number; OI: Opportunistic Infections; TB: Tuberculosis; WHO: World Health Organization.

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AUTHORS' CONTRIBUTION

All authors made a significant contribution to the work reported. **AA** conceived the idea and design for work, participated in the data collection process, analyze and interpretation of data and also draft the manuscript. **BS, EG, MW** and **BC** approved the designed work with some revisions, participated in data analysis and reviewed the manuscript. All authors gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

COMPETING INTERESTS

The authors have declared that they have no competing interests.

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AVAILABILITY OF DATA AND MATERIALS

The datasets used during the current study is available from the corresponding author.

CONSENT FOR PUBLICATION

Not applicable.

REFERENCES

- Geneva, S. and W.H. Organization, Haemoglobin Concentrations for the Diagnosis of Anaemia and Assessment of Severity. Vitamin and Mineral Nutrition Information System. Document Reference WHO. 2011, NMH/NHD/MNM/11.1. <u>http://www</u>. who. int/entity/vmnis/indicators/haemoglobin
- WHO, *The global prevalence of anaemia in 2011*. Geneva: World Health Organization, 2015.
- Organization, W.H., Global nutrition targets 2025: anemia policy brief. Geneva: World Health Organization; 2014. WHO/NMH/NHD/14.4)[cited 2020 Feb 20]. Available at: https://apps. who. int
- 4. Brentlinger, P.E., et al., *Practical management of HIV-associated anemia in resource-limited settings: prospective observational evaluation of a new Mozambican guideline.*AIDS research and human retroviruses, 2016. 32(1): p. 12-25.
- Aynalem, Y.A., W. Shibabaw Shiferaw, and Z. Woldiye, Prevalence of Anemia and Its Associated Factors in Antiretroviral-Treated HIV/AIDS-Positive Adults from 2013 to 2018 at Debre Berhan Referral Hospital, Ethiopia. Advances in Hematology, 2020. 2020.
- Turner, J., M. Parsi, and M. Badireddy, *Anemia*, in *StatPearls [Internet]*. 2020, StatPearls Publishing.
- Chaparro, C.M. and P.S. Suchdev, *Anemia epidemiology, pathophysiology, and etiology in low-and middle-income countries*. Annals of the New York Academy of Sciences, 2019. 1450(1): p. 15.
- 8. Kerkhoff, A.D., et al., *Predictive value of anaemia for tuberculosis in HIV-infected patients in sub-Saharan Africa: an indication for routine microbiological investigation using new*

rapid assays. Journal of acquired immune deficiency syndromes (1999), 2014. **66**(1): p. 33.

- 9. Meidani, M., et al., *Prevalence, severity, and related factors of anemia in HIV/AIDS patients.* Journal of research in medical sciences: the official journal of Isfahan University of Medical Sciences, 2012. **17**(2): p. 138.
- Petraro, P., 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. 94(2): p. 384-392.
- Durandt, C., et al., *HIV and haematopoiesis*. South African Medical Journal, 2019. 109(8, Supplement 1): p. S41-S46.
- 12. Ezeamama, A.E., et al., Evolution of anemia types during antiretroviral therapy implications for treatment outcomes and quality of life among HIV-infected adults. Nutrients, 2019. **11**(4): p. 755.
- Shen, Y., et al., Prevalence of anemia among adults with newly diagnosed HIV/AIDS in China. PLoS One, 2013. 8(9): p. e73807.
- Gardner, W. and N. Kassebaum, Global, Regional, and National Prevalence of Anemia and Its Causes in 204 Countries and Territories, 1990–2019. Current Developments in Nutrition, 2020. 4(Supplement_2): p. 830-830.
- 15. Kassebaum, N.J., *The global burden of anemia*. Hematology/Oncology Clinics, 2016. **30**(2): p. 247-308.
- 16. Melese, H., et al., *Anemia among adult HIV patients in Ethiopia: a hospital-based crosssectional study*. Hiv/aids (Auckland, NZ), 2017. **9**: p. 25.
- 17. Martin, C., K. Poudel-Tandukar, and K.C. Poudel, *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. **9**(12): p. e116263.
- Takuva, S., et al., Anemia among HIV-infected patients initiating antiretroviral therapy in South Africa: improvement in hemoglobin regardless of degree of immunosuppression and the initiating ART regimen. Journal of tropical medicine, 2013. 2013.
- 19. Assefa, M., et al., *Prevalence and correlates of anemia among HIV infected patients on highly active anti-retroviral therapy at Zewditu Memorial Hospital, Ethiopia.* BMC hematology, 2015. **15**(1): p. 6.

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20	Adape A et al HIV-associated anaemia before and after initiation of antiretroviral
20.	therapy at Art Centre of Minilik II Hospital. Addis Ababa, Ethiopia, Ethiopian Medical
	Journal, 2012. 50 (1): p. 13-21.
21.	Alamdo, A.G., et al., Anemia and its associated risk factors at the time of antiretroviral
	therapy initiation in public health facilities of Arba Minch Town, Southern Ethiopia.
	Health, 2015. 7 (12): p. 1657.
22.	Daka, D., D. Lelissa, and A. Amsalu, Prevalence of anaemia before and after the initiation
	of antiretroviral therapy at ART centre of Hawassa University Referral Hospital, Hawassa,
	South Ethiopia. Sch J Med, 2013. 3(1): p. 1-6.
23.	Tesfaye, Z. and B. Enawgaw, Prevalence of anemia before and after initiation of highly
	active antiretroviral therapy among HIV positive patients in Northwest Ethiopia: a
	retrospective study. BMC research notes, 2014. 7(1): p. 1-5.
.4	Woldeamanuel, G.G. and D.H. Wondimu, 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. 18(1): p. 7.
25.	ICF, C.S.A.C.E.a., Ethiopia demographic and health survey 2016. Addis Ababa, Ethiopia,
	and Rockville, Maryland, USA: CSA and ICF, 2016.
6.	Moges, N. and G. Kassa, Prevalence of opportunistic infections and associated factors
	among HIV positive patients taking anti-retroviral therapy in DebreMarkos Referral
	Hospital, Northwest Ethiopia. J AIDs Clin Res, 2014. 5(5): p. 1-300.
7.	Aemro, A., A. Jember, and D.Z. Anlay, Incidence and predictors of tuberculosis
	occurrence among adults on antiretroviral therapy at Debre Markos referral hospital,
	Northwest Ethiopia: retrospective follow-up study. BMC Infectious Diseases, 2020. 20(1):
	p. 1-11.
28.	Zerihun, K.W., G.A. Bikis, and E.A. Muhammad, 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 research notes, 2019. 12(1):
	p. 168.
29.	Muluken, W. and M. Epherem, Assessment of the prevalence of zidovudine induced anemia
	among adult HIV/AIDS patients on HAART in an ethiopian hospital. Occup Med Health
	Aff, 2018. 6 (271): p. 2.
	20
	20

31. Ageru, T.A., et al., *Anemia and its associated factors among adult people living with human immunodeficiency virus at Wolaita Sodo University teaching referral hospital.* PloS one, 2019. **14**(10): p. e0221853.

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FIGURE LEGEND:

Figure 1: Level of Anemia at the time of ART initiation among HIV infected adults at Debre Markos Referral Hospital.

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Markos Referral Hospital.

Prevalence of anemia and its associated factors among HIVinfected adults at the time of ART initiation at Debre Markos comprehensive specialized hospital, Northwest Ethiopia: a retrospective cross-sectional study

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Prevalence of anemia and its associated factors among HIV-infected adults at
 the time of ART initiation at Debre Markos comprehensive specialized hospital,
 Northwest Ethiopia: a retrospective cross-sectional study

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Abstract **Objective**: The aim of this study was to assess the prevalence of anemia and its associated factors at the time of antiretroviral therapy (ART) initiation among HIV-infected adults at Debre-Markos comprehensive specialized hospital. Methods: an institution-based retrospective cross-sectional study was conducted among 473 patients' charts enrolled from 2014 to 2018 at Debre-Markos comprehensive specialized hospital. Patients' chart numbers were selected from the computer using a simple random sampling technique. Data was entered using EPI INFO version 7.2.2.6 and analyzed with Stata 14.0. Anemia prevalence at the time of ART initiation was computed and described using frequency tables. To identify factors for anemia, bivariate and multivariate logistic regression models were fitted. Model fitness was checked using the Hosmer-Lemeshow goodness of fit test. **Results**: From 473 patients' charts, 468 charts were included in the analysis, and a total of 164 anemia cases were recorded. The overall prevalence of anemia among HIV-infected adults at the time of ART initiation was 35.04% (95% Confidence interval (CI): 30.84-39.49). After multivariate analysis, an increased risk of anemia was seen among males (Adjusted odds ratio (AOR) = 2.45; 95% CI: 1.51–3.98); not attending formal education (AOR = 2.38; 95% CI: 1.12– 5.05); baseline CD4+ T-cell count \leq 200 cells/mm³ (AOR = 4.67; 95% CI: 2.78–7.85); body mass index (BMI) $<18.5 \text{ kg/m}^2$ (AOR = 2.43; 95% CI: 1.42–4.16); and ambulatory/bedridden baseline functional status (AOR = 2.69; 95% CI: 1.41–5.12). **Conclusion**: The current study showed that a significant proportion of HIV-infected adults developed anemia at the time of ART initiation. Hence, giving special attention to those who have not attended formal education, males, and late presenters is crucial to reduce the health impact of

anemia. The result will provide insight into the development of new anemia preventive strategies.

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46 Keywords: Anemia; ART; Associated factors; Ethiopia; HIV/AIDS; Prevalence

This study provided baseline information about anemia status before starting ART. To make a representative sample, reviewed charts were selected randomly. But, due to the retrospective nature of the study, the current study lacks some variables like smoking, alcohol consumption, chat chewing, and type of anemia. Additionally, this study was conducted among ART naïve adults, which lacks comparison

with anemia after ART initiation.

Strengths and limitations of this study

54 Introduction

Anemia is a serious global public health problem that affects all age groups of the population. It affects up to one-third of the global population, and if it is undiagnosed or left untreated for a prolonged period of time, it can lead to multi-organ failure and can even death [1, 2]. It can also have a negative effect on the quality of life and adversely impact the social and economic development of a patient and the country at large [3, 4].

There are varieties of hematologic abnormalities associated with HIV infection, of which anemia remains a public health challenge in HIV-positive patients around the world, particularly in sub-Saharan Africa, including Ethiopia. It is a well-known complication of HIV infection that is linked to an increased risk of morbidity and mortality in HIV patients [5, 6]. Anemia is the most common hematologic abnormality associated with HIV infection, especially among patients with advanced HIV disease [6]. In addition to the weakening of the immune system, HIV infection has a negative impact on the hematopoietic system of infected individuals, which results in a decreased

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concentration of hemoglobin in the blood. On the other hand, anemia contributes to the progression
of HIV infection to the acquired immunodeficiency syndrome (AIDS) stage and this, in turn,
accelerates progression to mortality [5, 7-10].

Globally, in 2019, a total of 1.74 billion anemia cases with an overall prevalence of 22.8% were reported [11]. Anemia is more prevalent in developing countries, particularly sub-Saharan Africa, which accounts for more than 89% of overall anemia [12, 13]. This anemia prevalence increased more among HIV-infected patients who didn't start ART [6]. In different study settings, the prevalence of anemia at the time of ART initiation among HIV-infected patients was estimated to be about 55.8%, 51.9%, and 25.8% in Nepal, China, and Johannesburg, South Africa [10, 14, 15], respectively.

Ethiopia is one of the most seriously affected countries by HIV, and anemia is a known predictor
of disease progression and death among HIV-infected patients [3, 16]. Studies conducted in
Ethiopia showed that the prevalence of anemia at the time of ART initiation ranged from 21.2%
to 52.6% [16-22].

Identifying risk factors for anemia prevalence is crucial for developing effective interventions and monitoring anemia control programs among HIV-infected patients. A cross-sectional survey conducted in China showed that advanced age, low CD4+ T-cell count, and ethnicity were significant factors in increased anemia [10]. Another study conducted in Tanzania revealed that female gender, low body mass index (BMI), lower CD4+ T-cell count, and concurrent tuberculosis treatment were associated with an increased risk of anemia [8]. Studies conducted in Ethiopia reported that female sex, World Health Organization (WHO) clinical stage III/IV, TB/HIV co-infection, Lower CD4+ T-cell counts, presence of opportunistic infection (OI), lower BMI, and

history of tuberculosis (TB) treatment were independent predictors of anemia occurrence at

Ethiopia is strongly committed to promote health and wellbeing among HIV-infected patients and

the community at large, and anemia control is among its priorities. However, the relative contribution of different risk factors to anemia among HIV-infected patients in Ethiopia still varies from one setting to another. So, knowing the factors at local levels is important to intervene accordingly. Therefore, this study aimed to assess the prevalence of anemia and its associated factors at the time of ART initiation among HIV-infected patients at Debre-Markos comprehensive specialized hospital. Method and materials Study design, setting and period

baseline [16-21, 23].

An institution-based retrospective cross-sectional study was conducted at Debre Markos comprehensive specialized hospital from January 1, 2014, to December 31, 2018, among HIVinfected adults. Patients' charts were reviewed to collect the data from randomly selected charts. Debre-Markos comprehensive specialized hospital is located in Debre Markos town in the East

104 Gojjam Zone of Amhara Nation Regional State (ANRS). It is located 299 kilometers from

105 Ethiopia's capital, Addis Ababa, and 265 kilometers from Bahir Dar, the capital city of ANRS [24].

106 Source and Study Population

Source Population: All adult people living with HIV aged 15 years old and above attended the
 ART Clinic at Debre-Markos comprehensive specialized hospital in Northwest Ethiopia.

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Study population: Randomly selected HIV-positive adults aged 15 years old and above who were
newly enrolled in the ART Clinic at Debre-Markos comprehensive specialized hospital between
January 1, 2014, and December 31, 2018, Northwest Ethiopia.

112 Inclusion and exclusion criteria

Adults, aged 15 years and above who were newly enrolled in the ART Clinic at Debre-Markos comprehensive specialized hospital at the time of the study were included in this study. Patients' charts with transferred in record information were excluded because these charts may lack baseline information. Additionally, being pregnant at baseline was excluded from the study.

117 Sample size and sampling procedure

118 The sample size was determined by using a formula to estimate single population proportion with 119 the assumption of a 95% level of confidence, 23.4% proportion [19], and a 4% marginal error.

 $n_1 = \frac{(za/2)^2 \cdot p(1-p)}{w^2}$

Where, n_1 = initial sample size, a = precision level or level of significance, P = population proportion of anemia, w= marginal error, and $Z_{a/2}$ = the value under the standard normal table. Finally, the sample size was calculated using the EPI INFO statistical package version 7.2.2.6 and, with consideration of 10% expected incomplete records, the final sample size was 473. During the study period, a total of 1264 patients were newly enrolled in the Debre-Markos ART Clinic. Of these, 1117 patient charts fulfill the inclusion criteria. Then, by generating a random number on the computer, a total of 473 patients' charts were selected through a simple random sampling technique, and data was collected from them.

131 Operational definition of variables

Anemia in this study was defined as anemic or non-anemic based on WHO criteria: hemoglobin
concentration < 13 g/dl for males and < 12 g/dl for females [25].

Functional status was classified based on WHO criteria as: Working (W) = capable of going out
of home and doing routine activities, including daily work; Ambulatory (A) = capable of self-care
and going to the toilet unsupported; Bed-ridden (B) = can't go even to the toilet unsupported [26].

Baseline WHO Clinical stages: taken from the chart record at enrolment to ART based on WHO
classification criteria, labeled as stage I to IV.

Body mass index (BMI): Defined as the weight of the individual in kilograms divided by their
height in meters squared.

141 Data collection tools and procedures

First, an extraction tool was developed from HIV/AIDS care monitoring and evaluation tools. Forms used for laboratory requests and ART intake were also incorporated into the development of the extraction tool. The tool contains socio-demographic and related baseline clinical variables. Prior to data collection, training was given to three nurses regarding the tool and the way they extract the data from the chart. With the help of medical record numbers (MRN), patients' charts were selected by a computer-generated simple random sampling technique. Patient charts were picked up from the chart room using MRN and then data was extracted from the patient's medical charts using the tool. A common code was given for each selected chart after the data was extracted, so that there was no chance of recollection of data from a similar chart. In this way, all selected patients' charts that fulfill the inclusion criteria were reviewed and data extraction was completed.

Data quality assurance

A pretested data extraction tool was used to maintain data quality. Quality is also maintained by extracting data using trained nurses and close monitoring of the procedure by the supervisor. Data clerks were involved in the selection of patients' charts from the computer as well as from the chart room. Before returning the chart to the shelf, the completeness of the data extraction tool was checked and a necessary correction was made.

Statistical analysis

After the data was extracted from the chart, it was first checked for consistency and completeness. After that, it was coded and entered into EPI INFO version 7.2.2.6 and exported to STATA version 14.0 for analysis. A frequency table was used to describe the socio-demographic and clinical variables of the study. The prevalence of anemia with a 95% confidence interval at the time of ART initiation was estimated. Model fitness was checked by using the Hosmer-Lemeshow goodness of fit test (p-value = 0.6106) and the model was fitted well. Bivariate analysis was executed for each variable, and those variables with a p-value < 0.2 were entered into multivariate binary logistic regression to identify factors associated with anemia prevalence at the time of ART initiation. An odds ratio with a 95% CI was computed, and variables having a p-value < 0.05 in the multivariate logistic regression were considered as statistically independent factors for anemia at ART initiation.

Patient and public involvement

Since the study was based on chart review without active involvement of patients, no patients were involved.

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176 Ethics approval and consent to participate

Ethical clearance was obtained from the Institutional Review Board (IRB) of the University of Gondar (Ref. No. :-S/N/1600/06/2011). Upon the ethical clearance, a letter of cooperation was obtained from the school of nursing to collect data. Permission was also obtained from Debre Markos comprehensive specialized hospital medical director and ART focal person. Confidentiality was maintained by avoiding the registration of personal identifiers like names to the extraction tool. Also, no raw data was given to anyone other than the investigator, and it was fully anonymized.

Result

185 Socio-demographic characteristics of HIV-infected adults

Out of all the patients enrolled in the ART Clinic from January 1, 2014, to December 31, 2018, a total of 473 charts were selected and reviewed based on the inclusion criteria. From these reviewed charts, 468 charts were included in the analysis, and only five charts were excluded due to data incompleteness. Of all the patients' charts included in the analysis, 281 (60.04%) were females, and about 190 (40.60%) of the participants were grouped under the category of age 25 to 34 years (Table 1).

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Characteristics	Frequency (%)	Ane	P-value	
		Anemic (%)	Not Anemic (%)	-
Sex			, , , , , , , , , , , , , , , , , , ,	
Male	187 (39.96)	86 (45.99)	101 (54.01)	< 0.001
Female	281 (60.04)	77 (27.40)	204 (72.60)	
Age in years				
15-24	51 (10.90)	11 (21.57)	40 (78.43)	0.138
25-34	190 (40.60)	65 (34.21)	125 (65.79)	
35-44	157 (33.55)	61 (38.85)	96 (61.15)	
≥45	70 (14.96)	27 (38.57)	43 (61.43)	-
Religion				
Orthodox	447 (95.51)	158 (35.35)	289 (64.65)	0.677
Muslim	20 (4.27)	6 (30.00)	14 (70.00)	
Protestant	1 (0.21)	0	1 (100.00)	
Marital status				
Single	56 (11.97)	18 (32.14)	38 (67.86)	0.813
Married	251 (53.63)	85 (33.86)	166 (66.14)	-
Divorced/separated	125 (26.71)	47 (37.60)	78 (62.40)	
Widowed	36 (7.69)	14 (38.89)	22 (61.11)	
Educational level				
No education	171 (36.54)	62 (36.26)	109 (63.74)	0.365
Primary	109 (23.29)	38 (34.86)	71 (65.14)	
Secondary	113 (24.15)	44 (38.94)	69 (61.06)	
College +	75 (16.03)	20 (26.67)	55 (73.33)	
Residence				
Rural	101 (21.58)	45 (44.54)	56 (55.45)	0.024
Urban	367 (78.42)	119 (32.43)	248 (67.57)	
Occupation				
Employed	153 (32.69)	50 (32.68)	103 (67.32)	0.455
Unemployed	315 (67.31)	114 (36.19)	201 (63.81)	-
Family size				
< 2 person	187 (39.96)	55 (29.41)	132 (70.59)	0.112
3-4 person	213 (45.51)	82 (38.50)	131 (61.50)]
>4 person	68 (14.53)	27 (39.71)	41 (60.29)]
HIV disclosure status				
Disclosed	426 (91.03)	149 (34.98)	277 (65.02)	0.924
Not disclosed	42 (8.97)	15 (35.71)	27 (64.29)	1

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203 Clinical and immunological related characteristics of HIV-infected adults

Of all the study participants included in the analysis, around 136 (29.06%) had started ART six months or above after HIV status had been confirmed, and 78 (16.67%) of the study subjects had past OIs. From the group, about 121 (25.85%) and 29 (6.20%) of patients were grouped under baseline WHO clinical staging of three and four, respectively. One-third of patients included in the analysis had a baseline CD4+ T-cell count of less than 200 cells/µl and 134 (28.63%) of patients were grouped under the category of BMI of less than 18.5kg/m². Regarding the functional status of HIV-infected patients in this study, around 98 (20.84%) had ambulatory or bedridden functional status at enrolment into highly active antiretroviral therapy (HAART) (Table 2).

Table 2: Prevalence of anemia at the time of ART initiation stratified by clinical and immunologic
related characteristics of HIV-infected adults at Debre-Markos comprehensive specialized hospital
from January 1, 2014, to December 31, 2018 (n = 468).

Characteristics	Frequency	Aner	Anemia status		
	(%)	Anemic (%)	Not Anemic (%)		
Pre-ART duration					
< 6 month	332 (70.94)	122 (36.75)	210 (63.25)	0.227	
\geq 6 month	136 (29.06)	42 (30.88)	94 (69.12)		
Past OI					
Yes	78 (16.67)	34 (43.59)	44 (56.41)	0.083	
No	390 (83.33)	130 (33.33)	260 (66.67)		
Past CPT treatment					
Yes	93 (19.87)	32 (34.41)	61 (65.59)	0.886	
No	375 (80.13)	132 (35.02)	243 (64.80)		
Past INH prophylaxis					
Yes	15 (3.21)	3 (20.00)	12 (80.00)	0.215	
No	453 (96.79)	161 (35.54)	292 (64.46)		
Past TB treatment history					
Yes	14 (2.99)	8 (57.14)	6 (42.86)	0.078	
No	454 (97.01)	156 (34.36)	298 (65.64)		
Baseline WHO clinical staging					
Ι	197 (42.09)	43 (21.83)	154 (78.17)	< 0.001	
II	121 (25.85)	35 (28.93)	86 (71.07)		
III	121 (25.85)	63 (52.07)	58 (47.93)		
IV	29 (6.20)	23 (79.31)	6 (20.69)		
Baseline CD4 count (cells/µl)					
<100	89 (19.02)	62 (69.66)	27 (30.34)	< 0.001	

100 - 199	74 (15.81)	41 (55.41)	33 (44.59)	
200 - 349	124 (26.50)	34 (27.42)	90 (72.58)	
\geq 350	181 (38.68)	27 (14.92)	154 (85.08)	
Baseline BMI				
< 18.5	134 (28.63)	78 (58.21)	56 (41.79)	< 0.001
18.5-24.9	286 (61.11)	76 (26.57)	210 (73.43)	
>24.9	48 (10.26)	10 (20.83)	38 (79.17)	
Baseline functional status				
Working	370 (79.06)	93 (25.14)	277 (74.86)	< 0.001
Ambulatory	90 (19.23)	65 (72.22)	25 (27.78)	
Bedridden	8 (1.71)	6 (75.00)	2 (25.00)	

215	ART=Antiretroviral Therapy; OI=Opportunistic Infection; CPT=Cotrimoxazole preventive therapy;
216	INH=Isoniazid; TB=Tuberculosis; CD4=Cluster of Differentiation four; BMI=Body Mass Index
217	Anemia prevalence among HIV-infected adults at the time of ART initiation
218	The overall prevalence of anemia at the time of ART initiation in this study was 35.04% (95% CI:
219	30.84–39.49). Of these, about 74 (45.12%) were grouped under the category of moderate anemia
220	level (Figure 1).
221	Factors that determine anemia prevalence at the time of ART initiation
222	After applying bivariate logistic regression, variables with a p-value of 0.2 or less were taken into
223	multivariate logistic regression. Variables included in multivariate analysis were sex, age at
224	enrolment, level of education, residence, family size, pre-ART duration, past OIs, CD4+ T-cell
225	count at enrollment, Body Mass Index, WHO clinical stage, and functional status at enrollment.
226	After multivariate logistic regression, five variables, including sex, level of education, CD4+ T-
227	cell count, BMI, and functional status at enrollment, were found to be statistically independent
228	predictors of anemia prevalence at the time of ART initiation at a p-value of less than 0.5.
229	The current study revealed that the odds of being anemic at the time of ART initiation among
230	males was 2.45 times that of females (AOR = 2.45 ; 95% CI: $1.51-3.98$). Similarly, the odds of
231	developing anemia among patients who had not attended formal education was 2.38 times that of

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those with a college degree and above educational level (AOR = 2.38; 95% CI: 1.12-5.05). The CD4+ T-cell count was also another significant factor of anemia at the time of ART initiation. The likelihood of developing anemia at the time of ART initiation among patients with a CD4+ T-cell count of less than 200 cells/ μ l was 4.67 times that of 200 cells/ μ l or more (AOR = 4.67; 95% CI: 2.78–7.85). In the same manner, the odds of being anemic at enrolment into ART was 2.43 times higher among patients with a BMI of less than 18.5 kg/m² than among patients with a normal BMI (AOR = 2.43; 95% CI: 1.42-4.16). Lastly, the odds of being anemic among ambulatory and/or bedridden patients was 2.69 times that of working functional status at the time of ART initiation (AOR = 2.69; 95% CI: 1.41-5.12) (Table 3).

Table 3: Bivariate and multivariable logistic regression analysis of factors associated with anemia
at the time of ART initiation among HIV infected adults at Debre-Markos comprehensive
specialized hospital from January 1, 2014, to December 31, 2018 (n = 468).

Characteristics	Fr	requency	COR (95% CI)	AOR (95% CI)	P-Value	
	Anemic Not anemic					
Sex of the patient						
Male	86	101	2.30 (1.56, 3.40)	2.45 (1.51, 3.98)	<0.001*	
Female	77	204	1.00	1.00		
Age at enrolment (in year	ar)					
15-24	11	40	1.00	1.00		
25-34	65	125	1.89 (0.91, 3.93)	1.96 (0.79, 4.85)	0.145	
35-44	60	97	2.31 (1.10, 4.85)	1.65 (0.65, 4.22)	0.295	
45+	27	43	2.28 (1.003, 5.19)	1.65 (0.58, 4.67)	0.346	
Level of education			4			
No education	62	109	1.57 (0.88, 2.82)	2.38 (1.12, 5.05)	0.024*	
Primary	37	72	1.32 (0.70, 2.51)	1.69 (0.76, 3.77)	0.195	
Secondary	44	69	1.87 (1.01, 3.45)	1.88 (0.87, 4.04)	0.107	
College+	20	55	1.00	1.00		
Patient's residence						
Rural	118	249	1.67 (1.07, 2.62)	1.58 (0.91, 2.75)	0.105	
Urban	45	56	1.00	1.00		
Family size						
$\leq 2 \text{ person}$	55	132	1.00	1.00		
3–4 person	81	132	1.50 (0.99, 2.28)	1.30 (0.76, 2.22)	0.333	
\geq 5 person	27	41	1.58 (0.89, 2.82)	1.41 (0.68, 2.94)	0.352	
Pre-ART duration			· · · · ·			
< 6 months	122	210	1.00	1.00		

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\geq 6 months	42	94	0.77 (0.50, 1.17)	0.93 (0.55, 1.60)	0.807
Presence of past OI					
Yes	34	44	1.55 (0.94, 2.53)	0.88 (0.46, 1.69)	0.708
No	130	260			
CD4+ T-cell count at enr	olment (cell	s/µl)			
< 200	103	60	6.86 (4.49, 10.49)	4.67 (2.78, 7.85)	<0.001*
\geq 200	61	244	1.00	1.00	
Body Mass Index (kg/m ²)					
<18.5	78	56	3.85 (2.49, 5.93)	2.43 (1.42, 4.16)	0.001*
18.5 - 24.9	76	210	1.00	1.00	
> 24.9	10	38	0.73 (0.35, 1.53)	1.26 (0.54, 2.93)	0.593
WHO Clinical staging			· · · · · · · · · · · · · · · · · · ·		
Stage I	43	158	1.00	1.00	
Stage II	35	86	1.49 (0.89, 2.51)	0.94 (0.51, 1.73)	0.850
Stage III/IV	86	60	5.27 (3.29, 8.44)	1.78 (0.96, 3.30)	0.068
Functional status at enrolment					
Working	93	277	1.00	1.00	
Ambulatory/bedridden	71	27	7.83 (4.74, 12.93)	2.69 (1.41, 5.12)	0.003*

244 *significance at a p-value <0.05

AOR=Adjusted Odds Ratio; ART=Antiretroviral therapy; CD4+=Cluster of Differentiation;
 COR=Crude Odds Ratio; OI=Opportunistic Infection; WHO=World Health Organization

247 **Discussion**

The overall prevalence of anemia at the time of ART initiation in the current study was 35.04% 248 (95% CI: 30.84–39.49), which is higher than studies conducted at the University of Gondar 249 Referral Hospital (21.2%) [20], and Hawassa University Referral Hospital (23.4%) [19]. However, 250 251 anemia prevalence in the current study is lower than in studies from Addis Ababa [16, 17] and Arba Minch Town [18]. Similarly, anemia prevalence in the current study is lower than in a similar 252 study at Black Lion Specialized Hospital (41.9%) [21]. This could be due to a higher mean of 253 baseline CD4+ T-cell count in the current study (289.5 cells/ μ l ±167.8) than that of Black Lion 254 255 Specialized Hospital (162.5 cells/ μ l ± 108.6). This indicates that the likelihood of anemia will be 256 increased as the HIV infection advances due to immunologic deterioration [27].

Anemia prevalence is also higher than a study done in Johannesburg, South Africa, with a
prevalence of 25.8% [15]. The variation may be due to socio-demographic differences. However,

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it is also lower than studies conducted in China and Nepal, with a prevalence of 51.9% [10] and 55.8% [14], respectively. This lower prevalence of anemia in the current study could be related to differences in socio-demographic characteristics, or it could be due to differences in the time period in which better interventions to reduce anemia have been applied recently than in previous times. Additionally, the majority of patients (72.3%) from China had a CD4+ T-cell count of less than 200 cells/mm3 [10] compared to the current study, which is about 34.83%. This might have an important biological implication in that the lower CD4+ T-cell count was associated with an increased risk of anemia [5, 28].

In this study, the male sex was found to be an independent predictor of increased anemia at the time of ART initiation. This is in line with studies conducted in Zewditu memorial hospital and Arba Minchi town, Ethiopia [16, 18]. More alcohol consumption among males than females might contribute to this difference between males and females. As males consume more alcohol, the rate of Vitamin B12 absorption into the circulatory system becomes lower and may result in anemia [29]. In contrast to the current study, the odds of being anemic at the time of ART initiation at Hawassa University referral hospital was higher in females than in males [19]. In the previous study, more than two-thirds of the subjects were females, and this might have contributed to increased anemia due to the presence of menstrual blood loss and in the drains on iron stores during pregnancy and delivery [16].

Similarly, the current study showed that the odds of being anemic among patients who had not
attended formal education was 2.38 times higher than those with a college degree and above
educational status. This is supported by a retrospective cross-sectional study from Mizan-Aman
General Hospital, Ethiopia [30]. This may be explained by patients who have not attended formal
education are less aware of better nutrition and better health care. When HIV infection is observed

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among those who have not attended formal education, the risk of poor nutrition and the occurrence of anemia will be double burdened. Additionally, non-educated patients are not fully aware of anemia symptoms, so they will come to the hospital quite late with high anemic grades [31, 32]. The current study revealed that the odds of being anemic among patients with a CD4+ T-cell count of less than 200 cells/ mm³ was 4.67 times that of a CD4+ T-cell count greater than 200 cells/ mm³. This is congruent with studies from the University of Gondar referral hospital, Arba Minchi town, and Black Lion specialized hospital [18, 20, 21]. It could be due to the fact that bone marrow abnormalities are found at all stages of HIV disease and increase in frequency and severity as the disease advances. So, the risk of anemia occurrence increases with progressive immunologic deterioration and a CD4+ T-cell count of less than 200 cells/mm3 is related to the development of anemia [33].

Anemia was 2.43 times more likely in patients with a lower BMI (18.5 kg/m2) than in those with a normal BMI. This is congruent with a study from Wolaita Sodo University teaching referral hospital, Ethiopia [34]. This might be as a result of deficiencies in micronutrients such as iron, folate, and vitamin B12 in patients with under nutrition. This deficiency of micronutrients directly contributes to the development of anemia among those with a BMI of less than 18.5 kg/m^2 . Lastly, being in an ambulatory or bedridden functional status increased the likelihood of developing anemia among HIV patients. This might be explained by being in ambulatory or bedridden functional status, which could be an indicator of HIV infection advancement and the occurrence of other opportunistic infections that may also be at risk for loss of appetite, expose them to malnutrition, and result in anemia [35].

In this study, we noted a few limitations. Since the cause of anemia in HIV-infected adults is multifactorial and the study was based on chart review, we noted that a few variables were missed.

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> Furthermore, this study did not collect data on dietary habits, substance use status, menstrual habits in females, or the type of anemia. Additionally, this study was conducted among ART-naïve adults, which lacks comparison with anemia after ART initiation.

Conclusion

The current study showed that a significant proportion of HIV-infected adults developed anemia at the time of ART initiation. Male sex, lack of formal education, a CD4+ T-cell count of less than 200 cells/mm3, under nutrition, and ambulatory or bedridden functional status were discovered to be independent predictors of anemia. Hence, giving special attention to patients not attending formal education, males, and late presenters is crucial to reduce anemia occurrence and its health impact. Finally, the findings of this study will provide baseline information to healthcare providers in order to select ART drugs accordingly, and may provide additional insight into the development Lie of new anemia preventive strategies.

Abbreviations

AIDS: Acquired Immunodeficiency Syndrome; AOR: Adjusted Odds Ratio; ART: Antiretroviral Therapy; BMI: Body Mass Index; CD4+: Cluster of Differentiation Four; CI: Confidence Interval; COR: Crude Odds Ratio; CPT: Cotrimoxazole Prophylactic Therapy; HAART: Highly Active Antiretroviral Therapy; HIV: Human Immunodeficiency Virus; INH: Isoniazid; MRN: Medical Record Number; OI: Opportunistic Infections; TB: Tuberculosis; WHO: World Health Organization.

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7 8 9	329	collaboration during the data collection. Also, the authors' heartfelt thanks go to the University of
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12 13	331	Competing interests
14 15 16	332	The authors have declared that they have no competing interests.
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23 24	335	not-for-profit sectors.
25 26 27	336	Availability of data and materials
28 29	337	The dataset used during the current study is available from the corresponding author.
30 31 22	338	Consent for publication
33 34	339	Not applicable.
35 36 37	340	Authors' contribution
37 38 39	341	All authors made a significant contribution to the work reported. AA conceived the idea and design
40 41	342	for the work, participated in the data collection process, analyzed and interpreted the data, and also
42 43 44	343	drafted the manuscript. BS, EG, MW, and BC approved the designed work with some revisions,
45 46	344	participated in data analysis, and reviewed the manuscript. All authors gave final approval of the
47 48	345	version to be published; have agreed on the journal to which the article has been submitted; and
49 50 51	346	agree to be accountable for all aspects of the work.
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59 60		For peer review only - http://bmiopen.bmi.com/site/about/guidelines.xhtml
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3349References53501.Turner, J., M. Parsi, and M. Badireddy, Anemia, in StatPearls [Internet]. 2020, StatPearls6351Publishing.73522.Chaparro, C.M. and P.S. Suchdev, Anemia epidemiology, pathophysiology, and etiology in9353and middle-income countries. Annals of the New York Academy of Sciences, 2019. 1450(11035415.113553.Aynalem, Y.A., W. Shibabaw Shiferaw, and Z. Woldiye, Prevalence of Anemia and Its Assoc12356Factors in Antiretroviral-Treated HIV/AIDS-Positive Adults from 2013 to 2018 at Debre Ber13357Referral Hospital, Ethiopia. Advances in Hematology, 2020. 2020.143584.15359settings: prospective observational evaluation of a new Mozambican guideline. AIDS researce	low- : p. iated han d
53501.Turner, J., M. Parsi, and M. Badireddy, Anemia, in StatPearls [Internet]. 2020, StatPearls6351Publishing.73522.Chaparro, C.M. and P.S. Suchdev, Anemia epidemiology, pathophysiology, and etiology in9353and middle-income countries. Annals of the New York Academy of Sciences, 2019. 1450(11035415.113553.12356Factors in Antiretroviral-Treated HIV/AIDS-Positive Adults from 2013 to 2018 at Debre Ber13357Referral Hospital, Ethiopia. Advances in Hematology, 2020. 2020.143584.15359settings: prospective observational evaluation of a new Mozambican guideline. AIDS researce	low- : p. iated han d
6351Publishing.73522.Chaparro, C.M. and P.S. Suchdev, Anemia epidemiology, pathophysiology, and etiology in9353and middle-income countries. Annals of the New York Academy of Sciences, 2019. 1450(11035415.113553.Aynalem, Y.A., W. Shibabaw Shiferaw, and Z. Woldiye, Prevalence of Anemia and Its Assoc12356Factors in Antiretroviral-Treated HIV/AIDS-Positive Adults from 2013 to 2018 at Debre Ber13357Referral Hospital, Ethiopia. Advances in Hematology, 2020. 2020.143584.Brentlinger, P.E., et al., Practical management of HIV-associated anemia in resource-limite15359settings: prospective observational evaluation of a new Mozambican guideline. AIDS researce	low- : p. iated han d
73522.Chaparro, C.M. and P.S. Suchdev, Anemia epidemiology, pathophysiology, and etiology in9353and middle-income countries. Annals of the New York Academy of Sciences, 2019. 1450(11035415.113553.12356Aynalem, Y.A., W. Shibabaw Shiferaw, and Z. Woldiye, Prevalence of Anemia and Its Assoc12356Factors in Antiretroviral-Treated HIV/AIDS-Positive Adults from 2013 to 2018 at Debre Ber13357Referral Hospital, Ethiopia. Advances in Hematology, 2020. 2020.143584.15359settings: prospective observational evaluation of a new Mozambican guideline. AIDS researce	low- : p. iated han d
0353and middle-income countries. Annals of the New York Academy of Sciences, 2019. 1450(11035415.113553.12356Factors in Antiretroviral-Treated HIV/AIDS-Positive Adults from 2013 to 2018 at Debre Ber13357Referral Hospital, Ethiopia. Advances in Hematology, 2020. 2020.143584.15359settings: prospective observational evaluation of a new Mozambican guideline. AIDS researce	: p. iated han d
1035415.113553.Aynalem, Y.A., W. Shibabaw Shiferaw, and Z. Woldiye, Prevalence of Anemia and Its Assoc12356Factors in Antiretroviral-Treated HIV/AIDS-Positive Adults from 2013 to 2018 at Debre Ber13357Referral Hospital, Ethiopia. Advances in Hematology, 2020.143584.15359settings: prospective observational evaluation of a new Mozambican guideline. AIDS researce	iated han d
113553.Aynalem, Y.A., W. Shibabaw Shiferaw, and Z. Woldiye, Prevalence of Anemia and Its Assoc12356Factors in Antiretroviral-Treated HIV/AIDS-Positive Adults from 2013 to 2018 at Debre Ber13357Referral Hospital, Ethiopia. Advances in Hematology, 2020. 2020.143584.Brentlinger, P.E., et al., Practical management of HIV-associated anemia in resource-limite15359settings: prospective observational evaluation of a new Mozambican guideline. AIDS researce	iated han d
12356Factors in Antiretroviral-Treated HIV/AIDS-Positive Adults from 2013 to 2018 at Debre Ber13357Referral Hospital, Ethiopia. Advances in Hematology, 2020. 2020.143584.Brentlinger, P.E., et al., Practical management of HIV-associated anemia in resource-limite15359settings: prospective observational evaluation of a new Mozambican guideline. AIDS research	han d
13357Referral Hospital, Ethiopia. Advances in Hematology, 2020.2020.143584.Brentlinger, P.E., et al., Practical management of HIV-associated anemia in resource-limite15359settings: prospective observational evaluation of a new Mozambican guideline. AIDS research	d
143584.Brentlinger, P.E., et al., Practical management of HIV-associated anemia in resource-limite15359settings: prospective observational evaluation of a new Mozambican guideline. AIDS research	d rch
¹⁵ 359 settings: prospective observational evaluation of a new Mozambican guideline. AIDS resea	rch
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360 and human retroviruses, 2016. 32 (1): p. 12-25.	
17 361 5. Durandt, C., et al., <i>HIV and haematopoiesis</i> , South African Medical Journal, 2019, 109 (8,	
10 362 Supplement 1): n S41-S46	
20 363 6 Kerkhoff A D et al Predictive value of angemig for tuberculosis in HIV-infected natients	n suh-
21 364 Saharan Africa: an indication for routine microhiological investigation using new ranid ass	71/5/10
22 365 Iournal of acquired immune deficiency syndromes (1999) 2014 66 (1): n 33	<i>xy</i> 5.
23 366 7 Meidani M et al Prevalence severity and related factors of anemia in HIV/AIDS nation	c
24 267 Journal of research in medical sciences: the official journal of Isfahan University of Medici	з. I
25 269 Sciences 2012 17 (2): p 129	1
26 360 Sciences, 2012. $1/(2)$. p. 156.	adulta
27 369 8. Petraro, P., et al., Determinants of allering among numun immunoueficiency virus-positive	uuuns
$_{28}$ 370 <i>at care and treatment clinics in dar es saladam, Tanzania.</i> The American journal of tropical	
29 371 medicine and hygiene, 2016. 94 (2): p. 384-392.	
30 372 9. Ezeamama, A.E., et al., Evolution of anemia types during antiretroviral therapy—implication	ons for
31 373 treatment outcomes and quality of life among HIV-infected adults. Nutrients, 2019. 11 (4):	р.
375 10. Shen, Y., et al., <i>Prevalence of anemia among adults with newly diagnosed HIV/AIDS in Chir</i>	1a.
376 PLOS One, 2013. 8(9): p. e/3807.	
36 377 11. Gardner, W. and N. Kassebaum, <i>Global, Regional, and National Prevalence of Anemia and</i>	lts
37 378 <i>Causes in 204 Countries and Territories, 1990–2019.</i> Current Developments in Nutrition, 2	020.
38 379 4 (Supplement_2): p. 830-830.	
39 380 12. Kassebaum, N.J., <i>The global burden of anemia</i> . Hematology/Oncology Clinics, 2016. 30 (2) ⁻	р.
40 381 247-308.	
41 382 13. Melese, H., et al., Anemia among adult HIV patients in Ethiopia: a hospital-based cross-ser	tional
⁴² 383 <i>study.</i> Hiv/aids (Auckland, NZ), 2017. 9 : p. 25.	
43 384 14. Martin, C., K. Poudel-Tandukar, and K.C. Poudel, HIV symptom burden and anemia among	HIV-
385 positive individuals: cross-sectional results of a community-based positive living with HIV (POLH)
45 386 study in Nepal. PloS one, 2014. 9 (12): p. e116263.	
47 387 15. Takuva, S., et al., Anemia among HIV-infected patients initiating antiretroviral therapy in S	outh
48 388 Africa: improvement in hemoglobin regardless of degree of immunosuppression and the	
49 389 <i>initiating ART regimen.</i> Journal of tropical medicine, 2013. 2013 .	
50 390 16. Assefa, M., et al., Prevalence and correlates of anemia among HIV infected patients on hic	hly
⁵¹ 391 <i>active anti-retroviral therapy at Zewditu Memorial Hospital, Ethiopia.</i> BMC hematology, 2)15.
⁵² 392 15 (1): p. 6.	
⁵³ 393 17. Adane, A., et al., <i>HIV-associated anaemia before and after initiation of antiretroviral therc</i>	py at
54 57 394 Art Centre of Minilik II Hospital. Addis Ababa. Ethiopia. Ethiopian Medical Journal. 2012. 5) (1): p.
55 rc 395 13-21.	V / F
50 555 10 11 57	
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2	206	10	Alamdo, A.G., at al. Anomia and its associated risk factors at the time of antiratroviral therapy
4	207	10.	initiation in public health facilities of Arba Minch Town, Southern Ethionia, Hoolth, 2015, 7(12):
5	308		n 1657
6	200	10	p. 1037. Daka D. D. Lelissa and A. Amsalu, <i>Brevalence of angemia before and after the initiation of</i>
7	399	19.	antiratroviral therapy at APT centre of Hawassa University Peferral Hespital Hawassa South
8	400		Ethiopia Sch Mod 2012 2 (1), p. 1.6
9 10	401	20	Ethiopia. Sch J Mea, 2013. 3 (1): P. 1-0.
10 11	402	20.	Testaye, Z. and B. Enawgaw, Prevalence of anemia before and after initiation of highly active
12	403		antiretroviral therapy among HIV positive patients in Northwest Ethiopia: a retrospective study.
13	404	24	BIMC research holes, 2014. 7(1): p. 1-5.
14	405	21.	woldeamanuel, G.G. and D.H. wondimu, <i>Prevalence of anemia before and after initiation of</i>
15	406		antiretroviral therapy among HIV infected patients at black lion specialized hospital, Addis
16	407		Ababa, Ethiopia: a cross sectional study. BMC hematology, 2018. 18(1): p. 7.
17	408	22.	ICF, C.S.A.C.E.a., Ethiopia demographic and health survey 2016. Addis Ababa, Ethiopia, and
18	409		Rockville, Maryland, USA: CSA and ICF, 2016.
19	410	23.	Negesse, A., et al., Prevalence of anemia and its associated factors in human immuno deficiency
20	411		virus infected adult individuals in Ethiopia. A systematic review and meta-analysis. BMC
21	412		hematology, 2018. 18 (1): p. 32.
22	413	24.	Moges, N. and G. Kassa, Prevalence of opportunistic infections and associated factors among HIV
25 24	414		positive patients taking anti-retroviral therapy in DebreMarkos Referral Hospital, Northwest
24	415		<i>Ethiopia</i> . J AIDs Clin Res, 2014. 5 (5): p. 1-300.
26	416	25.	Geneva, S. and W.H. Organization, Haemoglobin Concentrations for the Diagnosis of Anaemia
27	417		and Assessment of Severity. Vitamin and Mineral Nutrition Information System. Document
28	418		Reference WHO. 2011, NMH/NHD/MNM/11.1. <u>http://www</u> . who.
29	419		int/entity/vmnis/indicators/haemoglobin
30	420	26.	Aemro, A., A. Jember, and D.Z. Anlay, Incidence and predictors of tuberculosis occurrence among
31	421		adults on antiretroviral therapy at Debre Markos referral hospital, Northwest Ethiopia:
32	422		retrospective follow-up study. BMC Infectious Diseases, 2020. 20(1): p. 1-11.
33	423	27.	Gedefaw, L., et al., Anemia and risk factors in HAART naive and HAART experienced HIV positive
34 25	424		persons in south west Ethiopia: a comparative study. PloS one, 2013. 8(8): p. e72202.
36	425	28.	Zerihun, K.W., G.A. Bikis, and E.A. Muhammad, Prevalence and associated factors of anemia
37	426		amona adult human immune deficiency virus positive patients on anti-retroviral therapy at
38	427		Debre tabor Hospital. Northwest Ethiopia. BMC research notes. 2019. 12 (1): p. 168.
39	428	29.	Fragasso, A., Vitamin B12 deficiency in alcoholics, in Alcohol, nutrition, and health consequences.
40	429		2013. Springer, p. 131-134.
41	430	30.	Muluken, W, and M. Epherem, Assessment of the prevalence of zidovudine induced gnemia
42	431	50.	among adult HIV/AIDS natients on HAART in an ethionian hospital. Occup Med Health Aff. 2018
43	432		6(271)· n 2
44	132	31	Sunguya BE et al Poor nutrition status and associated feeding practices among HIV-positive
45	131	51.	children in a food secure region in Tanzania: a call for tailored nutrition training PloS one 2014
40 47	434		$\mathbf{q}(5)$: n $\mathbf{q}(23)$
47 48	433	27	J(J), p. E30300.
49	430	52.	Ethnic Groups Attending Antengtal Care at Drovincial Loval Hespital of Drovince 2, Nonal
50	437		Anomia 2021 2021
51	430	22	Anemia, 2021. 2021 .
52	439	55.	of homotology and infectious diseases, 2012 E(1)
53	440	24	or mematology and interctions diseases, 2013. $\mathbf{J}(1)$.
54	441	54.	Ageru, T.A., et al., Anemia and its associated jactors among dault people living with numan
55	442		inimunouejiciency virus at vvoiaita soao University teaching referral nospital. Plos one, 2019.
56	443		14 (10): p. e0221853.
5/			
50 59			20

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3	444	35.	Gebremichael, M.A., M.K. Gurara, and H.N. Weldehawaryat, Incidence and predictors of initial
4	445		antiretroviral therapy reaimen change among HIV-infected Adults receiving antiretroviral
5	446		therapy at Arba Minch general hospital Southern Ethiopia HIV/AIDS (Auckland N7) 2020 12 n
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1 2 3 4	462	Figure legend:
5 6 7	463	Figure 1: Level of anemia at the time of ART initiation among HIV-infected adults at Debre
9 10	464	Markos comprehensive specialized hospital.
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Figure 1: Level of anemia at the time of ART initiation among HIV-infected adults at Debre

Markos comprehensive specialized hospital.

STROBE Statement—checklist of items that should be included in reports of observational studies

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	Item No.	Recommendation	Page No.	Relevant text from Handscript
Title and abstract	1	(a) Indicate the study's design with a commonly used term in the title or the abstract	2	Line (27); An institution based retrospective cross-sectional study was conducted among 47 betweents' charts enrolled from 2014 to 2018 at Debre-Markos compressive specialized hospital.
		(b) Provide in the abstract an informative and balanced summary of what was done and what was found	2	Lines (23 – 45); Abstracta
Introduction				ata m
Background/ratio nale	2	Explain the scientific background and rationale for the investigation being reported	3, 4 and 5	Lines (54 – 94); Introduction
Objectives	3	State specific objectives, including any prespecified hypotheses	5	Lines (95 – 97); This study aimed to assess the prevalence of anemia and its associated factors at the time of ART initiation among HIV- infected patients at Debre Markos comprehensive specialized hospital.
Methods				similar
Study design	4	Present key elements of study design early in the paper	5	Lines (100 – 102); An institution-based retrospective cross-sectional study was conducted at Debre Markos comprehensive specialized hospital from January 1, 2014, to December 31, 2018, among HIV- infected adults.
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5	Lines (199 – 105); Study design, setting and period
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Participants	6	(a) Cohort study—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	5 and	Lines (106 – 111); Source and study population Lines (112 – 116); Ingluston and exclusion criteria (eligibility criteria)
		Case-control study—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls	6	Lines (126 – 128); By generating a random number on the computer, a total of 473 patient selected through a simple random sampling technique, and selected from them.
		Cross-sectional study—Give the eligibility criteria, and the sources and methods of selection of participants		ext and c
		(b) Cohort study—For matched studies, give matching criteria and number of exposed and unexposed	N/A	This was a cross-section is study
		Case-control study—For matched studies, give matching criteria and the number of controls per case		, Al trair
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	7	Lines (131 – 140); Operational definition of variables
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	7	Lines (141 – 152); Data Gellection tools and procedures
Bias	9	Describe any efforts to address potential sources of bias	8	Lines (154–159); A pretended data extraction tool was used to maintain data quality. Quality is also maintained by extracting data using trained nurses and close monitoring of the procedure by the supervisor. Data clerks were involved in the selection of patients' charts from the computer as well as from the chart room. Before returning the chart to

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				the shelf, the completences of the data extraction tool was checked a a necessary correction was made.
Study size	10	Explain how the study size was arrived at	6	Lines (117–124); The same ple size was determined by using a form to estimate single population proportion with the assumption of a 95 level of confidence, by g proportion, and a 4% marginal error.
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	8	Lines (166–171); Biggin & analysis was executed for each variable and those variables with p-value < 0.2 were entered into multivaria binary logistic regression to identify factors associated with anemia. A odds ratio with a 95% as computed, and variables having a p-val < 0.05 in the multivariate logistic regression were considered statistically independing factors for anemia at ART initiation.
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding	8	Lines (160–171); State and the second
		(b) Describe any methods used to examine subgroups and interactions	N/A	There were no subgroups
		(c) Explain how missing data were addressed	N/A	There was no missing dag
		(d) Cohort study—If applicable, explain how loss to follow-up was addressedCase-control study—If applicable, explain how matching of cases and controls was addressed	N/A	Lines (126–128); By generating a random number on the computer total of 473 patients beckarts were selected through a simple rando sampling technique.
		Cross-sectional study—If applicable, describe analytical methods taking account of sampling strategy		Agence E
		(e) Describe any sensitivity analyses	N/A	siblio g
Results				raphiq

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study with only one stage.	This was a cross-sectiona ing for	N/A	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	13*	Participants
ne 2	inseig ies rei	N/A	(b) Give reasons for non-participation at each stage		
992 D	nemer ated to	N/A	(c) Consider use of a flow diagram		
The special sector of	Line (197); Table 1: Prove stratified by socio denne at Debre-Markos compre- 2014 to December 31 Line (212); Table 2: Prev stratified by clinical and infected adults at Depre- from January 1, 2014	10 and 11	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	14*	Descriptive data
วi ณฑก/o	There was no missing dat	N/A	(b) Indicate number of participants with missing data for each variable of interest		
study	This was a cross-sectiona	N/A	(c) Cohort study—Summarise follow-up time (eg, average and total amount)		
Southand States Study	This was a cross-section a	N/A	Cohort study—Report numbers of outcome events or summary measures over time	15*	Outcome data
study <u>B</u>	This was a cross-sectiona	N/A	Case-control study—Report numbers in each exposure category, or summary measures of exposure		
The second seco	Lines (218–219); The over initiation in this study wa	12	Cross-sectional study—Report numbers of outcome events or summary measures		

Page 2	29 of	29
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Main results	16	 (a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included 	12, 13 and 14	Lines (218–219); The second and prevalence of anemia at the time of ART initiation in this study was 35.04% (95% CI: 30.84–39.49). Lines (241); Table 3 Bis ariate and multivariable logistic regression analysis of factors associated with anemia at the time of ART initiation among HIV infection and the time of ART initiation among HIV infection and the time of the second analysis of the second analysis at Debre-Markos comprehensive specialized hospital analysis of 1, 2014, to Dec 31, 2018 (n = 468).
		(b) Report category boundaries when continuous variables were categorized	N/A	There was no continuous pariable.
		(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	N/A	There was no estimate spot relative risk.
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	N/A	There was no sub groups and sensitivity analysis.
Discussion		10		g, Al
Key results	18	Summarise key results with reference to study objectives	14–16	Lines (247–307); Disgussion
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	16	Lines (303–307); Singe the cause of anemia in HIV-infected adults is multi-factorial and the study was based on chart review, we noted that a few variables were missed. Furthermore, this study did not collect data on dietary habits substance use status, menstrual habits in females, or the type of anemia Additionally, this study was conducted among ART-naïve adults, variables lacks comparison with anemia after ART initiation.
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	14–16	Lines (247–307); Discussion
Generalizability	21	Discuss the generalizability (external validity) of the study results	17	Lines (308–316); The gurrent study showed that a significant proportion of HIV-infected adults developed anemia at the time of ART

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Other informatio	n			initiation. Male sex, is less than 200 cells/m functional status we anemia. Hence, givin education, males, an occurrence and its he provide baseline infor ART drugs accordin development of new	Solution in the study will Solution in the study will So
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	18	This research received in the public, comm	ອີອີອີອີອີອີອີອີອີອີອີອີອີອີອີອີອີອີອ
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Prevalence of anemia and its associated factors among HIVinfected adults at the time of ART initiation at Debre-Markos comprehensive specialized hospital, Northwest Ethiopia: a retrospective cross-sectional study

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the time of ART initiation at Debre-Markos comprehensive specialized hospital, Northwest Ethiopia: a retrospective cross-sectional study

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20 Word count: 3,715 (Introduction to conclusion; excluding tables and figures).

Abstract

Objective: The aim of this study was to assess the prevalence of anemia and its associated factors at the time of antiretroviral therapy (ART) initiation among HIV-infected adults at Debre-Markos comprehensive specialized hospital.

Methods: An institution-based retrospective cross-sectional study was conducted among 473 patients' charts enrolled from 2014 to 2018 at Debre-Markos comprehensive specialized hospital. Patients' chart numbers were selected from the computer using a simple random sampling technique. Data was entered using EPI INFO version 7.2.2.6 and analyzed with Stata 14.0. Anemia prevalence at the time of ART initiation was computed and described using frequency tables. To identify factors for anemia, bivariate and multivariate logistic regression models were fitted. Model fitness was checked using the Hosmer-Lemeshow goodness of fit test. **Results**: From 473 patients' charts, 468 charts were included in the analysis, and a total of 164 anemia cases were recorded. The overall prevalence of anemia among HIV-infected adults at the time of ART initiation was 35.04% (95% Confidence interval (CI): 30.84-39.49). After multivariate analysis, an increased risk of anemia was seen among males (Adjusted odds ratio (AOR) = 2.45; 95% CI: 1.51–3.98); not attending formal education (AOR = 2.38; 95% CI: 1.12– 5.05); baseline CD4+ T-cell count ≤ 200 cells/mm³ (AOR = 4.67; 95% CI: 2.78–7.85); body mass index (BMI) $<18.5 \text{ kg/m}^2$ (AOR = 2.43; 95% CI: 1.42–4.16); and ambulatory/bedridden baseline functional status (AOR = 2.69; 95% CI: 1.41-5.12).

Conclusion: The current study showed that a significant proportion of HIV-infected adults developed anemia at the time of ART initiation. Hence, giving special attention to those who have not attended formal education, males, decreased baseline CD4+ T-cell count, lower BMI, and patients with ambulatory/bedridden baseline functional status is crucial to reduce the health

2		
3 4	46	impact of anemia. The result will provide insight into the development of new anemia preventive
5 6 7	47	strategies.
7 8 9	48	Keywords: Anemia; ART; Associated factors; Ethiopia; HIV/AIDS; Prevalence
10 11 12 13	49	Strengths and limitations of this study
14 15 16	50	• This study provided baseline information about anemia status before starting ART.
17 18	51	• To make a representative sample, reviewed charts were selected randomly.
19 20 21	52	• But, due to the retrospective nature of the study, the current study lacks some variables
21 22 23	53	like smoking, alcohol consumption, chat chewing, and type of anemia.
24 25	54	• It is also difficult to determine the temporal link between the outcome and exposure
26 27 28	55	variables.
28 29 30	56	• Additionally, this study was conducted among ART naïve adults, which lacks
31 32 33	57	comparison with anemia after ART initiation.
34 35 36	58	Introduction
37 38	59	Anemia is a serious global public health problem that affects all age groups of the population. It
39 40	60	affects up to one-third of the global population, and if it is undiagnosed or left untreated for a
41 42 43	61	prolonged period of time, it can lead to multi-organ failure and can even death [1, 2]. It can also
44 45	62	have a negative effect on the quality of life and adversely impact the social and economic
46 47 48	63	development of a patient and the country at large [3, 4].
49 50	64	There are varieties of hematologic abnormalities associated with HIV infection, of which anemia
51 52 53	65	remains a public health challenge in HIV-positive patients around the world, particularly in sub-
54 55 56 57 58	66	Saharan Africa, including Ethiopia. Anemia is a well-known complication and the most common

hematologic abnormality associated with HIV infection, especially among patients with advanced HIV disease [5, 6]. In addition to the weakening of the immune system, HIV infection has a negative impact on the hematopoietic system of infected individuals, which results in a decreased concentration of hemoglobin in the blood. On the other hand, anemia contributes to the progression of HIV infection to the acquired immunodeficiency syndrome (AIDS) stage and this in turn accelerates progression to mortality [5, 7-10].

Globally, in 2019, a total of 1.74 billion anemia cases with an overall prevalence of 22.8% were reported [11]. Anemia is more prevalent in developing countries, particularly sub-Saharan Africa, which accounts for more than 89% of overall anemia [12, 13]. This anemia prevalence increased more among HIV-infected patients who didn't start ART [6]. In different study settings, the prevalence of anemia at the time of ART initiation among HIV-infected patients was estimated to be 55.8%, 51.9%, and 25.8% in Nepal, China, and Johannesburg, South Africa [10, 14, 15], respectively.

Ethiopia is one of the most seriously affected countries by HIV, and anemia is a known predictor
of disease progression and death among HIV-infected patients [3, 16]. Studies conducted in
Ethiopia showed that the prevalence of anemia at the time of ART initiation ranged from 21.2%
to 52.6% [16-22].

Identifying risk factors for anemia prevalence is crucial for developing effective interventions and monitoring anemia control programs among HIV-infected patients. A cross-sectional survey conducted in China showed that advanced age, low CD4+ T-cell count, and ethnicity were significant factors in increased anemia [10]. Another study conducted in Tanzania revealed that female gender, low body mass index (BMI), lower CD4+ T-cell count, and concurrent tuberculosis treatment were associated with an increased risk of anemia [8]. Studies conducted in

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Ethiopia reported that female sex, World Health Organization (WHO) clinical stage III/IV,
TB/HIV co-infection, Lower CD4+ T-cell counts, presence of opportunistic infection (OI), lower
BMI, and history of tuberculosis (TB) treatment were independent predictors of anemia
occurrence at baseline [16-21, 23].

Ethiopia is strongly committed to promote health and wellbeing among HIV-infected patients and the community at large, and anemia control is among its priorities. However, the relative contribution of different risk factors to anemia among HIV-infected patients in Ethiopia still varies from one setting to another. So, knowing the factors at local levels is important to intervene accordingly. Therefore, this study aimed to assess the prevalence of anemia and its associated factors at the time of ART initiation among HIV-infected patients at Debre-Markos comprehensive specialized hospital.

01.0

101 Method and materials

102 Study design, setting and period

An institution-based retrospective cross-sectional study was conducted at Debre Markos
comprehensive specialized hospital from January 1, 2014, to December 31, 2018, among HIVinfected adults. Patients' charts were reviewed to collect the data from randomly selected charts.
Debre-Markos comprehensive specialized hospital is located in Debre Markos town in the East
Gojjam Zone of Amhara Nation Regional State (ANRS). It is located 299 kilometers (km) from
Ethiopia's capital, Addis Ababa, and 265 km from Bahir Dar, the capital city of ANRS [24].

109 Source and Study Population

Source Population: All adult people living with HIV aged 15 years old and above attended the

111 ART Clinic at Debre-Markos comprehensive specialized hospital in Northwest Ethiopia.

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Study population: Randomly selected HIV-positive adults aged 15 years old and above who were newly enrolled in the ART Clinic at Debre-Markos comprehensive specialized hospital between January 1, 2014, and December 31, 2018, Northwest Ethiopia.

Inclusion and exclusion criteria

Adults aged 15 years and above who were newly enrolled in the ART Clinic at Debre-Markos comprehensive specialized hospital at the time of the study were included in this study. Patients' charts with transferred in record information were excluded because these charts may lack baseline information. Additionally, being pregnant at baseline was excluded from the study.

Sample size and sampling procedure

The sample size was determined by using a formula to estimate single population proportion with the assumption of a 95% level of confidence, 23.4% proportion [19], and a 4% marginal error.

 $n_{!} = \frac{(za/2)^2 \cdot p(1-p)}{w^2}$

Where, n_1 = initial sample size, a = precision level or level of significance, P = population proportion of anemia, w= marginal error, and $Z_{a/2}$ = the value under the standard normal table. Finally, the sample size was calculated using the EPI INFO statistical package version 7.2.2.6 and, with consideration of 10% expected incomplete records, the final sample size was 473. During the study period, a total of 1264 patients were newly enrolled in the Debre-Markos ART Clinic. Of these, 1117 patient charts fulfill the inclusion criteria. Then, by generating a random number on the computer, a total of 473 patients' charts were selected through a simple random sampling technique, and data was collected from them.

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Operational definition of variables

Anemia in this study was defined as anemic or non-anemic based on WHO criteria: hemoglobin
concentration < 13 g/dl for males and < 12 g/dl for females [25].

Functional status was classified based on WHO criteria as: Working (W) = capable of going out
of home and doing routine activities, including daily work; Ambulatory (A) = capable of self-

139 care and going to the toilet unsupported; Bed-ridden (B) = can't go even to the toilet unsupported

140 [26].

Baseline WHO Clinical stages: taken from the chart record at enrolment to ART based on
WHO classification criteria, labeled as stage I to IV.

Body mass index (BMI): Defined as the weight of the individual in kilograms divided by their
height in meters squared.

145 Data collection tools and procedures

First, an extraction tool was developed from HIV/AIDS care monitoring and evaluation tools. Forms used for laboratory requests and ART intake were also incorporated into the development of the extraction tool. The tool contains socio-demographic and related baseline clinical variables. Prior to data collection, training was given to three nurses regarding the tool and the way they extract the data from the chart. With the help of medical record numbers (MRN), patients' charts were selected by a computer-generated simple random sampling technique. Patient charts were picked up from the chart room using MRN and then data was extracted from the patient's medical charts using the tool. A common code was given for each selected chart after the data was extracted, so that there was no chance of recollection of data from a similar chart. In this way, all selected patients' charts that fulfill the inclusion criteria were reviewed and data extraction was completed.

157 Data quality assurance

A pretested data extraction tool was used to maintain data quality. Quality is also maintained by extracting data using trained nurses and close monitoring of the procedure by the supervisor. Data clerks were involved in the selection of patients' charts from the computer as well as from the chart room. Before returning the chart to the shelf, the completeness of the data extraction tool was checked and a necessary correction was made.

163 Statistical analysis

After the data was extracted from the chart, it was first checked for consistency and completeness. After that, it was coded and entered into EPI INFO version 7.2.2.6 and exported to STATA version 14.0 for analysis. A frequency table was used to describe the socio-demographic and clinical variables of the study. The prevalence of anemia with a 95% confidence interval at the time of ART initiation was estimated. Model fitness was checked by using the Hosmer-Lemeshow goodness of fit test (p-value = 0.6106) and the model was fitted well. Bivariate analysis was executed for each variable, and those variables with a p-value < 0.2 were entered into multivariate binary logistic regression to identify factors associated with anemia prevalence at the time of ART initiation. An odds ratio with a 95% CI was computed, and variables having a p-value < 0.05 in the multivariate logistic regression were considered as statistically independent factors for anemia at ART initiation.

7 175 **Patient and public involvement**

Since the study was based on chart review without active involvement of patients, no patientswere involved.

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179 Ethics approval and consent to participate

Ethical clearance was obtained from the Institutional Review Board (IRB) of the University of Gondar (Ref. No. :-S/N/1600/06/2011). Upon the ethical clearance, a letter of cooperation was obtained from the school of nursing to collect data. Permission was also obtained from Debre Markos comprehensive specialized hospital medical director and ART focal person. Confidentiality was maintained by avoiding the registration of personal identifiers like names to the extraction tool. Also, no raw data was given to anyone other than the investigator, and it was fully anonymized.

Result

188 Socio-demographic characteristics of HIV-infected adults

Out of all the patients enrolled in the ART Clinic from January 1, 2014, to December 31, 2018, a total of 473 charts were selected and reviewed based on the inclusion criteria. From these reviewed charts, 468 charts were included in the analysis, and only five charts were excluded due to data incompleteness. Of all the patients' charts included in the analysis, 281 (60.04%) were females, and about 190 (40.60%) of the participants were grouped under the category of age 25 to 34 years (**Table 1**).

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Table 1: Prevalence of Anemia at the time of ART initiation stratified by socio demographic characteristics of HIV-infected adults at Debre-Markos comprehensive specialized hospital from January 1, 2014 to December 31, 2018 (n = 468).

Characteristics	Frequency (%)	Ane	mia status	P-value	
		Anemic (%)	Not Anemic (%)		
Sex					
Male	187 (39.96)	86 (45.99)	101 (54.01)	< 0.001	
Female	281 (60.04)	77 (27.40)	204 (72.60)		
Age in years		, , , , , , , , , , , , , , , , , , ,			
15-24	51 (10.90)	11 (21.57)	40 (78.43)	0.138	
25-34	190 (40.60)	65 (34.21)	125 (65.79)		
35-44	157 (33.55)	61 (38.85)	96 (61.15)		
≥45	70 (14.96)	27 (38.57)	43 (61.43)		
Religion					
Orthodox	447 (95.51)	158 (35.35)	289 (64.65)	0.677	
Muslim	20 (4.27)	6 (30.00)	14 (70.00)	1	
Protestant	1 (0.21)	0	1 (100.00)		
Marital status					
Single	56 (11.97)	18 (32.14)	38 (67.86)	0.813	
Married	251 (53.63)	85 (33.86)	166 (66.14)	1	
Divorced/separated	125 (26.71)	47 (37.60)	78 (62.40)	-	
Widowed	36 (7.69)	14 (38.89)	22 (61.11)	1	
Educational level					
No education	171 (36.54)	62 (36.26)	109 (63.74)	0.365	
Primary	109 (23.29)	38 (34.86)	71 (65.14)		
Secondary	113 (24.15)	44 (38.94)	69 (61.06)		
College +	75 (16.03)	20 (26.67)	55 (73.33)		
Residence					
Rural	101 (21.58)	45 (44.54)	56 (55.45)	0.024	
Urban	367 (78.42)	119 (32.43)	248 (67.57)		
Occupation					
Employed	153 (32.69)	50 (32.68)	103 (67.32)	0.455	
Unemployed	315 (67.31)	114 (36.19)	201 (63.81)		
Family size					
< 2 person	187 (39.96)	55 (29.41)	132 (70.59)	0.112	
3-4 person	213 (45.51)	82 (38.50)	131 (61.50)	1	
>4 person	68 (14.53)	27 (39.71)	41 (60.29)		
HIV disclosure status					
Disclosed	426 (91.03)	149 (34.98)	277 (65.02)	0.924	
Not disclosed	42 (8.97)	15 (35.71)	27 (64.29)	1	

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205 Clinical and immunological related characteristics of HIV-infected adults

Of all the study participants included in the analysis, around 136 (29.06%) had started ART six months or above after HIV status had been confirmed, and 78 (16.67%) of the study subjects had past OIs. From the group, about 121 (25.85%) and 29 (6.20%) of patients were grouped under baseline WHO clinical staging of three and four, respectively. One-third of patients included in the analysis had a baseline CD4+ T-cell count of less than 200 cells/ul and 134 (28.63%) of patients were grouped under the category of BMI of less than 18.5kg/m². Regarding the functional status of HIV-infected patients in this study, around 98 (20.84%) had ambulatory or bedridden functional status at enrolment into highly active antiretroviral therapy (HAART) (Table 2).

Table 2: Prevalence of anemia at the time of ART initiation stratified by clinical and immunologic related characteristics of HIV-infected adults at Debre-Markos comprehensive specialized hospital from January 1, 2014, to December 31, 2018 (n = 468).

Characteristics	Frequency	Anemia status		P-value
	(%)	Anemic (%)	Not Anemic (%)	1
Pre-ART duration				
< 6 month	332 (70.94)	122 (36.75)	210 (63.25)	0.227
\geq 6 month	136 (29.06)	42 (30.88)	94 (69.12)	
Past OI			~	
Yes	78 (16.67)	34 (43.59)	44 (56.41)	0.083
No	390 (83.33)	130 (33.33)	260 (66.67)	
Past CPT treatment				
Yes	93 (19.87)	32 (34.41)	61 (65.59)	0.886
No	375 (80.13)	132 (35.02)	243 (64.80)	
Past INH prophylaxis				
Yes	15 (3.21)	3 (20.00)	12 (80.00)	0.215
No	453 (96.79)	161 (35.54)	292 (64.46)	
Past TB treatment history				
Yes	14 (2.99)	8 (57.14)	6 (42.86)	0.078
No	454 (97.01)	156 (34.36)	298 (65.64)	
Baseline WHO clinical staging				
Ι	197 (42.09)	43 (21.83)	154 (78.17)	< 0.001
II	121 (25.85)	35 (28.93)	86 (71.07)]
III	121 (25.85)	63 (52.07)	58 (47.93)	1

IV	29 (6.20)	23 (79.31)	6 (20.69)	
Baseline CD4 count (cells/µl)				
<100	89 (19.02)	62 (69.66)	27 (30.34)	< 0.001
100 - 199	74 (15.81)	41 (55.41)	33 (44.59)	
200 - 349	124 (26.50)	34 (27.42)	90 (72.58)	
≥ 350	181 (38.68)	27 (14.92)	154 (85.08)	
Baseline BMI				
< 18.5	134 (28.63)	78 (58.21)	56 (41.79)	< 0.001
18.5-24.9	286 (61.11)	76 (26.57)	210 (73.43)	
>24.9	48 (10.26)	10 (20.83)	38 (79.17)	
Baseline functional status				
Working	370 (79.06)	93 (25.14)	277 (74.86)	< 0.001
Ambulatory	90 (19.23)	65 (72.22)	25 (27.78)	
Bedridden	8 (1.71)	6 (75.00)	2 (25.00)	

ART=Antiretroviral Therapy; OI=Opportunistic Infection; CPT=Cotrimoxazole preventive therapy;
 INH=Isoniazid; TB=Tuberculosis; CD4=Cluster of Differentiation four; BMI=Body Mass Index

Anemia prevalence among HIV-infected adults at the time of ART initiation The overall prevalence of anemia at the time of ART initiation in this study was 35.04% (95%)

222 CI: 30.84–39.49). Of these, about 74 (45.12%) were grouped under the category of moderate 223 anemia level (Figure 1).

Factors that determine anemia prevalence at the time of ART initiation

After applying bivariate logistic regression, variables with a p-value of 0.2 or less were taken into multivariate logistic regression. Variables included in multivariate analysis were sex, age at enrolment, level of education, residence, family size, pre-ART duration, past OIs, CD4+ T-cell count at enrollment, Body Mass Index, WHO clinical stage, and functional status at enrollment. After multivariate logistic regression, five variables, including sex, level of education, CD4+ Tcell count, BMI, and functional status at enrollment, were found to be statistically independent predictors of anemia prevalence at the time of ART initiation at a p-value of less than 0.05.

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232	The current study revealed that the odd of being anemic at the time of ART initiation among
233	males was 2.45 times that of females (AOR = 2.45 ; 95% CI: $1.51-3.98$). Similarly, the odd of
234	developing anemia among patients who had not attended formal education was 2.38 times that of
235	those with a college degree and above educational level (AOR = 2.38 ; 95% CI: $1.12-5.05$). The
236	CD4+ T-cell count was also another significant factor of anemia at the time of ART initiation.
237	The likelihood of developing anemia at the time of ART initiation among patients with a CD4+
238	T-cell count of less than 200 cells/ μ l was 4.67 times that of 200 cells/ μ l or more (AOR = 4.67;
239	95% CI: 2.78–7.85). In the same manner, the odds of being anemic at enrolment into ART was
240	2.43 times higher among patients with a BMI of less than 18.5 kg/m ² than among patients with a
241	normal BMI (AOR = 2.43; 95% CI: 1.42-4.16). Lastly, the odds of being anemic among
242	ambulatory and/or bedridden patients was 2.69 times that of working functional status at the time
243	of ART initiation (AOR = 2.69; 95% CI: 1.41–5.12) (Table 3).

Table 3: Bivariate and multivariable logistic regression analysis of factors associated with anemia at the time of ART initiation among HIV infected adults at Debre-Markos comprehensive specialized hospital from January 1, 2014, to December 31, 2018 (n = 468).

Characteristics	Frequency		COR (95% CI)	AOR (95% CI)	P-Value
	Anemic	Not anemic			
Sex of the patient					
Male	86	101	2.30 (1.56, 3.40)	2.45 (1.51, 3.98)	<0.001*
Female	77	204	1.00	1.00	
Age at enrolment (in yea	ur)				
15-24	11	40	1.00	1.00	
25-34	65	125	1.89 (0.91, 3.93)	1.96 (0.79, 4.85)	0.145
35-44	60	97	2.31 (1.10, 4.85)	1.65 (0.65, 4.22)	0.295
45+	27	43	2.28 (1.003, 5.19)	1.65 (0.58, 4.67)	0.346
Level of education					
No education	62	109	1.57 (0.88, 2.82)	2.38 (1.12, 5.05)	0.024*
Primary	37	72	1.32 (0.70, 2.51)	1.69 (0.76, 3.77)	0.195
Secondary	44	69	1.87 (1.01, 3.45)	1.88 (0.87, 4.04)	0.107
College+	20	55	1.00	1.00	
Patient's residence					
Rural	118	249	1.67 (1.07, 2.62)	1.58 (0.91, 2.75)	0.105
Urban	45	56	1.00	1.00	
Family size					
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\leq 2 person	55	132	1.00	1.00	
3–4 person	81	132	1.50 (0.99, 2.28)	1.30 (0.76, 2.22)	0.3
\geq 5 person	27	41	1.58 (0.89, 2.82)	1.41 (0.68, 2.94)	0.3
Pre-ART duration					
< 6 months	122	210	1.00	1.00	
\geq 6 months	42	94	0.77 (0.50, 1.17)	0.93 (0.55, 1.60)	0.8
Presence of past OI					
Yes	34	44	1.55 (0.94, 2.53)	0.88 (0.46, 1.69)	0.7
No	130	260			
CD4+ T-cell count at ent	olment (cell	s/µl)			
< 200	103	60	6.86 (4.49, 10.49)	4.67 (2.78, 7.85)	<0.
\geq 200	61	244	1.00	1.00	
Body Mass Index (kg/m ²					
<18.5	78	56	3.85 (2.49, 5.93)	2.43 (1.42, 4.16)	0.0
18.5 - 24.9	76	210	1.00	1.00	
> 24.9	10	38	0.73 (0.35, 1.53)	1.26 (0.54, 2.93)	0.5
WHO Clinical staging					
Stage I	43	158	1.00	1.00	
Stage II	35	86	1.49 (0.89, 2.51)	0.94 (0.51, 1.73)	0.8
Stage III/IV	Stage III/IV 86 60 5.27 (3.29, 8.44)		1.78 (0.96, 3.30)	0.0	
Functional status at enrol	ment				
Working	93	277	1.00	1.00	
A mala valata may la a dui d dan	71	27	7 82 (4 74 12 02)	260(141512)	0.0

AOR=Adjusted Odds Ratio; ART=Antiretroviral therapy; CD4+=Cluster of Differentiation; COR=Crude Odds Ratio; OI=Opportunistic Infection; WHO=World Health Organization

Discussion

The overall prevalence of anemia at the time of ART initiation in the current study was 35.04% (95% CI: 30.84–39.49), which is higher than studies conducted at the University of Gondar Referral Hospital (21.2%) [20], and Hawassa University Referral Hospital (23.4%) [19]. However, anemia prevalence in the current study is lower than in studies from Addis Ababa [16, 17] and Arba Minch Town [18]. Similarly, anemia prevalence in the current study is lower than in a similar study at Black Lion Specialized Hospital (41.9%) [21]. This could be due to a higher mean of baseline CD4+ T-cell count in the current study (289.5 cells/ μ l ±167.8) than that of

Black Lion Specialized Hospital (162.5 cells/ μ l ± 108.6). This indicates that the likelihood of anemia will be increased as the HIV infection advances due to immunologic deterioration [27]. Anemia prevalence is also higher than a study done in Johannesburg, South Africa, with a prevalence of 25.8% [15]. The variation may be due to socio-demographic differences. However, it is also lower than studies conducted in China and Nepal, with a prevalence of 51.9% [10] and 55.8% [14], respectively. This lower prevalence of anemia in the current study could be related to differences in socio-demographic characteristics, or it could be due to differences in the time period in which better interventions to reduce anemia have been applied recently than in previous times. Additionally, the majority of patients (72.3%) from China had a CD4+ T-cell count of less than 200 cells/mm3 [10] compared to the current study, which is about 34.83%. This might have an important biological implication in that the lower CD4+ T-cell count was associated with an increased risk of anemia [5, 28]. In this study, the male sex was found to be an independent predictor of increased anemia at the time of ART initiation. This is in line with studies conducted in Zewditu memorial hospital and Arba Minchi town, Ethiopia [16, 18]. More alcohol consumption among males than females might contribute to this difference between males and females. As males consume more alcohol, the rate of Vitamin B12 absorption into the circulatory system becomes lower and may result in anemia [29]. In contrast to the current study, the odds of being anemic at the time of ART

initiation at Hawassa University referral hospital was higher in females than in males [19]. In the previous study, more than two-thirds of the subjects were females, and this might have contributed to increased anemia due to the presence of menstrual blood loss and in the drains on iron stores during pregnancy and delivery [16].

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Similarly, the current study showed that the odds of being anemic among patients who had not attended formal education was 2.38 times higher than those with a college degree and above educational status. This is supported by a retrospective cross-sectional study from Mizan-Aman General Hospital, Ethiopia [30]. This may be explained by patients who have not attended formal education are less aware of better nutrition and better health care. When HIV infection is observed among those who have not attended formal education, the risk of poor nutrition and the occurrence of anemia will be double burdened. Additionally, non-educated patients are not fully aware of anemia symptoms, so they will come to the hospital quite late with high anemic grades [31, 32].

The current study revealed that the odds of being anemic among patients with a CD4+ T-cell count of less than 200 cells/ mm³ was 4.67 times that of a CD4+ T-cell count greater than 200 cells/ mm³. This is congruent with studies from the University of Gondar referral hospital, Arba Minchi town, and Black Lion specialized hospital [18, 20, 21]. It could be due to the fact that bone marrow abnormalities are found at all stages of HIV disease and increase in frequency and severity as the disease advances. So, the risk of anemia occurrence increases with progressive immunologic deterioration and a CD4+ T-cell count of less than 200 cells/mm3 is related to the development of anemia [33].

Anemia was 2.43 times more likely in patients with a lower BMI (18.5 kg/m2) than in those with a normal BMI. This is congruent with a study from Wolaita Sodo University teaching referral hospital, Ethiopia [34]. This might be as a result of deficiencies in micronutrients such as iron, folate, and vitamin B12 in patients with under nutrition. This deficiency of micronutrients directly contributes to the development of anemia among those with a BMI of less than 18.5 kg/m². Lastly, being in an ambulatory or bedridden functional status increased the likelihood of

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developing anemia among HIV patients. This might be explained by being in ambulatory or bedridden functional status, which could be an indicator of HIV infection advancement and the occurrence of other opportunistic infections that may also be at risk for loss of appetite, expose them to malnutrition, and result in anemia [35].

In this study, we noted a few limitations. Since the cause of anemia in HIV-infected adults is multi-factorial and the study was based on chart review, we noted that a few variables were missed. Furthermore, this study did not collect data on dietary habits, substance use status, menstrual habits in females, or the type of anemia. Additionally, this study was conducted among ART-naïve adults, which lacks comparison with anemia after ART initiation.

312 Conclusion

The current study showed that a significant proportion of HIV-infected adults developed anemia at the time of ART initiation. Male sex, lack of formal education, a CD4+ T-cell count < 200 cells/mm3, decreased BMI, and ambulatory or bedridden functional status were discovered to be independent predictors of anemia. Hence, giving special attention to patients not attending formal education, males, and late presenters is crucial to reduce anemia occurrence and its health impact. Finally, the findings of this study will provide baseline information to healthcare providers in order to select ART drugs accordingly, and may provide additional insight into the development of new anemia preventive strategies.

321 Abbreviations

AIDS: Acquired Immunodeficiency Syndrome; AOR: Adjusted Odds Ratio; ART: Antiretroviral
 Therapy; BMI: Body Mass Index; CD4+: Cluster of Differentiation Four; CI: Confidence
 Interval; COR: Crude Odds Ratio; CPT: Cotrimoxazole Prophylactic Therapy; HAART: Highly

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Organization.

Acknowledgments

Competing interests

not-for-profit sectors.

Not applicable.

Consent for publication

Authors' contribution

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Availability of data and materials

The authors have declared that they have no competing interests.

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Active Antiretroviral Therapy; HIV: Human Immunodeficiency Virus; INH: Isoniazid; MRN: Medical Record Number; OI: Opportunistic Infections; TB: Tuberculosis; WHO: World Health Protected by copyright, including for uses related to text and The authors would like to acknowledge the hospital director and data collectors for their collaboration during the data collection. Also, the authors' heartfelt thanks go to the University This research received no specific grant from any funding agency in the public, commercial, or ining, Al training, and similar technologies The dataset used during the current study is available from the corresponding author. All authors made a significant contribution to the work reported. AA conceived the idea and design for the work, participated in the data collection process, analyzed and interpreted the data, and also drafted the manuscript. BS, EG, MW, and BC approved the designed work with some revisions, participated in data analysis, and reviewed the manuscript. All authors gave final 18

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4	346	approv	val of the version to be published; have agreed on the journal to which the article has bee	n
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8	348	Refe	rences	
9 10	510	11010		
11	349	1.	Turner, J., M. Parsi, and M. Badireddy, Anemia, in StatPearls [Internet]. 2020, StatPearls	
12	350		Publishing.	
13	351	2.	Chaparro, C.M. and P.S. Suchdev, Anemia epidemiology, pathophysiology, and etiology in low-	
14	352		and middle-income countries. Annals of the New York Academy of Sciences, 2019. 1450(1): p.	
15	353		15.	
16	354	3.	Aynalem, Y.A., W. Shibabaw Shiferaw, and Z. Woldiye, Prevalence of Anemia and Its Associated	
1/	355		Factors in Antiretroviral-Treated HIV/AIDS-Positive Adults from 2013 to 2018 at Debre Berhan	
10	356		Referral Hospital, Ethiopia. Advances in Hematology, 2020. 2020.	
20	357	4.	Brentlinger, P.E., et al., Practical management of HIV-associated anemia in resource-limited	
21	358		settings: prospective observational evaluation of a new Mozambican guideline. AIDS research	
22	359		and human retroviruses, 2016. 32 (1): p. 12-25.	
23	360	5.	Durandt, C., et al., HIV and haematopoiesis. South African Medical Journal, 2019. 109(8,	
24	361		Supplement 1): p. S41-S46.	
25	362	6.	Kerkhoff, A.D., et al., Predictive value of anaemia for tuberculosis in HIV-infected patients in sub	1-
26	363		Saharan Africa: an indication for routine microbiological investigation using new rapid assays.	
27	364		Journal of acquired immune deficiency syndromes (1999), 2014. 66(1): p. 33.	
28	365	7.	Meidani, M., et al., Prevalence, severity, and related factors of anemia in HIV/AIDS patients.	
30	366		Journal of research in medical sciences: the official journal of Isfahan University of Medical	
31	367		Sciences, 2012. 17(2): p. 138.	
32	368	8.	Petraro, P., et al., Determinants of anemia among human immunodeficiency virus-positive adult	ts
33	369		at care and treatment clinics in dar es salaam, Tanzania. The American journal of tropical	
34	370		medicine and hygiene, 2016. 94 (2): p. 384-392.	
35	371	9.	Ezeamama, A.E., et al., Evolution of anemia types during antiretroviral therapy—implications fo	r
36	372		treatment outcomes and quality of life among HIV-infected adults. Nutrients, 2019. 11 (4): p.	
3/	373		755.	
20 20	374	10.	Shen, Y., et al., Prevalence of anemia among adults with newly diagnosed HIV/AIDS in China.	
40	375		PLoS One, 2013. 8 (9): p. e73807.	
41	376	11.	Gardner, W. and N. Kassebaum, Global, Regional, and National Prevalence of Anemia and Its	
42	377		<i>Causes in 204 Countries and Territories, 1990–2019.</i> Current Developments in Nutrition, 2020.	
43	378		4 (Supplement_2): p. 830-830.	
44	379	12.	Kassebaum, N.J., The global burden of anemia. Hematology/Oncology Clinics, 2016. 30(2): p.	
45	380		247-308.	
46	381	13.	Melese, H., et al., Anemia among adult HIV patients in Ethiopia: a hospital-based cross-sectiona	ıl
4/ 10	382		<i>study.</i> Hiv/aids (Auckland, NZ), 2017. 9 : p. 25.	
40 49	383	14.	Martin, C., K. Poudel-Tandukar, and K.C. Poudel, HIV symptom burden and anemia among HIV-	
50	384		positive individuals: cross-sectional results of a community-based positive living with HIV (POLH)
51	385		<i>study in Nepal.</i> PloS one, 2014. 9 (12): p. e116263.	
52	386	15.	Takuva, S., et al., Anemia among HIV-infected patients initiating antiretroviral therapy in South	
53	387		Africa: improvement in hemoglobin regardless of degree of immunosuppression and the	
54	388		initiating ART regimen. Journal of tropical medicine, 2013. 2013.	
55				
56 57				
57 58				0
59			-	.9

BMJ Open

389 200	16.	Assefa, M., et al., Prevalence and correlates of anemia among HIV infected patients on highly active anti-retroviral therapy at Zewdity Memorial Hospital. Ethiopia, BMC homotology 2015
201		15 (1): n 6
392	17	Adape A et al HIV-associated angemia before and after initiation of antiretroviral therapy at
393	17.	Art Centre of Minilik II Hospital Addis Ababa Ethionia Ethionian Medical Journal 2012 50 (1): n
394		
395	18	Alamdo A G et al Anemia and its associated risk factors at the time of antiretroviral therapy
396	10.	initiation in public health facilities of Arba Minch Town, Southern Ethionia, Health, 2015, 7(12):
397		n 1657
398	19	Daka, D., D. Lelissa, and A. Amsalu, <i>Prevalence of angemig before and after the initiation of</i>
399	19.	antiretroviral therapy at ART centre of Hawassa University Referral Hospital, Hawassa, South
400		Ethionia, Sch I Med 2013, 3 (1): n 1-6
401	20.	Tesfave, Z. and B. Enawgaw. Prevalence of anemia before and after initiation of highly active
402	20.	antiretroviral therapy among HIV positive patients in Northwest Ethiopia: a retrospective study.
403		BMC research notes, 2014, 7(1): p. 1-5.
404	21.	Woldeamanuel, G.G. and D.H. Wondimu. <i>Prevalence of anemia before and after initiation of</i>
405		antiretroviral therapy among HIV infected patients at black lion specialized hospital. Addis
406		Ababa, Ethiopia: a cross sectional study. BMC hematology, 2018. 18 (1): p. 7.
407	22.	ICF, C.S.A.C.E.a., Ethiopia demographic and health survey 2016. Addis Ababa, Ethiopia, and
408		Rockville, Maryland, USA: CSA and ICF, 2016.
409	23.	Negesse, A., et al., Prevalence of anemia and its associated factors in human immuno deficiency
410		virus infected adult individuals in Ethiopia. A systematic review and meta-analysis. BMC
411		hematology, 2018. 18 (1): p. 32.
412	24.	Moges, N. and G. Kassa, Prevalence of opportunistic infections and associated factors among HI
413		positive patients taking anti-retroviral therapy in DebreMarkos Referral Hospital, Northwest
414		<i>Ethiopia.</i> J AIDs Clin Res, 2014. 5 (5): p. 1-300.
415	25.	Geneva, S. and W.H. Organization, Haemoglobin Concentrations for the Diagnosis of Anaemia
416		and Assessment of Severity. Vitamin and Mineral Nutrition Information System. Document
417		<i>Reference WHO</i> . 2011, NMH/NHD/MNM/11.1. <u>http://www</u> . who.
418		int/entity/vmnis/indicators/haemoglobin
419	26.	Aemro, A., A. Jember, and D.Z. Anlay, Incidence and predictors of tuberculosis occurrence among
420		adults on antiretroviral therapy at Debre Markos referral hospital, Northwest Ethiopia:
421		retrospective follow-up study. BMC Infectious Diseases, 2020. 20(1): p. 1-11.
422	27.	Gedefaw, L., et al., Anemia and risk factors in HAART naive and HAART experienced HIV positive
423		persons in south west Ethiopia: a comparative study. PloS one, 2013. 8 (8): p. e72202.
424	28.	Zerihun, K.W., G.A. Bikis, and E.A. Muhammad, Prevalence and associated factors of anemia
425		among adult human immune deficiency virus positive patients on anti-retroviral therapy at
426		Debre tabor Hospital, Northwest Ethiopia. BMC research notes, 2019. 12 (1): p. 168.
427	29.	Fragasso, A., Vitamin B12 deficiency in alcoholics, in Alcohol, nutrition, and health consequences
428		2013, Springer. p. 131-134.
429	30.	Muluken, W. and M. Epherem, Assessment of the prevalence of zidovudine induced anemia
430		among adult HIV/AIDS patients on HAART in an ethiopian hospital. Occup Med Health Aff, 2018
431		6 (271): p. 2.
432	31.	Sunguya, B.F., et al., Poor nutrition status and associated feeding practices among HIV-positive
433		children in a food secure region in Tanzania: a call for tailored nutrition training. PloS one, 2014
434		9 (5): p. e98308.

Page 22 of 29

BMJ Open

1			
2			
5 ⊿	435	32.	Yadav, U.K., et al., Factors Associated with Anemia among Pregnant Women of Underprivileged
5	436		Ethnic Groups Attending Antenatal Care at Provincial Level Hospital of Province 2, Nepal.
6	437		Anemia, 2021. 2021 .
7	438	33.	Dhurve, S.A. and A.S. Dhurve, Bone marrow abnormalities in HIV disease. Mediterranean journal
8	439		of hematology and infectious diseases, 2013. 5(1).
9	440	34.	Ageru, T.A., et al., Anemia and its associated factors among adult people living with human
10	441		immunodeficiency virus at Wolaita Sodo University teaching referral hospital. PloS one, 2019.
11	442		14 (10): p. e0221853.
12	443	35.	Gebremichael, M.A., M.K. Gurara, and H.N. Weldehawaryat, Incidence and predictors of initial
13	444		antiretroviral therapy regimen change among HIV-infected Adults receiving antiretroviral
14	445		therapy at Arba Minch general hospital, Southern Ethiopia. HIV/AIDS (Auckland, NZ), 2020. 12: p.
15	446		315.
16 17			
17	447		
10			
20	110		
21	448		
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26	450		
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1 2 3 4	459	Figure legend:
5 6 7	460	Figure 1: Level of anemia at the time of ART initiation among HIV-infected adults at Debre
9 10	461	Markos comprehensive specialized hospital.
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53 54 55 56 57 58 59 60		22 For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml



Figure 1: Level of anemia at the time of ART initiation among HIV-infected adults at Debre

Markos comprehensive specialized hospital.

STROBE Statement—checklist of items that should be included in reports of observational studies

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	Item No.	Recommendation	Page No.	Relevant text from Handscript
Title and abstract	1	(a) Indicate the study's design with a commonly used term in the title or the abstract	2	Line (27); An institution based retrospective cross-sectional study was conducted among 47 betweents' charts enrolled from 2014 to 2018 at Debre-Markos compressive specialized hospital.
		(b) Provide in the abstract an informative and balanced summary of what was done and what was found	2	Lines (23 – 45); Abstracta
Introduction				ata m
Background/ratio nale	2	Explain the scientific background and rationale for the investigation being reported	3, 4 and 5	Lines (54 – 94); Introduction
Objectives	3	State specific objectives, including any prespecified hypotheses	5	Lines (95 – 97); This study aimed to assess the prevalence of anemia and its associated factors at the time of ART initiation among HIV- infected patients at Debre Markos comprehensive specialized hospital.
Methods				similar
Study design	4	Present key elements of study design early in the paper	5	Lines (100 – 102); An institution-based retrospective cross-sectional study was conducted at Debre Markos comprehensive specialized hospital from January 1, 2014, to December 31, 2018, among HIV- infected adults.
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5	Lines (199 – 105); Study design, setting and period
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Participants	6	(a) Cohort study—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	5 and	Lines (106 – 111); Source and study population Lines (112 – 116); Ingluston and exclusion criteria (eligibility criteria)
		Case-control study—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls	6	Lines (126 – 128); By generating a random number on the computer, a total of 473 patient selected through a simple random sampling technique, and selected from them.
		Cross-sectional study—Give the eligibility criteria, and the sources and methods of selection of participants		ext and c
		(b) Cohort study—For matched studies, give matching criteria and number of exposed and unexposed	N/A	This was a cross-section is study
		Case-control study—For matched studies, give matching criteria and the number of controls per case		, Al trair
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	7	Lines (131 – 140); Operational definition of variables
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	7	Lines (141 – 152); Data Gellection tools and procedures
Bias	9	Describe any efforts to address potential sources of bias	8	Lines (154–159); A pretended data extraction tool was used to maintain data quality. Quality is also maintained by extracting data using trained nurses and close monitoring of the procedure by the supervisor. Data clerks were involved in the selection of patients' charts from the computer as well as from the chart room. Before returning the chart to

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				the shelf, the completeness of the data extraction tool was checked a a necessary correction was made.		
Study size	10	Explain how the study size was arrived at	6	Lines (117–124); The same ple size was determined by using a form to estimate single population proportion with the assumption of a 9 level of confidence, 2015 proportion, and a 4% marginal error.		
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	8	Lines (166–171); Bi the analysis was executed for each variable and those variables with p-value < 0.2 were entered into multivariable binary logistic regression identify factors associated with anemia. odds ratio with a 95% as computed, and variables having a p-value < 0.05 in the multivariate logistic regression were considered statistically independent factors for anemia at ART initiation.		
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding	8	Lines (160–171); Stal 400 I Analysis		
		(b) Describe any methods used to examine subgroups and interactions	N/A	There were no subgraups		
		(c) Explain how missing data were addressed	N/A	There was no missing dag		
		(d) Cohort study—If applicable, explain how loss to follow-up was addressedCase-control study—If applicable, explain how matching of cases and controls was addressed	N/A	Lines (126–128); By generating a random number on the computer total of 473 patients charts were selected through a simple rand sampling technique.		
		Cross-sectional study—If applicable, describe analytical methods taking account of sampling strategy		g en ce B		
		(<u>e</u>) Describe any sensitivity analyses	N/A	ibliog		
Results				raphiq		

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study with only one stage.	This was a cross-sectiona ing for	N/A	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	13*	Participants
ne 2	inseig ies rei	N/A	(b) Give reasons for non-participation at each stage		
992 D	nemer ated to	N/A	(c) Consider use of a flow diagram		
The special sector of	Line (197); Table 1: Prove stratified by socio denne at Debre-Markos compre- 2014 to December 31 Line (212); Table 2: Prev stratified by clinical and infected adults at Depre- from January 1, 2014	10 and 11	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	14*	Descriptive data
วi ณฑก/o	There was no missing dat	N/A	(b) Indicate number of participants with missing data for each variable of interest		
study	This was a cross-sectiona	N/A	(c) Cohort study—Summarise follow-up time (eg, average and total amount)		
Southand States Study	This was a cross-section a	N/A	Cohort study—Report numbers of outcome events or summary measures over time	15*	Outcome data
study <u>B</u>	This was a cross-sectiona	N/A	Case-control study—Report numbers in each exposure category, or summary measures of exposure		
The second seco	Lines (218–219); The over initiation in this study wa	12	Cross-sectional study—Report numbers of outcome events or summary measures		

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Main results	16	 (a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included 	12, 13 and 14	Lines (218–219); The over all prevalence of anemia at the time of ART initiation in this study was 35.04% (95% CI: 30.84–39.49). Lines (241); Table 3, Bis ariate and multivariable logistic regression analysis of factors associated with anemia at the time of ART initiation among HIV infection and the time of ART initiation specialized hospital from January 1, 2014, to Dec 31, 2018 (n = 468).
		(b) Report category boundaries when continuous variables were categorized	N/A	There was no continue Bariable.
		(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	N/A	There was no estimates be relative risk.
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	N/A	There was no sub group and sensitivity analysis.
Discussion				g, // A
Key results	18	Summarise key results with reference to study objectives	14–16	Lines (247–307); Dissussion
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	16	Lines (303–307); Single the cause of anemia in HIV-infected adults i multi-factorial and the study was based on chart review, we noted that a few variables were missed. Furthermore, this study did not collect data on dietary habits substance use status, menstrual habits in females or the type of anemia Additionally, this study was conducted amon ART-naïve adults, which lacks comparison with anemia after ART initiation.
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	14–16	Lines (247–307); Discussion
Generalizability	21	Discuss the generalizability (external validity) of the	17	Lines (308–316); The surrent study showed that a significant

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Other informat Funding *Give information	ion 22 n separatel	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based y for cases and controls in case-control studies and, if applic	18 cable, for	initiation. Male sex, I less than 200 cells/m functional status we anemia. Hence, givin education, males, an occurrence and its he provide baseline info ART drugs accordin development of new This research receiv in the public, comm	king and an and similar technologies	of formal education, a CD4+ T-cell count of nder nutrition, and ambulatory or bedridden scovered to be independent predictors of ocial attention to patients not attending formal mpact. Finally, the findings of this study will be not be healthcare providers in order to select and may provide additional insight into the may provide additional insight into the may provide additional insight into the may provide additional insight into the a preventive strategies.
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