scientific reports

Check for updates

OPEN

Predictors of anemia among HIV-infected children in Ethiopia: systematic review and meta-analysis

Desalegn Girma[1]✉, Zinie Abita[2], Wubetu Agegnehu[2], Daniel Asmelash[3], Amanuel Adugna[1], Nigusie Shifera[2], Melsew Setegn Alie[2] & Gossa Fetene Abebe[1]

Anemia continues to be one of the common complications among HIV-infected children. In Ethiopia, though there is a systematic review and meta-analysis study on anemia among HIV-infected children, it only disclosed the effect Highly Active Antiretroviral Treatment on HIV/AIDS-anemia comorbidity, and yet, the meta effect of other potential factors such as type of ART, presence of opportunistic infection, advanced stage of HIV/AIDS, and cotrimoxazole therapy on HIV/AIDS-anemia comorbidity have not been explored in the previous review. Therefore, this systematic review and meta-analysis aimed to identify the factors associated with anemia among HIV-infected children. Moreover, this study provides an up-to-date pooled estimate of anemia among HIV-infected children in Ethiopia. We systematically searched PubMed, HINARI, Science Direct, Cochrane Library, Google Scholar, and African Journals Online on February 3, 2024, to identify relevant primary research articles. The Briggs Institute (JBI) Checklist was used to check the quality of the original studies. Meta package for proportions (Metapro) was used to estimate the pooled prevalence of anemia among HIV-infected children using the random-effects model. Heterogeneity across studies was checked using the I-square test. Funnel plots visual inspection and Egger's tests were done to detect publication bias. The pooled prevalence of anemia among HIV-infected children in Ethiopia was 23.79% (95% CI 17.28, 31.81). Age < 7 years (OR 3.71, 95% CI 2.58; 5.33), advanced HIV disease (OR 2.78, 95% CI 2.00; 3.87), intestinal parasitic infection (OR 2.28, 95% CI 1.02; 5.09), poor ART treatment adherence (OR 1.96, 95% CI 1.23; 3.10), opportunistic infection (OR 2.81, 95% CI 1.59; 4.95), viral load > 1000 copies/ml (OR 4.29, 95% CI 2.28; 8.09), and zidovudine containing regimen (OR 5.07, 95% CI 2.41; 10.64) were identified as factors associated with a higher risk of anemia. Whereas, cotrimoxazole prophylaxis therapy (OR 0.49, 95% CI 0.35; 0.72) reduces the risk of anemia among HIV-infected children. In Ethiopia, anemia remains a public health concern among children living with HIV. Therefore, regular screening and management of anemia are important for HIV-infected children, particularly for those with advanced HIV disease, opportunistic infection, high viral load, and who are taking zidovudine-containing regimens for better clinical outcomes. Moreover, preventive chemotherapy (deworming) and counseling on infection prevention should be provided for children living with HIV to prevent parasitic infection.

Keywords Anemia, Children, HIV, Systematic review, Meta-analysis, Ethiopia

Abbreviations

WHO	World Health Organization
HIV	Human Immunodeficiency Virus
JBI	The Joanna Briggs Institute Critical Appraisal Checklist
HAART	Highly Active Antiretroviral Treatment
PRISMA	Preferred Reporting Items for Systematic Review and Meta-Analysis Statement
OR	Odds ratio
CI	Confidence interval

[1]Department of Midwifery, College of Health Science, Mizan-Tepi University, Mizan-Teferi, Ethiopia. [2]Department of Public Health, College of Health Science, Mizan-Tepi University, Mizan-Teferi, Ethiopia. [3]Department of Medical Laboratory, College of Health Science, Mizan Tepi University, Mizan-Teferi, Ethiopia. ✉email: desegir@gmail.com

Anemia in children is defined as a hemoglobin concentration below < 11 g/L for children aged < 5 years, < 11.5 g/dl for children aged 5–11.9 years, and < 12 g/dl for children aged 12–14.9 years after altitude adjustment[1]. According to the World Health Organization (WHO), the prevalence of anemia ≥ 40%, 20–39%, 5–19%, and < 5% in the country is considered a severe public health problem, moderate public health problem, mild public health problem, and no public health problem, respectively[2]. Anemia can affect children in many aspects, such as it impairs the growth and development of children[3–7], reduces school performance[7,8] and in the long run decreases productivity in adulthood and affects the quality of life of an individual[8].

Anemia is one of the common complications among people living with human immunodeficiency virus (HIV) infection[9]. Evidence shows that the envelope protein of HIV and/or abnormal levels of cytokine milieu in the bone marrow (BM) is one of the pathophysiological mechanisms responsible for HIV-related anemia[10,11]. Moreover, anemia is an independent predictor of disease progression and deaths among people living with HIV[12,13]. Globally, an estimated 39.7% of children (aged < 15 years) living with HIV were affected by anemia[14]. Similarly, a high prevalence of anemia was reported among HIV-infected children in East Africa. In this region, an estimated 36.17% of HIV-infected children were affected by anemia[15]. This shows the succeeding public health impact of anemia among people living with HIV.

In Ethiopia, the prevalence of anemia among HIV-infected children varies considerably, ranging from the lowest in the Tigray region (7%)[16] to the highest in the Afar region (53.9%)[17]. Moreover, WHO clinical staging, opportunistic infection, age, viral load, antiretroviral therapy (ART) drug type, cotrimoxazole prophylaxis therapy, intestinal parasitic infection, ART adherence, dietary diversity, and residence of caregiver were identified as factors associated with anemia among HIV positive children[17–29]. However, in previous literature, mixed results were reported on some of the associated factors. For instance, factors such as advanced WHO clinical staging[17,22,25,26], opportunistic infection[25,27], not receiving cotrimoxazole prophylaxis therapy[20,26] and intestinal parasitic infection[20,23,27] were associated with an increased risk of anemia among HIV infected children. However, in other previous studies, advanced WHO clinical staging[19,20,23], opportunistic infection[19,20,26], cotrimoxazole prophylaxis therapy[27,29], and intestinal parasitic infection[19] have no association with anemia among HIV infected children. In Ethiopia, though there is a systematic review and meta-analysis study on anemia among HIV-infected children, it only explored the association of anemia with Highly Active Antiretroviral Treatment (HAART)[30] and yet, the meta effect of other potential factors such as type of ART, presence of opportunistic infection, advanced stage of HIV/AIDS, and cotrimoxazole therapy on HIV/AIDS-anemia comorbidity have not been explored in the previous review with the known inconsistency. Therefore, this systematic review and meta-analysis amid to identify the potential factors contributing to anemia among HIV-infected children. Moreover, this study provides an up-to-date pooled estimate of anemia among HIV-infected children in Ethiopia, which is important to evaluate the progress made against anemia. Having up-to-date information about the prevalence and risk factors of anemia among children living with HIV could help policymakers, program implementers, and other responsible bodies to mobilize and prioritize resources for the appropriate interventions. Moreover, it could help healthcare professionals to take a preventive measure for children who are at higher risk for anemia and later, to improve the health of children living with HIV.

Methods

Reporting and protocol registration

This systematic review and meta-analysis was carried out according to the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA2020) guidelines (Additional Table 1)[31]. The protocol was registered in the International Prospective Register of Systematic Reviews (PROSPERO) with the registration number CRD42024567824.

Search strategy

We systematically searched PubMed, HINARI, Science Direct, and Cochrane Library other sources such as Google Scholar, and African Journals Online on February 3, 2024, to obtain studies, which is conducted related to anemia among HIV-infected children. We Searched the databases using the following terms and phrases: "Human Immunodeficiency virus", "HIV", "Acquired Immunodeficiency syndrome", "antiretroviral therapy", "anemia", anaemia", "iron status", "abnormal hematology", "associated factors", "risk factors", "determinants", "predictors", "pediatrics", "children", "under-five children", "child", "infant" and "Ethiopia". The Boolean search operators such as "AND" and "OR" were used separately and in combination during searching (Additional Table 2).

Eligibility criteria

We included original studies that determine the prevalence of anemia and identify its associated factors among HIV-infected children (aged < 15 years old). We incorporated studies conducted using a cross-sectional or case-control study design. In case-control study design, we included studies that reported the cases as all HIV-positive children (aged < 15 years old) who were anemic and the controls as all HIV-positive children (aged < 15 years old) on ART who were not anemic. Moreover, studies available in the electronic source till February 3, 2024, were incorporated. On the other hand, citations without abstract and/or full-text, anonymous reports, editorial reports, qualitative studies, and conference abstracts were excluded from the analysis.

Data extraction

All records were exported to EndnoteX7 to identify and remove duplication. Four authors (GF, DA, ZA, and MS) independently extracted data using a standardized form. Finally, the author's name, publication year, number of

children with anemia (event), study design, prevalence, study regions, and the predictor of anemia with its odd ratios were extracted.

Quality assessment/critical appraisal

The quality of the original studies was checked using the Joanna Briggs Institute (JBI) Checklist tools[32]. Two authors (AA and WA) independently assessed the qualities of the primary studies. The mean scores of the two authors were used to handle the discrepancy in scoring. The tool has Yes, No, Unclear, and Not Applicable options: "1" is given for "Yes" and "0" is given for other options. The scores were summed and changed to percentages. Finally, 15 studies that received a quality score of > 50% were included in the final analysis (Additional Table 3).

Outcome measurement

This systematic review and meta-analysis have two main outcomes. The primary outcome was the prevalence of anemia among HIV-infected children. The second outcome was to identify predictors of anemia among HIV-infected children in Ethiopia. Accordingly, the odd ratio of factors associated with anemia with its 95% confidence intervals (CI) was extracted from the primary studies to compute the pooled odd ratio.

Advanced HIV disease: children older than five years whose WHO clinical stages are III and IV. Whereas, children younger than five years living with HIV are considered as having advanced HIV disease, regardless of the clinical stages. Mild WHO clinical stages: HIV-positive children whose WHO clinical stages are stages I and II[33].

ART Adherence: Good (> 95%)—if missed doses is ≤ 2 doses of 30 doses or ≤ 3 doses of 60 doses; Fair: (85–94%) if missing doses is between 3 and 4 of 30 doses or 4–9 of 60 doses; poor: (< 85%) if missed doses are > 5 doses of 30 doses or 10 and above doses of 60 doses of ART drug[33].

Statistical analysis

Data entry was done using Microsoft Excel 2013 and then the data was imported into R- software version 4.1.3 for further analysis. The Meta package for proportions (Metapro) was used to estimate the pooled prevalence of anemia. Heterogeneity across studies was checked using the I-square test[34]. Sub-group analyses were conducted to explore potential differences among studies. Meta-regression analysis was done using sample size and the publication years to identify the possible source of heterogeneity. Sensitivity analysis was performed to assess the impact of each study on the overall pooled estimate of anemia. Funnel plots analysis and Egger's test were done to detect publication bias. Forest plots and tables were used to present the prevalence of anemia and odd ratio, respectively, along with its 95% confidence interval. The random-effect model was fitted to estimate the pooled prevalence of anemia among HIV-infected children.

Results

Searching results and characteristics of included studies

A total of 4847 studies were searched from PubMed, HINARI, Science Direct, Cochrane Library, Google Scholar, and African journals online. Out of the total records, 477 studies were eliminated due to duplication. An additional 4339 articles were removed because of not relevant by titles and abstracts. The remaining 31 studies were browsed for full-text review. Hence, after reviewing the full text, a total of 16 studies were excluded due to noncompliance with the inclusion criteria. Finally, 15 studies met the eligibility criteria and were incorporated into the final analysis[16–29,35] (Fig. 1). In this study, a total of 3516 study participants were included. Among the studies included in the study, thirteen of the studies were conducted using a cross-sectional study design, and the rest two of the studies were conducted using a case-control study design. These studies were done in different regionals of Ethiopia (Addis Ababa, Amhara, Oromia, SNNPR (South Nation, Nationalities and People Regional), and Bnishangul Gumuz, Tigray, Afar and Harari) (Table 1).

The pooled prevalence of anemia among HIV-infected children in Ethiopia

We incorporated 13 studies to estimate the pooled prevalence of anemia among HIV-infected children[16–25,28,29,35]. Based on this, the pooled prevalence of anemia among HIV-infected children was 23.79% (95% CI: 17.28, 31.81) using the random effect model. Heterogeneity was identified between studies ($I^2 = 93\%$, $P < 0.01$) (Fig. 2).

Subgroup analysis

We identified heterogeneity across the studies, which were used to estimate the prevalence of anemia among HIV-positive children. Hence, we conducted a subgroup analysis using the study region and sample size. Accordingly, the prevalence of anemia among HIV-infected children was higher in the Afar regions [53.92% (95%CI: 44.22; 6333)] than in other regions of Ethiopia. Moreover, the prevalence of anemia by sample sizes was [25.49% (95%CI:16.95; 36.45)] and [20.37% (95%CI:11.70; 33.08)] for studies incorporated less than 250 and greater than or equal to 250 study participants, respectively (Table 2).

Sensitivity analysis

Leave one out sensitivity analysis was carried out to determine the contribution of each study in the final estimate of anemia. Accordingly, the sensitivity analysis revealed that the overall pooled estimate of anemia among HIV infected children was not affected by a single study, and all of the leave-one-out point estimates are within the lower and upper confidence interval of the overall estimate of anemia (Fig. 3).

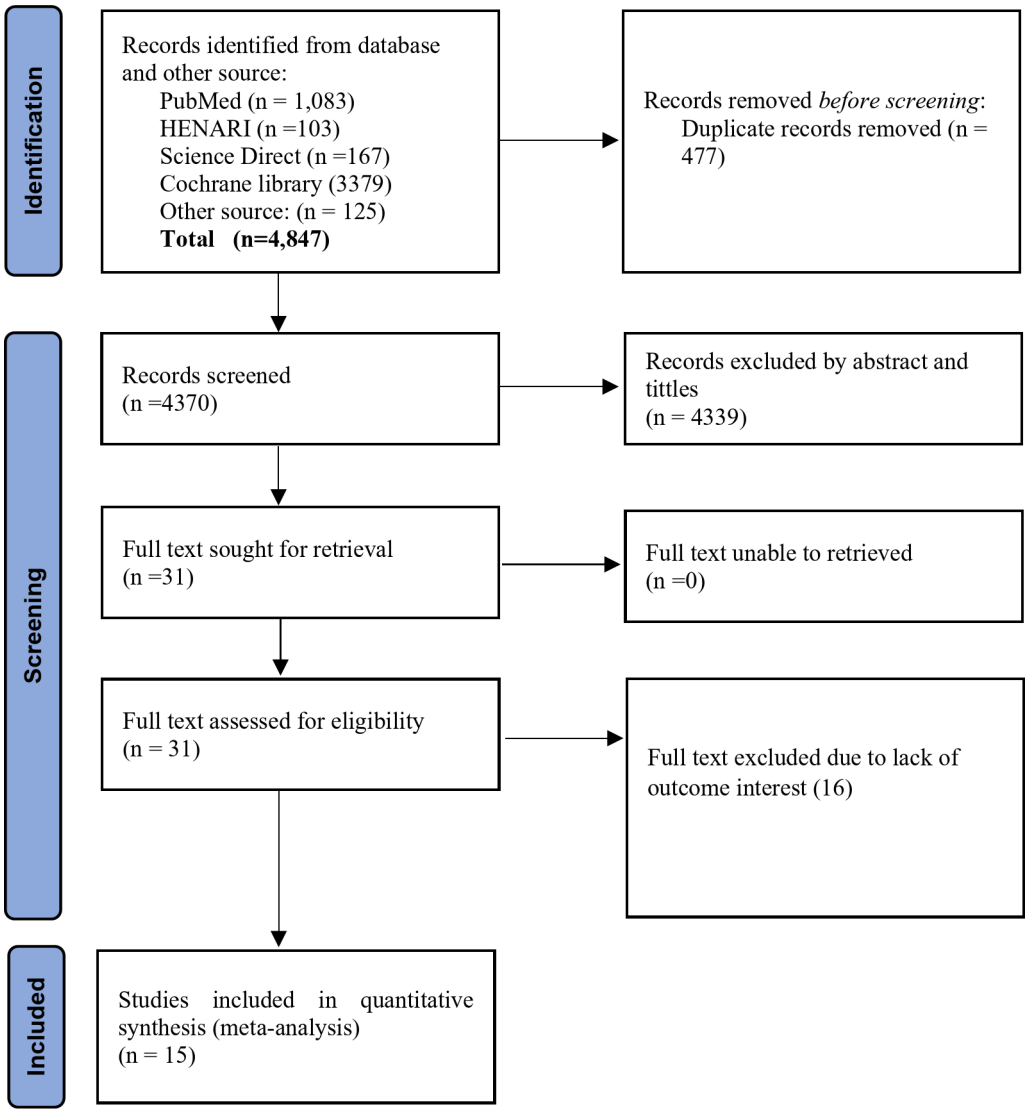

Fig. 1. PRISMA flow chart describing screening protocols of studies for meta-analysis.

Author	Publication year	Region	Sample sizes	Study design	Number of children with anemia	Prevalence
Teklemariam et al. (2015)[18]	2015	Harari	66	Cross-sectional	26	39.2
Enawgaw et al. (2015)[19]	2015	Amhara	265	Cross-sectional	43	16.2
Geleta et al. (2021)[20]	2021	SNNPR	256	Cross-sectional	98	38.8
Tsegay et al. (2017)[21]	2017	Amhara	224	Cross-sectional	66	29.5
Melaku et al. (2020)[22]	2020	Amhara	200	Cross-sectional	75	37.5
Mihiretie et al. (2015)[23]	2015	Addis Ababa	180	Cross-sectional	40	22.2
Fentaw et al. (2015)[17]	2020	Afar	102	Cross-sectional	55	53.9
Bayleyegn et al. (2021)[24]	2021	Amhara	255	Cross-sectional	54	21.2
Abebe et al. (2009)[35]	2009	Oromia	64	Cross-sectional	14	21.9
Geletaw et al. (2017)[25]	2017	Amhara	222	Cross-sectional	42	18.9
Tiruneh et al. (2023)[26]	2023	Benishangul Gumz	712	Case control	–	–
Beletew et al. (2020)[27]	2020	Amhara	350	Case control	–	–
Debasu et al. (2015)[28]	2015	Addis Ababa	106	Cross-sectional	20	18.9
Fanta et al. (2020)[29]	2020	SNNPR	273	Cross-sectional	31	11.4
Tesfay et al. (2021)[16]	2021	Tigray	241	Cross-sectional	16	7

Table 1. Characteristics of studies included in the systematic review and meta-analysis, Ethiopia, 2024.

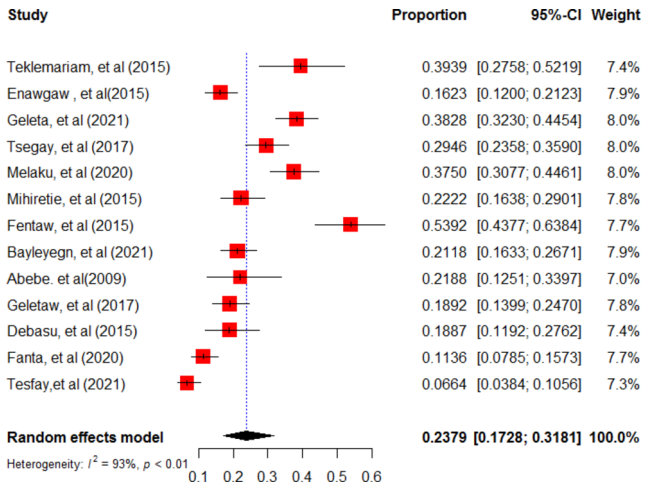

Fig. 2. The forest plot shows the pooled prevalence of anemia among HIV infected children, Ethiopia, 2024.

Variables	Characteristics	Prevalence of anemia (95% CI)
Regions	Afar	0.5392 [0.4422; 0.6333]
	Tigray	0.0 664 [0.0411; 0.1056]
	Amhara	0.2398 [0.1739; 0.3210]
	Oromia	0.2188 [0.1341; 0.3362]
	SNNPR	0.2210 [0.0570; 0.5709]
	Harari	0.3939 [0.2840; 0.5157]
	Addis Ababa	0.2103 [0.1668; 0.2614]
Sample size	Less than 250	0.2549 [0.1695; 0.3645]
	Greater than 250	0.2037 [0.1170; 0.3308]

Table 2. Sub-group analysis of anemia among HIV-infected children by regions and sample size, Ethiopia, 2024.

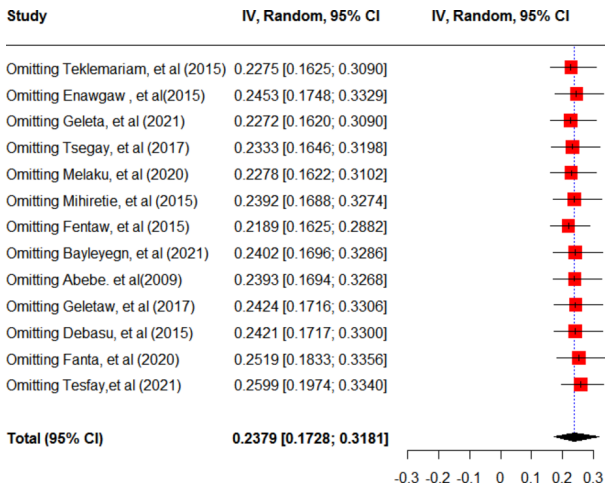

Fig. 3. Sensitivity analysis for the pooled prevalence of anemia among HIV-infected children, Ethiopia, 2024.

Meta-regression analysis

Meta-regression analysis was carried out considering sample size and publication years to identify the possible source heterogeneity for the pooled estimate of anemia among HIV-infected children. However, none of the sample sizes and publications years were statistically significant to be a source of heterogeneity (Table 3).

Variables	Coefficients	*P*-value
Publication years	−0.0068 (−0.1174, 0.1310)	0.92
Sample size	−0.0043 (−0.0094, 0.0008)	0.09

Table 3. Meta-regression analysis using publication years and sample sizes for the possible source of heterogeneity of anemia among HIV-infected children, Ethiopia, 2024.

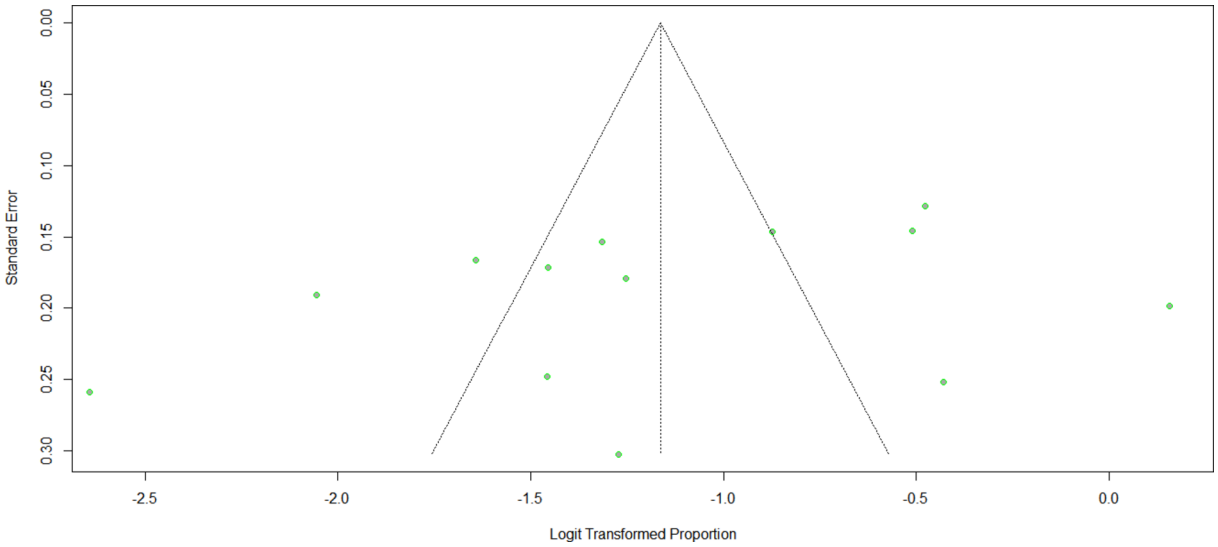

Fig. 4. Funnel plot showing publication bias among studies used to compute the pooled prevalence of anemia among HIV positive children, Ethiopia, 2024.

Publication bias

Asymmetric distribution was observed in funnel plot visual inspection (Fig. 4). However, Eggers's test showed that there was no statistically significant publication bias with (B_0 −0.117, p-value = 0.23). Hence, we didn't conduct any further Meta trim and fill analysis.

Predictors of anemia among HIV-infected children in Ethiopia

Fifteen studies were used to identify factors associated with anemia among HIV-infected children[16–29,35]. Accordingly, the likelihood of anemia was 3.71 times (OR 3.71, 95% CI 2.58; 5.33) higher among HIV-positive children whose ages are < 7 years as compared to children whose ages are ≥ 7 years[18,21,24,25,29]. The odds of being anemic were 2.78 times (OR 2.78, 95% CI 2.00; 3.87) higher among children with advanced HIV disease than children with mild WHO clinical stages[17,19,20,22,23,26]. The likelihood of anemia was 2.28 times (OR 2.28, 95% CI 1.02; 5.09) higher among HIV-infected children who had an intestinal parasitic infection as compared to their counterparts[19,20,23,27]. The risk of anemia was lower by 51% (OR 0.49, 95% CI 0.35; 0.72) among HIV-infected children who received cotrimoxazole prophylaxis therapy as compared to children who didn't receive cotrimoxazole prophylaxis therapy[20,26,27,29]. The odds of anemia were 1.96 times (OR 1.96, 95% CI 1.23; 3.10) more likely among HIV-positive children with poor ART treatment adherence than children with good ART treatment adherence[26,27]. HIV-infected children with opportunistic infection were 2.81 times (OR 2.81, 95% CI 1.59; 4.95) higher risk for anemia than children without opportunistic infection[20,25,27]. The risk of anemia was 4.29 times (OR 4.29, 95% CI 2.28; 8.09) higher among HIV-positive children whose viral loads are greater than 1000 copies/ml[19,29]. The likelihood of anemia was 5.07 times (OR 5.07, 95% CI 2.41; 10.64) higher among children on zidovudine-containing regimen treatment[24,28]. However, residence (OR 2.44, 95% CI 0.74; 7.99)[26,27,29] and dietary diversity (OR 0.92, 95% CI 0.53; 1.61) were not associated with anemia among children living with HIV[20,27] (Table 4).

Discussion

Though the pooled effect of HAART on anemia-HIV/AIDS commodity has been identified in the previous literature, to the best of our knowledge, the effect of other contributing factors on HIV/AIDS-anemia comorbidity have not been investigated. Thus, this systematic review and meta-analysis explored the association of other factors with anemia among HIV-infected children in Ethiopia. Accordingly, age, advanced HIV disease, viral load, poor ART treatment adherence, opportunistic infection, cotrimoxazole prophylaxis therapy, intestinal parasitic infection, and zidovudine-containing regimen were identified as factors associated with anemia among children living with HIV.

Variables	Categories	Pooled OR (95% CI)	Q-statistic	*p*-value of Q	I^2 (%)	Tau^2	*p*-value of estimate	Included studies
Age of children	< 7 years	3.71 (2.58; 5.33)	2.25	0.6906	0	0	< 0.0001	5
	≥ 7 years	Ref.						
Residence	Rural	2.44 (0.74; 7.99)	9.83	0.0073	79.7	0.8590	0.1409	3
	Urban	Ref						
WHO clinical stage	Advanced HIV disease	2.78 (2.00; 3.87)	11.40	0.0767	47.4	0.2095	< 0.0001	7
	Mild WHO clinical stages	Ref.						
Viral load	> 1000 copies/ml	4.29 (2.28; 8.09)	0.50	0.4773	0	0	< 0.0001	2
	Not detected	Ref						
ART treatment adherence	Poor /fair	1.96 (1.23; 3.10)	0.39	0.5341	0	0	0.0044	2
	Good	Ref.						
Opportunistic infection	Yes	2.81 (1.59; 4.95)	2.61	0.2718	23.2%	0.0001	0.0003	5
	No	Ref						
CPT	Receive	0.49 (0.35; 0.72)	1.81	0.6126	0	0	0.0002	4
	Didn't received	Ref.						
Dietary diversity	Didn't receive	0.92 (0.53; 1.61)	11.07	0.0009	91	3.53	0.7761	2
	Received	Ref.						
Intestinal parasitic infection	Yes	2.28 (1.02; 5.09)	7.91	0.0479	62.1	0.39	0.0440	4
	No	Ref.						
Zidovudine containing regimen	Yes	5.07 (2.41; 10.64)	0.04	0.8472	0	0	< 0.0001	2
	No	Ref.						

Table 4. Meta-analysis of factors associated with anemia among HIV-infected children in Ethiopia, 2024. *OR* odd ratio.

This systematic review and meta-analysis revealed that the pooled prevalence of anemia among HIV-infected children was found to be 23.79% (95% CI 17.28, 31.81) using the random effect model. The finding is lower than the prevalence reported by a systematic review and meta-analysis conducted in East Africa[15] and globally[14]. The possible justification for the discrepancy might be related to the difference in the study period as there could be changes in the treatment and care of children living with HIV through time. Moreover, it may be related to the difference in geographic location variation where altitude difference may change the level of hemoglobin concentration.

In this systematic review and meta-analysis, the likelihood of anemia was higher among HIV-positive children whose ages are < 7 years as compared to children whose ages are ≥ 7 years. The finding is consistent with studies done elsewhere[36,37]. The possible elucidation might be that the young growing children require a high amount of iron for hemoglobin production. Moreover, young children may not be fed large quantities of iron-rich foods such as red meat and green leafy vegetables[38].

According to this systematic review and meta-analysis, the risk of anemia was lower among HIV-infected children who received cotrimoxazole prophylaxis therapy as compared to children who didn't receive cotrimoxazole prophylaxis therapy. The finding is supported by studies conducted elsewhere[39]. This is the fact that cotrimoxazole reduces the effect of pro-inflammatory cytokines that impair and perturb the expression of erythropoiesis and later, it causes cytokine-mediated anemia[40]. However, a study from Tanzania found that cotrimoxazole prophylaxis therapy has no association with anemia among HIV-positive children[41]. This might be related to ART treatment adherence, which implies that cotrimoxazole prophylaxis therapy might not have as such impact on children who have good ART drug adherence levels.

The other striking finding of this study was that advanced HIV disease and opportunistic infection are identified as factors associated with anemia. Previously, a similar finding was reported that advanced HIV disease[36] and opportunistic infection[42,43] were associated with an increased risk of anemia. This can be explained as children with advanced HIV disease and opportunistic infection may have difficulty in voluntary food intake, which can result in micronutrient deficiencies, such as iron, folate, vitamin B12, and vitamin A[44,45] and contributes to iron deficiency anemia. Moreover, the drug used to treat HIV-related opportunistic infection and advanced HIV disease may suppress bone marrow and later, can reduce the production of erythrocytes[46]. This implies the need for anemia preventive measures along with HIV care for HIV-positive children with advanced disease stages.

The likelihood of anemia was higher among HIV-infected children who had intestinal parasitic infections as compared to their counterparts. The finding is consistent with previous literature conducted elsewhere[37]. This can be explained as parasitic infections cause red blood cell destruction, gastrointestinal necrosis, and blood loss[47].

The other observed finding of this study was that the odds of being anemic were higher among HIV-positive children with poor ART treatment adherence than among children with good ART treatment adherence. This is the fact that poor ART treatment adherence can increase the risk of opportunistic infections and the progress of HIV disease, which leads to anemia through increased bone marrow suppression[48,49]. This implies that regular

evaluation of ART treatment adherence and counseling on ART drug adherence is important to gain optimal therapeutic effects and prevent HIV-related complications.

This systematic review and meta-analysis further identified that the risk of anemia was higher among HIV-positive children whose viral loads were greater than 1000 copies/ml. The finding is supported by studies conducted elsewhere[42,50]. This is the fact that high viral activity can reduce the proliferation and differentiation of hematopoietic progenitor cells, the activity of bone marrow stromal cells, and erythropoietin production[49]. This can increase the risk of anemia.

Lastly, the likelihood of being anemic was higher among children who received Zidovudine-containing regimen treatment as compared to another regimen. The finding is consistent with studies conducted elsewhere[43,51,52]. This could be the fact that Zidovudine has been found to exhibit cytotoxicity to the erythroid precursor cells in the bone marrow. Hence, Zidovudine containing regimen has to be substituted by Abacavir (ABC) or Tenofovir disoproxil fumarate (TDF) containing regimen for high anemia risk children. Generally, policies, strategies, and programs should consider the aforementioned predictors of anemia among HIV-infected children to reduce the burden of anemia among children living with HIV in the ART era.

Limitations

The limitations of this systematic review and meta-analysis are that only articles from seven regions were included to estimate the pooled prevalence of anemia, such that other regions may not be represented in the study. Some predictors that were reported in one primary study and/or classified in a different way from the included study were excluded from the analysis.

Conclusions

In Ethiopia, anemia remains a public health concern among children living with HIV. Age < 7 years, advanced HIV disease, intestinal parasitic infection, poor ART treatment adherence, opportunistic infection, viral load > 1000 copies/ml, and zidovudine-containing regimen were identified as factors associated with a higher risk of anemia. Whereas, cotrimoxazole prophylaxis therapy reduces the risk of anemia among HIV-infected children. Therefore, regular screening and management of anemia are important for HIV-infected children, particularly for those with advanced HIV disease, opportunistic infection, high viral load, and who are taking zidovudine-containing regimens for better clinical outcomes. Moreover, cotrimoxazole prophylaxis therapy should be given to all eligible HIV-infected children based on the national treatment guidelines. Furthermore, counseling on ART drug adherence should be strengthened. Lastly, preventive chemotherapy (deworming) and counseling on infection prevention should be provided for children living with HIV to prevent parasitic infection.

Data availability

The data is available at the corresponding author and can be provided upon request.

Received: 11 June 2024; Accepted: 1 January 2025
Published online: 18 February 2025

References

1. World Health Organization. *Haemoglobin Concentrations for the Diagnosis of Anaemia and Assessment of Severity* (World Health Organization, 2011).
2. World Health Organization. *Anaemia: What does this indicator tell us?* (2008). https://www.who.int/data/nutrition/nlis/info/anaemia [cited 2024 May 12].
3. Grantham-McGregor, S. & Ani, C. A review of studies on the effect of iron deficiency on cognitive development in children. *J. Nutr.* **131**(2), 649S–668S (2001).
4. Madanijah, S. et al. Assessment of anemia status on physical development skills of children under two years old in Aceh, Indonesia. *J. Nutr. Sci. Vitaminol.* **66**(Suppl), S463–S467 (2020).
5. Santos, J. N. et al. Consequences of anemia on language development of children from a public day care center. *Revista Paulista De Pediatria*. **27**, 67–73 (2009).
6. Labib, A. G. et al. The effect of chronic anemia on physical growth and development among children under five years. *Minia Sci. Nurs. J.* **4**(1), 11–21 (2018).
7. Gwetu, T. P. et al. Health and educational achievement of school-aged children: the impact of anaemia and iron status on learning. *Health SA Gesondheid*. **24**(1), 1–8 (2019).
8. Zavaleta, N. & Astete-Robilliard, L. Effect of anemia on child development: long-term consequences. *Revista Peruana De Med. Experimental y Salud Publica* **34**(4), 716–722 (2017).
9. Coyle, T. E. Hematologic complications of human immunodeficiency virus infection and the acquired immunodeficiency syndrome. *Med. Clin.* **81**(2), 449–470 (1997).
10. Akkina, R. New insights into HIV impact on hematopoiesis. *Blood* **122**(13), 2144–2146 (2013).
11. Babadoko, A., Muktar, H. & Mamman, A. Immuno-hematological abnormalities of human immunodeficiency virus-1 infected highly active antiretroviral naive adults in Zaria, Northern Nigeria. *Arch. Int. Surg.* **5**, 199 (2015).
12. Mocroft, A. et al. Anaemia is an independent predictive marker for clinical prognosis in HIV-infected patients from across Europe. *AIDS* **13**(8), 943–950 (1999).
13. O'Brien, M. E. et al. Anemia is an independent predictor of mortality and immunologic progression of disease among women with HIV in Tanzania. *JAIDS J. Acquir. Immune Defic. Syndr.* **40**(2), 219–225 (2005).
14. Cao, G. et al. Prevalence of anemia among people living with HIV: a systematic review and meta-analysis. *EClinicalMedicine*, 44 (2022).
15. Getu, F. et al. The prevalence of anemia among human immunodeficiency virus-infected individuals in East Africa (2023).
16. Tesfay, F. et al. Anemia among children living with HIV/AIDS on HAART in Mekelle Hospital, Tigray regional state of northern Ethiopia—A cross-sectional study. *BMC Pediatr.* **21**(1), 1–5 (2021).

17. Fentaw Mulaw, G., Ahmed Yesuf, F. & Temesgen Abebe, H. Magnitude of anemia and associated factors among HIV-infected children receiving antiretroviral therapy in pastoral community, Ethiopia: a retrospective cross-sectional study. *Adv. Hematol.*, 1–8 (2020).
18. Teklemariam, Z., Mitiku, H. & Mesfin, F. Prevalence of anemia and nutritional status among HIV-positive children receiving antiretroviral therapy in Harar, Eastern Ethiopia. *HIV/AIDS-Res. Palliat. Care*, 191–196 (2015).
19. Enawgaw, B. et al. Prevalence and associated risk factors of anemia among HIV infected children attending Gondar university hospital, Northwest Ethiopia: a cross sectional study. *BMC Hematol.* **15**, 1–6 (2015).
20. Geleta, M. L. et al. Predictors of anemia among HIV-infected children on antiretroviral therapy in wolaita zone, South Ethiopia: a facility-based cross-sectional study. *HIV/AIDS-Res. Palliat. Care*, 13–19 (2021).
21. Tsegay, Y. G. et al. Magnitude of cytopenias among HIV-infected children in Bahir Dar, Northwest Ethiopia: a comparison of HAART-naïve and HAART-experienced Childrenp. *HIV/AIDS-Res. Palliat. Care*, 31–42 (2017).
22. Melku, M. et al. Magnitude of anemia and undernutrition among HIV-infected children who took HAART: a retrospective follow-up study. *Am. J. Blood Res.* **10**(5), 198 (2020).
23. Mihiretie, H., Taye, B. & Tsegaye, A. Magnitude of anemia and associated factors among pediatric HIV/AIDS patients attending Zewditu Memorial Hospital ART Clinic, Addis Ababa, Ethiopia. *Anemia* **2015**, 479329 (2015).
24. Bayleyegn, B. et al. Magnitude and associated factors of peripheral cytopenia among HIV-infected children attending at University of Gondar Specialized Referral Hospital, Northwest Ethiopia. *PLoS One* **16**(3), e0247878 (2021).
25. Geletaw, T., Tadesse, M. Z. & Demisse, A. G. Hematologic abnormalities and associated factors among HIV infected children pre- and post-antiretroviral treatment, North West Ethiopia. *J. Blood Med.* **8**, 99–105 (2017).
26. Tiruneh, M. G. & Bizuneh, F. K. Determinates of anemia among human immune deficiency virus positive children on anti-retro viral therapy in selected health facilities, Northwest Ethiopia: a case-control study. *J. Nutr. Sci.* **12**, e95 (2023).
27. Beletew, B. et al. Determinants of anemia among HIV-positive children on highly active antiretroviral therapy attending hospitals of North Wollo Zone, Amhara Region, Ethiopia, 2019: a case-control study. *Anemia* **2020**, 3720572 (2020).
28. Debasu, M. et al. Anti-retroviral treatment related haematological disorders among HIV-infected children attending HIV clinic at yekatit 12 hospital, Addis Ababa, Ethiopia. *Int. Blood Res. Rev.* **4**(2), 1–18 (2015).
29. Fenta, D. A. et al. Anemia and related factors among highly active antiretroviral therapy experienced children in Hawassa comprehensive specialized hospital, southern Ethiopia: emphasis on patient management. *Drug Healthc. Patient Saf.* **12**, 49–56 (2020).
30. Wagnew, F. et al. Burden of anemia and its association with HAART in HIV infected children in Ethiopia: a systematic review and meta-analysis. *BMC Infect. Dis.* **19**(1), 1–9 (2019).
31. Page, M. J. et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. *Int. J. Surg.* **88**, 105906 (2021).
32. Lockwood, C. et al. Chap. 7: Systematic reviews of etiology and risk. In *JBI Manual for Evidence Synthesis* [Internet] (Joanna Briggs Institute, 2017).
33. Ethiopia, F. *National Consolidated Guidelines for Comprehensive HIV Prevention, care and Treatment*, 1–238 (FMOH, 2018).
34. Rücker, G. et al. Undue reliance on I 2 in assessing heterogeneity may mislead. *BMC Med. Res. Methodol.* **8**, 1–9 (2008).
35. Abebe, M. & Alemseged, F. Hematologic abormalities among children on Haart, in Jimma university specialized hospital, southwestern Ethiopia. *Ethiop. J. Health Sci.* **19**(2) (2009).
36. Nyesigire Ruhinda, E., Bajunirwe, F. & Kiwanuka, J. Anaemia in HIV-infected children: severity, types and effect on response to HAART. *BMC Pediatr.* **12**, 1–6 (2012).
37. Makubi, A. N. et al. Risk factors for anaemia among HIV infected children attending care and treatment clinic at Muhimbili National Hospital in Dar Es Salaam, Tanzania. *Tanzan. J. Health Res.* **14**(1), 68–74 (2012).
38. Alles, M. S., Eussen, S. R. & Van Der Beek, E. M. Nutritional challenges and opportunities during the weaning period and in young childhood. *Ann. Nutr. Metab.* **64**(3–4), 284–293 (2014).
39. Prendergast, A. et al. Improved growth and anemia in HIV-infected African children taking cotrimoxazole prophylaxis. *Clin. Infect. Dis.* **52**(7), 953–956 (2011).
40. Bourke, C. et al. Cotrimoxazole reduces systemic inflammation in HIV infection by altering the gut microbiome and immune activation. *Sci. Transl. Med.* **11**, 486 (2019).
41. Masao, A. F., Shayo, A. M. & Philemon, R. Prevalence of hematological abnormalities and factors associated among HIV infected children receiving care at Kilimanjaro Christian Medical Centre. *J. Clin. Pediatr. Child. Care Res.* **1**(1), 1–8 (2020).
42. Kaudha, R. et al. Anemia in HIV patients attending highly active antiretroviral therapy clinic at Hoima Regional Referral Hospital: prevalence, morphological classification, and associated factors. *HIV/AIDS-Res. Palliat. Care*, 621–632 (2023).
43. Ezechi, O. et al. The burden of anaemia and associated factors in HIV positive Nigerian women. *Arch. Gynecol. Obstet.* **287**, 239–244 (2013).
44. Castro, L. & Goldani, L. Z. Iron, folate and vitamin B12 parameters in HIV-1 infected patients with anaemia in southern Brazil. *Trop. Doctor*. **39**(2), 83–85 (2009).
45. Abioye, A. I. et al. Anemia, iron status, and HIV: a systematic review of the evidence. *Adv. Nutr.* **11**(5), 1334–1363 (2020).
46. Shah, I. & Murthy, A. Bone marrow abnormalities in HIV infected children, report of three cases and review of the literature. *J. Res. Med. Sci.* **19**(2), 181 (2014).
47. Tan, X. et al. Hookworm infection caused acute intestinal bleeding diagnosed by capsule: a case report and literature review. *Korean J. Parasitol.* **55**(4), 417 (2017).
48. Schaecher, K. L. The importance of treatment adherence in HIV. *Am. J. Manag Care*. **19**(12 Suppl), s231–s237 (2013).
49. Gibellini, D. et al. Effects of human immunodeficiency virus on the erythrocyte and megakaryocyte lineages. *World J. Virol.* **2**(2), 91 (2013).
50. Shet, A. et al. Anemia, diet and therapeutic iron among children living with HIV: a prospective cohort study. *BMC Pediatr.* **15**, 1–9 (2015).
51. Bunupuradah, T. et al. Incidence and predictors of severe anemia in Asian HIV-infected children using first-line antiretroviral therapy. *Int. J. Infect. Dis.* **17**(10), e806–e810 (2013).
52. Bello, S. O., Audu, E. S. & Hassan, I. Hematological profile of human immunodeficiency virus-infected children. *Sahel Med. J.* **23**(1), 36–40 (2020).

Acknowledgements

NA.

Author contributions

DG, GF, ZA, MS, AA, WA, NS, and DA are involved in the design, selection of articles, data extraction, quality appraisal, and statistical analysis. DG and GF were involved in manuscript writing. All authors read and approved the final draft of the manuscript.

Declarations

Competing interests
The authors declare no competing interests.

Additional information
Supplementary Information The online version contains supplementary material available at https://doi.org/10.1038/s41598-025-85285-8.

Correspondence and requests for materials should be addressed to D.G.

Reprints and permissions information is available at www.nature.com/reprints.

Publisher's note Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

Open Access This article is licensed under a Creative Commons Attribution-NonCommercial-NoDerivatives 4.0 International License, which permits any non-commercial use, sharing, distribution and reproduction in any medium or format, as long as you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons licence, and indicate if you modified the licensed material. You do not have permission under this licence to share adapted material derived from this article or parts of it. The images or other third party material in this article are included in the article's Creative Commons licence, unless indicated otherwise in a credit line to the material. If material is not included in the article's Creative Commons licence and your intended use is not permitted by statutory regulation or exceeds the permitted use, you will need to obtain permission directly from the copyright holder. To view a copy of this licence, visit http://creativecommons.org/licenses/by-nc-nd/4.0/.

© The Author(s) 2025