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Time to detection of anaemia and its predictors among women of reproductive-age living with HIV/AIDS initiating ART at public hospitals, Southwest Ethiopia: a multicentre retrospective follow-up study

Alemayehu Sayih Belay ,[1] Yalemtsehay Dagnaw Genie ,[2] Belete Fenta Kebede ,[3] Aychew Kassie,[1] Abebaw Molla [4]

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For numbered affiliations see end of article.

Correspondence to
Alemayehu Sayih Belay;
Alex.sayihalem2018@gmail.com

ABSTRACT

Objective To assess the time to development of anaemia and its predictors among women of reproductive-age receiving antiretroviral therapy (ART) in public hospitals, Southwest Ethiopia.

Design Hospital-based retrospective follow-up study

Setting Mizan-Tepi University Teaching Hospital, and Gebretsadik Shawo General Hospital Southwest Ethiopia.

Participants A total of 389 records of women living with HIV/AIDS at public hospitals were reviewed using a systematic sampling method. The data were entered using Epi-Data Manager V.4.2 and exported to STATA V.14 for data analysis. A Cox-regression model was used and variables with a p-value of <0.05% and 95% confidence level in multivariable analysis were declared as statistically significant predictors for anaemia.

Primary outcome Time to development of anaemia and its predictors among women of reproductive-age on ART in public hospitals.

Results Of 370 records of women of reproductive-age, 203 (54.86%, 95% CI (49.77% to 59.96%)) were anaemic with an incidence rate of 12.07 per 100 person months of observation, and the overall median survival time of 60 months. The total of 2.97%, and 80.26% of women were developed anaemia within the first 6 months and the last 6 months period of follow-up, respectively. Moreover, non-employed women, women with advanced WHO stage, women with baseline opportunistic infections and women who were on ART for long-duration were significantly associated with anaemia among women living with HIV/AIDS.

Conclusion In this study, the incidence rate of anaemia was significantly high. The development of anaemia among women on ART was also increased with increased follow-up time. The risk of anaemia is increased in women living with HIV/AIDS due to advanced baseline WHO staging, presence of OIs at baseline, an increased duration on ART and low occupational status. Therefore, early identification and treatment of opportunistic infections and other coinfections are required to decrease the incidence of anaemia among women living with HIV/AIDS.

Strengths and limitations of this study

- This study was conducted at the two hospitals, which increases the probability of generalisability.
- This study used a multivariate logistic regression analysis to control all possible confounders.
- In this study, the Cox Snell residual (r_C) was used to check the model goodness-of-fit graphically.
- Since this study was a retrospective follow-up study, there is loss of individuals to follow-up during the study.

BACKGROUND

Anaemia is the most common haematological problem associated with HIV infection worldwide.[1] WHO defined as haemoglobin (Hb) levels <12.0 g/L in women and <13.0 g/L in men.[2] It is a condition in which the number of red blood cells (RBCs) or the amount of Hb and their oxygen-carrying capacity are insufficient in the body to meet physiological needs.[3] However, normal Hb distribution varies with age, sex, altitude, ethnicity, cigarette use and pregnancy status.[2–4]

In 2019, the global prevalence of anaemia among women of reproductive-age was 29.9%, which is equivalent to over half a billion women aged 15–49 years. Since 2000, the global prevalence of anaemia in women of reproductive-age has been stagnant, although there has been a slight decrement in the prevalence of anaemia among pregnant women.[5]

In resource-limited settings, anaemia continues to be a challenge,[6] especially, in sub-Saharan Africa (SSA), with about an estimated 190 million cases occurring in SSA countries.[7] Of which, the preschool children account for 43% of the total anaemia cases, followed

by women of reproductive-age (29% non-pregnant and 38% pregnant women).[8] In Ethiopia, despite antiretroviral therapy (ART) service began in 2003 and the free ART programme launched in 2005,[9] the prevalence of HIV and other HIV-associated problems such as anaemia remains unduly high. In 2018, about 690 000 people were living with HIV. Women are disproportionally affected by HIV where about 410 000 were women. The prevalence of HIV among adults (15–49 years) was 1%.[10]

In HIV-infected individuals, the virus by itself and HIV-related opportunistic infections (OIs) and malignancies can directly affect the bone marrow which is responsible for the production of haematopoietic growth factors, and indirectly via cytokine-mediated bone-marrow suppression,[11] and due to this reason, anaemia is common in about 20%–80% of HIV-infected individuals. Thus, the introduction of highly active antiretroviral therapy (HAART) has improved the quality of life by suppressing viral replication and restoration of the immune system or increasing CD4+ T-cell count which in turn reduces the incidence of severe anaemia. However, the use of HAART (HAART-containing zidovudine and ganciclovir)[12] has been shown to be linked to the development of anaemia among HIV-infected patients due to bone marrow suppression.[4]

Anaemia is common in women of reproductive-age due to pregnancy, childbirth, internal bleeding due to certain medications and illnesses, lactation, heavy menstruation, endometriosis and insufficient dietary intake, or poor absorption of iron from food during their reproductive cycle.[13 14] It has enormous effects such as shock, loss of productivity, hypotension, cognitive impairment, coronary or pulmonary insufficiency, increased susceptibility to infections due to its effect on immunity, restless leg syndrome (also called Willis-Ekbom disease) and maternal mortality.[14 15] Besides, anaemia in women of reproductive-age can also result in poor feto-maternal outcomes such as premature birth, spontaneous abortion, stillbirth, low birth weight, postpartum depression and childhood mental, cognitive and motor developmental delays, which may result in infant/child mortality.[14–16]

Worldwide, mainly in developing countries, the prevalence and risk of developing anaemia among patients living with HIV relies on different economic, sociodemographic, behavioural and other health-related factors. Multifactorial causes contribute to the increase in the burden of anaemia and decrease survival includes rural residence,[17] being female, lower CD4 count, higher HIV viral loads, coinfection with tuberculosis (TB),[18–24] ethnicity, oral candidiasis,[25] the later stage of HIV disease, being pregnant,[20 21] lower levels of education, poorer housing, unemployment, poor diet, lower body mass index (BMI), immune dysregulation, neoplastic diseases, infections (viral, bacterial and parasitic), metabolic disorders.[26–29] and increased age were strongly associated with anaemia.[30]

Moreover, evidence also showed that the long-term use of multiple drugs used for the treatment of HIV/AIDS and other problems results in an increase in the occurrence of anaemia which is often argued to be associated with myelosuppression and reticuloendothelial iron block. For instance, long duration of HAART use, cotrimoxazole, pentamidine, amphotericin, interferon, dapsone, cancer chemotherapeutic medications (ie, used for the treatment of Kaposi's sarcoma; vinca alkaloids (eg, vincristine, bleomycin); chloramphenicol and trimethoprim/sulfamethoxazole and hydroxyurea-based drugs) can cause anaemia.[17 20 31–33]

Despite numerous attempts have been commenced to elucidate HIV-associated anaemia in Ethiopia, the burden of anaemia among women living with HIV/AIDS is remained strikingly high. Due to this reason, anaemia has attracted the attention of researchers and policymakers, where its' input helps the programmers to develop and implement strategies towards screening, early provision of treatment of anaemia and reduction of other morbidities and mortalities associated with advanced HIV disease and long-term use of HAART. Hence, this study aims to assess the time to development of anaemia and its predictors among women of reproductive-age on ART in public hospitals, Southwest Ethiopia.

METHOD AND MATERIALS

Study design and period

A retrospective follow-up study was conducted at public hospitals in southwest Ethiopia from 1 February 2020 to 30 March 2020, on women living with HIV/AIDS who attended ART clinic from 1 February 2010 to 5 February 2018.

Study setting

The study was carried out in two public hospitals of Southwest Ethiopia: Mizan-Tepi University Teaching Hospital (MTUTH) and Gebretsadik Shawo General Hospital (GSGH). These hospitals are located in Benchi-Sheko Zone and Kefa Zone, respectively.

MTUTH was established in 1986 GC. Previously during the Derg regime, this hospital was named 'Mizan-Teferi General Hospital'. Then, until 2016 GC, it was named 'Mizan Aman General Hospital'. Then, during 2016 GC, this hospital was incorporated into Mizan-Tepi University and named 'MTUTH'. This hospital was located in a town called Mizan Teferi (recently named Mizan-Aman Town) which is the capital town of the Bench Sheko Zone (previously the capital of the Bench Maji Zone). It is located 565 kms far from Addis Ababa; the Capital City of Ethiopia. Currently, MTUTH is expected to provide services to more than one million people. While GSGH was first established in the 1990 EC and named as 'Gebretsadik Shawo Primary Hospital'. Then, in 2005 EC, this hospital was named as 'GSGH'. Currently, the GSGH is expected to provide care for more than 500 000 people.[34]

Source population

All women of reproductive-age (15–49 years) who were receiving ART at the public hospitals.

Study population

All women of reproductive-age (15–49 years) who were receiving ART from 1 February 2010 to 5 February 2018 at public hospitals.

Inclusion and exclusion criteria

All women of reproductive-age (15–49 years) who were on ART and had a fixed follow-up time were included. Medical charts and ART registration logbooks of the study participants with incomplete data (ie, Hb status, weight, hypertension status and baseline CD4 count), and women who already had anaemia at baseline or before the start of the follow-up period were excluded from the study.

Sample size determination

The sample size was calculated using the STATA statistical package V.14 (Cox-Model) based on the following important assumptions: 95% confidence level, 80% optimum statistical power, variability of 0.5 and significance level of 0.05. By considering a study which was conducted in Felege Hiwot Referral Hospital, Northwest Ethiopia;[35] by taking the probability of failure (event) of 0.588 and considering HRs of different predictor variables; 2.98 for past pulmonary TB, 1.5 for baseline weight and 1.49 for nutritional status, the estimated sample sizes were 49.5, 357.5 and 369.6, respectively. Therefore, to increase the confidence in our estimate, to decrease the uncertainty and to have greater precision, we used a larger sample size of 370 and after a 5% non-response rate was added for the lost and incomplete medical charts, the final sample size was 389.

Sampling procedure

A systematic random sampling method was applied to select study participants. First, a total of 6224 women of reproductive-age (4108 from MTUTH and 2116 from GSGH) who started ART during the study period were identified in ART clinics. Then, the sample size was proportionally allocated to each hospital (257 from MTUTH and 132 from GSGH). The sampling interval (kth) was calculated as the total number of women of reproductive-age on ART divided by the sample size (6224/389=16). Then, every 16th participant was selected after the first eligible participant was selected by the lottery method (figure 1).

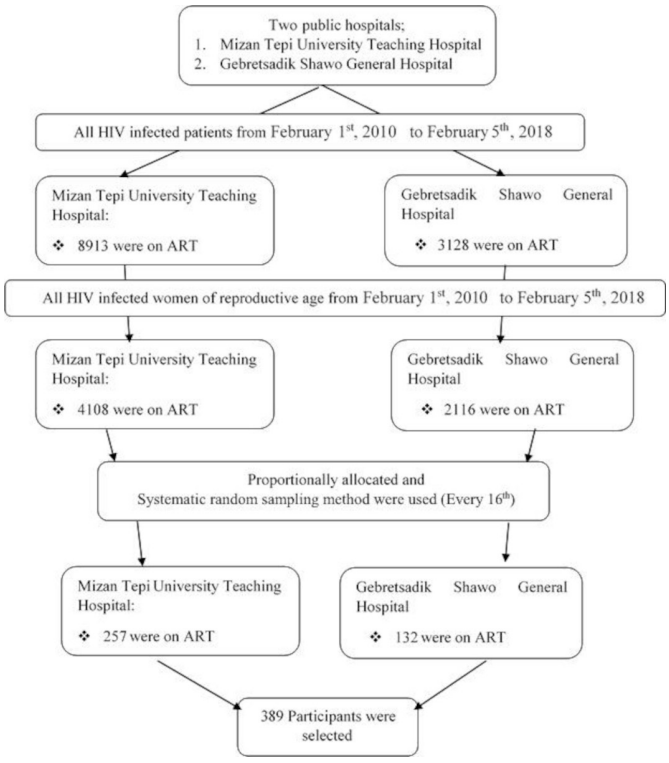

Figure 1 Schematic presentation of sampling procedure for time to detection of anaemia and its predictors among women of reproductive-age living with HIV/AIDS initiating ART at public hospitals, Southwest Ethiopia, 2020. ART, antiretroviral therapy.

Operational definition

Anaemia

A non-pregnant woman aged 15 years and above and a Hb level of less than 12.0 g/L were considered anaemic. Anaemia, further classified as mild (11–11.9 g/L), moderate (8–10.9 g/L) and severe (<8 g/L).[36] During pregnancy, Hb levels of less than 11.0 g/L were considered anaemic and can be categorised into mild anaemia (Hb levels 9–10.9 g/L), moderate anaemia (Hb levels 7–8.9 g/L) and severe anaemia (Hb levels less than 7 g/L).[37]

Time to detection of anaemia

Time calculated by subtracting dates from the period of women initiation of ART to the occurrence of the event (ie, anaemia) during the follow-up period.

Time measurement

The time was measured in months.

Time origin

First date of ART initiation and first starting time of follow-up

Censored

Study participants who were lost to follow-up, died before detection of anaemia, transferred to another service and end of the study period before developing anaemia were considered censored.

Baseline CD4+ T-cell count

It refers to the CD4+ T-cell count before initiation of ART.

Baseline weight

It refers to the weight of women of reproductive-age before initiation of ART.

Underweight, normal weight, overweight and obesity

It was defined as a BMI of <18.5 kg/m^2, 18.5–24.9 kg/m^2, 25–29.9 kg/m^2 and ≥30 kg/m^2, respectively.[38]

Baseline stages of hypertension

According to the 2020 International Society of Hypertension global hypertension practice guidelines, hypertension is classified as normal if BP is <130/85, high normal or prehypertension (130–139/85–89), grade 1 hypertension (140–159/90–99) and grade 2 hypertension (≥160/100).[39]

Baseline WHO clinical stages I– IV

Stage 1. Patients who were asymptomatic or had persistent generalised lymphadenopathy for longer than 6 months. *Stage 2*. Patients may demonstrate unexplained weight loss of less than 10% of their total body weight and recurrent respiratory infections as well as a range of dermatological problems. *Stage 3*. Those encompassed by a weight loss of greater than 10% of total body weight, prolonged (more than 1 month) unexplained diarrhoea, pulmonary TB and severe systemic bacterial infections including pneumonia, pyelonephritis, empyema, pyomyositis, meningitis, bone, and joint infections and bacteremia. *Stage 4*. Is the severely symptomatic stage, where the designation includes all AIDS-defining illnesses.[40]

Study variables

Dependent variables

Time to detection of anaemia

Independent variables

Sociodemographic characteristics such as age, residence, marital status, education, occupation and other clinical characteristics such as HIV/AIDS coinfection, baseline CD4+ T-cell count, baseline regimen type, baseline WHO clinical staging, viral load, adherence and weight at baseline.

Data collection tools and procedure

Data were collected using data extraction tools which were developed and adapted from reviewing different relevant literatures and derived from a standard national HIV follow-up form of Ethiopia.[35 41 42] Six data collectors and two supervisors were recruited from those who were working in ART clinics of respective hospitals and 1 day of training was given regarding the data collection procedure and how to extract appropriate data. The pretest was conducted among 5% of the sample size to check the consistency of the abstraction tools. The actual data were collected by four clinical nurses and supervised by two laboratory technicians in the selected public hospitals. Data regarding sociodemographic, clinical and treatment-related variables of women of the reproductive-age group were extracted from medical charts and ART registration logbooks. To address the potential sources of bias, a review of records was also conducted using the checklist.

Data quality assurance

The quality of data was assured by using a pretested and properly designed data extraction tool. Furthermore, the data were collected and supervised by trained data collectors and supervisors, respectively. The collected data were checked for completeness by the supervisor on a daily basis. Moreover, data cleaning and double data entry were carried out to check for any inconsistencies, coding errors and missing or out-of-range values.

Data processing and analysis

The data were entered using Epi-Data Manager V.4.2 and exported to STATA V.14 for data analysis. Descriptive statistics such as mean, median, IQR, frequencies and percentages were used to summarise data and to see the distribution of study variables.

The median survival time, the cumulative probability of anaemia and the survival curve difference between the different covariates were estimated by using the Kaplan–Meier analysis. The incidence rate of anaemia was calculated for women of reproductive-age with anaemia as the numerator divided by total months of follow-up in women of reproductive-age.

The survival curve difference was compared between categories of different predictor variables using the log-rank test. The cumulative probability of survival at the different time intervals was estimated by the life table. Multicollinearity among predictor variables was checked using variance inflation factor (VIF) and the mean VIF became 1.20 which shows no collinearity among explanatory variables.

Cox proportional hazards (CPH) regression model was used to identify the explanatory variables of anaemia. Those predictors having a p-value of <0.05 in the bivariate analysis were entered into the multivariable analysis and those variables having a p-value of <0.05 at 95% confidence level were declared as statistically significant predictors for anaemia. The Schoenfeld residual/global test was used to assess the assumptions of the Cox-proportional hazard model. The Cox Snell residual (r_C) was used to check the model goodness-of-fit graphically.

Patient and public involvement

Patients and/or the public were not involved in the design, or conduct, or reporting or dissemination plans of this research.

RESULTS

Socio-demographic characteristics of the respondents

A total of 370 records of women of reproductive-age on ART were reviewed with a complete response rate of 95%. The mean and SD of the age of the participants was 37.76±9.33 years. More than half 234 (63.2%) of the participants were urban residents, and 135 (36.5%) were orthodox religion followers. Concerning respondents' educational status, 233 (63.0%) were educated (table 1).

Clinical and treatment-related characteristics of women of reproductive-age on ART

Women living with HIV/AIDS were on ART for a median (IQR) of 7[2–10] years. At baseline, more than

Table 1 Sociodemographic characteristics of women of reproductive-age on ART (n=370) in public hospitals, South West Ethiopia, 2020

Variables	Frequency	%
Place of residence		
Urban	234	63.2
Rural	136	36.8
Age of participants		
<35	163	44.1
>35	207	55.9
Mean±SD	37.76±9.33	
Marital status		
Single	49	13.2
Married	168	45.4
Divorced	70	18.9
Widowed	83	22.4
Religion		
Orthodox	135	36.5
Protestant	117	31.6
Muslim	107	28.9
Others*	11	3.0
Ethnicity		
Kaffa	70	18.9
Amhara	60	16.2
Oromo	61	16.5
Bench	54	14.6
Sheka	57	15.4
Tigre	46	12.4
Other †	22	5.9
Respondent's educational status		
Non-educated	137	37.0
Educated	233	63.0
Respondent's occupational status		
Not employed	243	65.7
Employed	127	34.3
Monthly income		
Median (IQR)	1000.00 (642.50–2000.00)	

*Catholic, and Jehovah witnesses.
†Silte, Gurage, Hadiya, Wolayita.
ART, antiretroviral therapy.

Table 2 Clinical and treatment-related characteristics of women of reproductive-age on ART in public hospitals, South West Ethiopia, 2020

Variables	Frequency	%
Duration of HAART(in years)		
≤6	125	33.8
>6	245	66.2
Median (IQR) of ART duration (in years)	7.00 (2.00, 10.00)	
Baseline WHO clinical stage		
I	61	16.5
II	114	30.8
III	106	28.6
IV	89	24.1
Baseline CD4+ T-cell count (cells/mm^3)		
<200	177	47.8
200–349	107	28.9
350–499	55	14.9
≥500	31	8.4
Viral load count (copies/mm^3)		
≤1000	291	78.6
>1000	79	21.4
Initial HAART regimen		
AZT based	232	62.7
EFV based	138	37.3
Opportunistic infection at baseline		
Yes	199	53.8
No	171	46.2
Baseline status of hypertension		
No	304	82.2
Yes	66	17.8
Baseline stages of hypertension		
Norma1	275	74.3
High normal or prehypertension	29	7.8
Grade 1 hypertension	52	14.1
Grade 2 hypertension	14	3.8
Baseline weight		
Underweight	91	24.6
Normal weight	185	50.0
Overweight	55	14.9
Obesity	39	10.5

ART, antiretroviral therapy; AZT, zidovudine; CD4, cluster of differentiation 4; EFV, efavirenz; highly active antiretroviral therapy, HAART.

half 114 (30.8%) of the respondents were in WHO clinical stage II, 177 (47.8%) had a CD4+ T-cell count of <200 cells/mm^3, and 79 (21.4%) had a viral load of >1000 copies/mm^3. Regarding the initial treatment regimen, about 232 (62.7%) of the respondents were on AZT-based HAART regimen. Of the total respondents, about 199 (53.8%) had an OI, and 66 (17.8%) had hypertension (table 2).

Incidence and time to develop anaemia during the follow-up period

This study showed that 203 (54.86, 95% CI (49.77% to 59.96%)) of the women of reproductive-age were anaemic in 16818 person-months of observations (PMO), with an incidence rate of 12.07 per 100 PMO (95% CI: 10.51 to

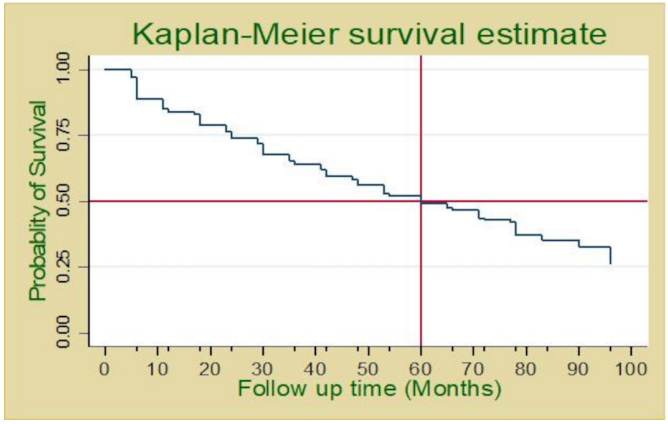

Figure 2 Kaplan–Meier survivor estimate of women of reproductive-age on ART in public hospitals, South West Ethiopia, 2020. ART, antiretroviral therapy.

13.85) during the follow-up period and 167 (45.14%) were censored; of which 13 (3.5%) of women of reproductive-age on ART were lost to follow-up, 13 (3.5%) were transferred out and 141 (38.1%) were remained non-anaemic until the end of the study. The two perpendicular lines in the Kaplan–Meier survivor function estimate graph show the overall median survival time of 60 months, where it is the time that half of the events occurred among women of reproductive-age. Using the Kaplan–Meier survival function estimator, the cumulative probability of not developing anaemia at the end of the 6th month, 48th month and 96th month period of follow-up were 88.92% (95% CI: 85.25 to 91.72), 56.05% (95% CI: 50.55 to 61.19) and 26.13% (95% CI: 14.73 to 39.04), respectively (figure 2).

Using the life table estimator of cumulative failure function, 2.97% (95% CI: 1.66 to 5.30), and 80.26% (95% CI: 62.11 to 93.37) of women of reproductive-age had developed anaemia within the first 6 months and the last 6 months period of follow-up, respectively (figure 3).

The median survival time free from anaemia among women of reproductive-age on ART who had a viral load count of below 1000 was 71 months, but for those who

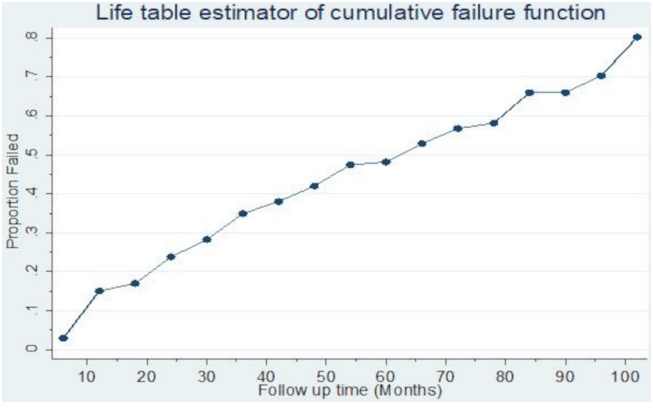

Figure 3 Life table estimator of cumulative failure function among women of reproductive-age on ART in public hospitals, South West Ethiopia, 2020. ART, antiretroviral therapy.

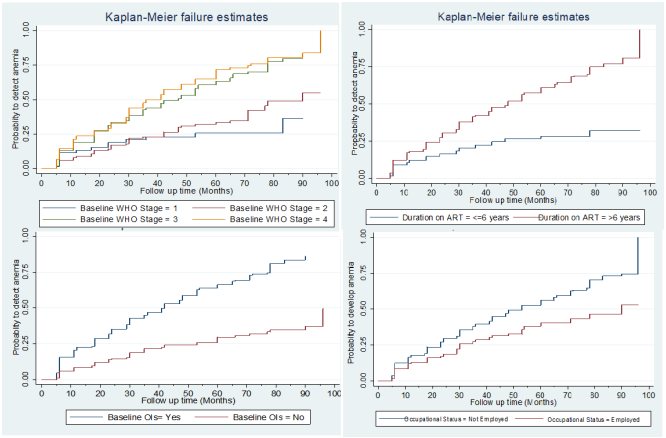

Figure 4 Kaplan–Meier failure estimate of anaemia in different groups' strong predictors among women of reproductive-age on ART in public hospitals, South West Ethiopia, 2020. ART, antiretroviral therapy.

had a viral load count of above 1000 was 42 months. The median survival time free from anaemia among educated women of reproductive-age on ART was 66 months, but for those who were uneducated, it was 60 months. The median survival time free from anaemia among employed women of reproductive-age receiving ART was 90 months, but for non-employed women, it was 53 months. The median anaemia-free survival times were 90, 47 and 41 months among women of reproductive-age on ART who had WHO stages II, III and IV, respectively. The probability of developing anaemia among women of reproductive-age who were on ART for ≥6 years, had baseline OIs and with their occupational status of not employed were higher as compared with their counterparts, respectively (figure 4).

Cox proportional hazard assumption test

Assumptions of the CPH model were assessed by using Schoenfeld residual/global test, which became non-significant (0.1022), indicates proportional hazard assumption of CPH regression was met. The multicollinearity of each independent variable was checked using the VIF and the mean VIF for those variables was 1.2.

Cox proportional hazard model fitness test

The fitness of the final model was checked graphically by using the Cox Snell residual; shows the hazard function follows the 45° line closely confirmed that the final model is a good fit (figure 5).

Predictors of time to development of anaemia

Considering the above-mentioned assumption and model fitness, the bivariable analysis of the CPH model was estimated and predictors including baseline WHO staging, OIs at baseline, duration on ART, age of the participant, educational status, occupational status, residence, baseline CD4 count and viral load were found to be significant predictors of anaemia. Besides, after adjusting the predictors using multivariable model, variables including baseline WHO staging, OIs at baseline, duration on ART

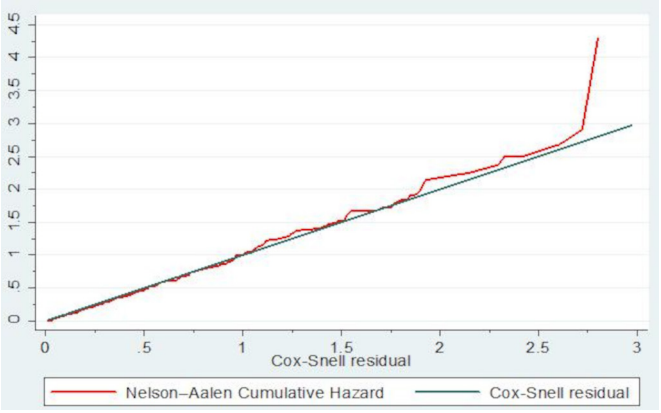

Figure 5 Cox-Snell residual and Nelson-Alen cumulative hazard graph among women of reproductive-age on ART in public hospitals, South West Ethiopia, 2020. ART, antiretroviral therapy.

and occupational status were found to be strong predictors of anaemia.

The HR of anaemia in non-employed women of reproductive-age were 1.465 times higher as compared with their counterparts (AHR: 1.47 (95% CI: 1.05 to 2.04)). The HR of anaemia in women of reproductive-age who had WHO stage IV were 2.493 times more likely compared with women of reproductive-age who had WHO stage I (AHR: 2.49 (95% CI: 1.40 to 4.43)). Besides, women who had a baseline OIs had almost three times more likely to increase in the HR of anaemia than their counterparts (AHR: 2.99 (95% CI: 2.12 to 4.23)). Moreover, women who were on ART for grater that 6 years had the higher hazards of anaemia than those who were on ART for duration of less than or equal to 6 years (AHR: 1.63 (95% CI: 1.04 to 2.55)) (table 3).

DISCUSSION

Background

Anaemia among women living with HIV/AIDS is common;[14] therefore, knowing the prevalence and predictors of anaemia will help different stakeholders develop an integrated preventive and control measure of anaemia.[43] Thus, this study aimed to assess the time to the development of anaemia and its predictors among women of reproductive-age on ART in public hospitals, Southwest Ethiopia.

General finding

In this study, about 54.86% of the participants developed anaemia with an incidence rate of 12.07 per 100 PMO, and the overall median survival time was 60 months. Of the total participants who developed anaemia, about 2.97% (95% CI: 1.66 to 5.30), and 80.26% (95% CI: 62.11 to 93.37) of women of reproductive-age living with HIV/AIDS developed anaemia within the first 6 months and the last 6 months period of follow-up, respectively. Moreover, non-employed women, women with advanced WHO clinical stage, women with baseline OIs and women who were on ART for a long-duration were significantly associated with anaemia among women living with HIV/AIDS.

Comparison with similar studies

In the current study, about 54.86% of women of reproductive-age developed anaemia during the follow-up period. This was higher than the studies conducted in the University of Gondar, Northwest Ethiopia, 35%,[44] in Addis Ababa, Ethiopia, 33%,[45] and Jimma University Specialised Hospital, southwest Ethiopia (16.2%).[46] This difference could be attributed to the difference in the cut-off value of Hb in defining anaemia and study participants. Moreover, this may be due to the difference in the proportion of patients on the zidovudine (AZT)-based regimen, whereas in our study, the proportion was 62.7% but 50% in the study conducted in Addis Ababa. Hence, the higher incidence rate of anaemia might be due to the myelosuppressive effect of the AZT-based regimen.[32]

In the current study, about 2.97% and 80.26% of women of reproductive-age living with HIV/AIDS developed anaemia within the first 6 months and last 6 months period of follow-up, respectively. This study was found to be inconsistent with the study conducted in Northwest Ethiopia,[35] where, about 13.8% and 18.1% of anaemia cases occurred in the first year, and in the third-year follow-up time, respectively. This discrepancy might be due to the differences in the time measurement and the total duration of follow-up period. For instance, in this study, the time was measured in months, whereas, in the study conducted in Northwest Ethiopia, the time was measured in years.

In the current study, numbers of factors, such as baseline WHO staging, OIs at baseline, duration on ART and occupational status were identified as independent predictors of anaemia among women living with HIV/AIDS.

In this study, the hazard of anaemia in women of reproductive-age with WHO clinical stage IV were higher than that in women of reproductive-age with WHO clinical stage I. This result is supported by studies conducted in different parts of Ethiopia like Tikur Anbessa Specialised Hospital, Addis Ababa,[47] and Debre Birhan[48] and other African countries like South Africa,[24] Mozambique[49] and Kenya.[50] The possible explanation could be attributed due to the advanced WHO clinical staging is associated with depletion of immunity and can lead to severe medical illnesses like anaemia due to the depletion of CD4+ T-cell count, viral replication and the additional burden of coinfections (oral candidiasis, cytomegalovirus, and others).[40]

Besides, women who had baseline OIs were more likely to have an increased HR of anaemia than their counterparts. This finding is congruent with the studies conducted in Isfahan, Iran[51] and in Jimma University Specialised Hospital, Ethiopia.[46] This may be due to the fact that OI among women living with HIV/AIDS causes immune dysregulation which in turn increases the risk of anaemia through RBC destruction (haemolysis) or ineffective RBC production.[52]

Table 3 Cox-regression analysis of predictors for anaemia among women of reproductive-age on ART in public hospitals, South West Ethiopia, 2020

Variables	Anaemia		Cox-regression analysis	
	No N (%)	Yes N (%)	CHR (95% CI)	AHR (95% CI)
Age of participant				
≤35	98 (60.1)	65 (39.9)	1.00†	1.00†
>35	69 (33.3)	138 (66.7)	**1.84 (1.37 to 2.48)***	0.98(0.70 to 1.36)
Residence				
Urban	127 (54.3)	107 (45.7)	1.00†	1.00†
Rural	40 (29.4)	96 (70.6)	**1.71 (1.30 to 2.26)***	1.08(0.79 to 1.47)
Educational status				
Uneducated	50 (36.5)	87 (63.5)	**1.32 (1.00 to 1.75)***	0.98(0.72 to 1.33)
Educated	117 (50.2)	116 (49.8)	1.00†	1.00†
Occupational status				
Non-employed	91 (37.4)	152 (62.6)	**1.75 (1.28 to 2.41)***	**1.47 (1.05 to 2.04)***
Employed	76 (59.8)	51 (40.2)	1.00†	1.00†
Baseline CD4 count				
<200	69 (39.0)	108 (61.0)	**2.27 (1.18 to 4.34)***	0.83(.41 to 1.66)
200–349	42 (39.3)	65 (60.7)	**2.08 (1.07 to 4.07)***	0.76(.37 to 1.55)
350–499	35 (63.6)	20 (36.4)	1.12(.53 to 2.39)	0.78(.36 to 1.69)
≥500	21 (67.7)	10 (32.3)	1.00†	1.00†
Viral load count				
≤1000	151 (51.9)	140 (48.1)	1.00†	1.00†
>1000	16 (20.3)	63 (79.7)	**1.88 (1.39 to 2.54)***	1.14(.81 to 1.62)
Baseline WHO clinical stage				
I	45 (73.8)	16 (26.2)	1.00†	1.00†
II	68 (59.6)	46 (40.4)	1.42 (0.80 to 2.50)	1.54 (0.86 to 2.74)
III	34 (32.1)	72 (67.9)	**3.08 (1.79 to 5.31)***	**2.48 (1.39 to 4.42)***
IV	20 (22.5)	69 (77.5)	**3.55 (2.06 to 6.12)***	**2.49 (1.40 to 4.43)***
OIs at baseline				
Yes	45 (22.6)	154 (77.4)	**3.38 (2.44 to 4.68)***	**2.99 (2.12 to 4.23)***
No	122 (71.3)	49 (28.7)	1.00†	1.00†
Duration of ART (in years)				
≤6	92 (73.6)	33 (26.4)	1.00†	1.00†
>6	75 (30.6)	170 (69.4)	**3.07 (2.11 to 4.47)***	**1.63 (1.04 to 2.55)***

*Adjusted for all significant variables p<0.05.
†Reference category.
AHR, adjusted HR; ART, antiretroviral therapy; CD4, cluster of differentiation 4; CHR, crude HR; OIs, opportunistic infections.

Moreover, women who received ART for a long duration had a higher hazard of anaemia than their counterparts. This study is in line with the studies conducted in San Francisco General Hospital[53] and in Jimma University Specialised Hospital, Ethiopia.[46 54] This similarity might be due to the toxic effect of AZT on the bone marrow which is the site of blood cell production.[55] Moreover, this drug is also argued to be associated with a reticuloendothelial iron block.[53]

The hazard of anaemia in unemployed women of reproductive-age was higher as compared with their counterparts. This is consistent with the studies conducted in Tamil Nadu, India[56] and North Showa, Ethiopia.[57] This might be due to the fact that the good occupational status of the women helps them to generate good income which in turn helps them to access for varieties of nutrition.[14]

This study had some of the strengths. First, since this study was conducted in two hospitals, it increases the

generalisability of anaemia among women living with HIV/AIDS in the study settings. Second, this study used fixed Hb measurement time of some study participants which is every 6 months. Despite these strengths, this study has also its own limitations. First, since it is a retrospective study, the study did not address some of the participant-related predictors of anaemia. Second, the total duration of follow-up time was not long enough. Therefore, in order to see the detail effects of HAART drug and other clinical findings to the development of anaemia, future researchers should do similar researches using prospective study by considering long duration of follow-up time.

Policy implication and future research

Ethiopian ministry of health has launched some programmes, plans and trials[58 59] for the reduction of anaemia and different complications among women living with HIV/AIDS who was initiating ART. Despite those trials and plans, the current study findings indicated that anaemia detection among women living with HIV/AIDS initiating ART was high due to different predictors. This highlights that reproductive-age women living with HIV/AIDS initiating ART are higher risky for the development of anaemia. Thus, the government of Ethiopia needs to strengthen existing programmes and strategies to decrease the proportion of early detection of anaemia by preventing predictive factors.

In addition to governmental organisations, other non-governmental organisations need to give attention to early detection of anaemia, its' reduction and intervention programmes to control the prevalence of anaemia in reproductive-age women living with HIV/AIDS initiating ART. Moreover, early detection of anaemia among women living with HIV/AIDS initiating ART should be promoted, especially for non-employed women, women with advanced WHO stage, women with baseline OIs and women who were on ART for long duration. For instance, the previous studies confirmed that non-employed women are associated with low socioeconomy status which in turn can affect early detection of anaemia.[56 57] The good occupational status of the women helps them to generate good income which in turn helps them to access varieties of nutrition for the prevention of anaemia.[14] Women who were on ART for long duration also showed a high incidence of anaemia.[46 54] Long-period use of AZT drug causes toxic effects on the bone marrow which is the site for blood cell production and associated with the reticuloendothelial iron block that leads for early anaemia detection.[53 55] Generally, in order to promote early detection of anaemia and reduce the prevalence of anaemia among women living with HIV/AIDS, health education should be given for non-employed women, patients with advanced WHO stage, women with baseline OIs and for women who were on ART for long duration. Moreover, health policy development should be considered in order to prevent OIs and comorbidities like anaemia and to increase the quality of life of women living with HIV/AIDS. Ultimately, close follow-up and monitoring of women living with HIV/AIDS initiating ART should be encouraged by concerned bodies at different health institutions including clinicians to minimise the risk of anaemia detection and its associated predictors.

CONCLUSION

In this study, the incidence rate of anaemia was significantly high. The development of anaemia among women on ART was also increased with increased follow-up time. The risk of anaemia is increased in women living with HIV/AIDS due to advanced baseline WHO staging, presence of OIs at baseline, an increased duration on ART and low occupational status. Therefore, early identification and treatment of OIs and other coinfections are required to decrease the incidence of anaemia among women living with HIV/AIDS.

Author affiliations
[1]Maternal and Reproductive Health Unit, Department of Nursing, College of Medicine and Health Sciences, Mizan-Tepi University, Mizan-Teferi, Ethiopia
[2]Child Health Unit, Department of Nursing, College of Medicine and Health Sciences, Mizan-Tepi University, Mizan Teferi, Ethiopia
[3]Department of midwifery, Faculty of Health Sciences, Jimma University, Jimma, Ethiopia
[4]Department of Nutrition, School of public health, College of Medicine and Health Sciences, Mizan-Tepi University, Mizan-Teferi, Ethiopia

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ORCID iDs
Alemayehu Sayih Belay http://orcid.org/0000-0001-7039-6600
Yalemtsehay Dagnaw Genie http://orcid.org/0000-0002-3764-3646
Belete Fenta Kebede http://orcid.org/0000-0001-8283-9667

Abebaw Molla http://orcid.org/0000-0001-5582-6449

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