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Prevalence and risk factors of anemia among people living with HIV/AIDS in Southeast Asia: a systematic review and meta-analysis

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Abstract

Background & objectives Anemia represents a critical hematological complication among people living with HIV/AIDS (PLHIV), significantly impacting morbidity and mortality. This systematic review and meta-analysis aimed to comprehensively evaluate anemia prevalence and identify key risk factors among PLHIV in Southeast Asia.

Methods We systematically searched PubMed, Scopus, Embase, and Web of Science (2000–2024) following PRISMA guidelines (PROSPERO: CRD42024610328). Random-effects meta-analysis was performed, with heterogeneity examined through meta-regression and subgroup analyses. Quality assessment utilized JBI critical appraisal tools.

Results Analysis of 39 studies ($n = 21,427$) revealed a striking pooled anemia prevalence of 50% (95% CI: 43–57%, $I^2 = 99.6\%$). Compelling disparities emerged across subgroups: ART-naïve individuals showed markedly higher prevalence (58%) versus those on ART (38%), children demonstrated elevated rates (52%) compared to adults (49%) and pregnant women (37%), and lower-middle-income countries exhibited greater burden (50%) versus upper-middle-income countries (39%). Meta-regression identified critical risk factors: CD4 count < 200 cells/mm^3 (OR = 3.56, 95% CI: 2.59–4.90), underweight BMI (OR = 4.75, 95% CI: 3.57–6.33), female gender (OR = 3.06, 95% CI: 2.71–3.45), and notably, zidovudine use (OR = 9.28, 95% CI: 1.18–73.0).

Conclusions Our findings reveal that anemia affects half of PLHIV in Southeast Asia, with vulnerable subgroups bearing a disproportionate burden. This evidence underscores the urgent need for enhanced screening protocols and targeted interventions, particularly among high-risk populations. Future research should prioritize intervention strategies for these vulnerable subgroups.

Keywords Anemia, HIV, Risk factors, Southeast Asia, Systematic review, Meta-Analysis

Introduction

The human immunodeficiency virus (HIV) belongs to the Ortho retro virinae subfamily, the Retrovirus family, and the genus Lentivo virus. Acquired immunodeficiency syndrome (AIDS) is caused by it [1, 2]. HIV can be passed From a mother to an infant during childbirth, through sexual contact, and tainted blood products. The virus can also spread after birth if it is consumed through breast milk [3]. The patient will begin to exhibit the signs of a primary infection two to four weeks after the infection enters the body. A protracted chronic infection that may persist for decades gradually emerges [4].Human Immunodeficiency Virus (HIV) continues to be a major public health problem in low-income countries and more importantly in Southeast Asia. For the last decade, access to Antiretroviral Therapy (ART) and its impact on improving quality of life and reducing HIV-related

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morbidity and mortality has significantly improved in Southeast Asia.

HIV reduces the number of clusters of differentiation 4 positive T-helper cells, leading to a steady deterioration in immune system function. As the disease progresses, it becomes AIDS when the cluster of differentiation 4 positive cell count falls below 200/mm3. A person with HIV typically develops complications that are directly related to the infection or an undesirable effect of the treatment [5, 6]. Old age, the presence of comorbidities, and lifestyle choices all increase the chance of developing chronic disorders such as diabetes and kidney disease. Since the beginning of the epidemic, 88.4 million [71.3–112.8 million] people have been infected with HIV, and about 42.3 million [35.7–51.1 million] people have died of HIV.

By the end of 2023, 39.9 million [36.1–44.6 million] people worldwide were HIV positive. Around the globe, an estimated 0.6% [0.6–0.7%] of adults between the ages of 15 and 49 are HIV positive [7], while the prevalence of the disease varies greatly across nations and geographical regions [8, 9].

Anemia, a prevalent hematological disorder characterized by reduced hemoglobin levels or red blood cell count, presents a significant health challenge for people living with HIV/AIDS (PLHIV). People living with HIV are at high risk of Anemia due to insufficient iron intake, HIV and opportunistic infections, inflammation, and as an adverse effect of antiretroviral therapy [10]. This comorbidity is of particular concern in Southeast Asia, a region grappling with a substantial HIV burden [11]. The interplay between HIV infection and Anemia is complex, with multiple contributing factors including the direct effects of the virus on hematopoiesis, opportunistic infections, nutritional deficiencies, and potential side effects of antiretroviral therapy (ART) [12].

The significance of this research lies in its potential to inform public health strategies and clinical practices in the region. By elucidating Anemia prevalence alongside associated risk factors, the findings can guide the creation of focused screening initiatives, influence treatment decisions, and highlight areas for intervention to improve outcomes for PLHIV. Moreover, this study may uncover knowledge gaps and areas requiring further investigation, thus contributing to the broader scientific understanding of HIV-related Anemia in diverse populations [13].

Many studies revealed that HIV/AIDS patients are at a high risk of developing Anemia. Though studies have been conducted on the prevalence of Anemia among HIV/AIDS patients, the findings have been inconsistent and inconclusive. Furthermore, the pooled prevalence of Anemia among HIV/AIDS patients in Southeast Asia has not been estimated by any systematic review or meta-analysis to date. Thus, the purpose of this systematic review and meta-analysis was to use the available data to estimate the pooled prevalence of Anemia among HIV/AIDS patients in Southeast Asia [14].

This systematic review and meta-analysis aims to synthesize the available evidence on the prevalence of Anemia among PLHIV in Southeast Asian countries. The specific objectives are:

1. To estimate the pooled prevalence of Anemia in PLHIV across studies from Southeast Asia
2. To identify demographic, clinical, and treatment-related variables linked to this population's Anemia
3. To assess the impact of antiretroviral therapy (ART) on the prevalence of Anemia

Methodology

Context and protocol development of the review

The Preferred Reporting Items for Systematic Review and Meta-Analysis guidelines had been adhered to in this systematic review [15]. Using published research from 2000 to 2024, the prevalence of Anemia among people living with HIV/AIDS in Southeast Asia has been determined.

This systematic review and meta-analysis were registered on the International Prospective Register of Systematic Reviews (CRD42024610328).

The initial retrieval was guided by the following PICOS algorithm principles:

P(population): People living with HIV/AIDS of all ages in Southeast Asia.

(Bangladesh, Bhutan, Democratic People's Republic of Korea, India, Indonesia, Maldives, Myanmar, Nepal, Sri Lanka, Thailand, Timor-Leste).
I (intervention): Not applicable (prevalence study);
C (comparison): no comparison;
O (outcome): Prevalence and risk factors of Anemia Among People Living with HIV/AIDS in Southeast Asia;
S (study): cross-sectional study/retrospective study/Cohort studies (baseline data)/Surveillance data Hospital-based studies/Community-based surveys/Randomized control trials/English language publication/Population-based surveys/Time series analysis.

Eligibility criteria

Inclusion criteria

- People living with HIV/AIDS of all ages.
- Residing in Southeast Asian countries.
- Both treatment-naive and those on ART.
- English language publications.

– Original research with primary data collection.

Exclusion criteria

– Studies conducted outside of Southeast Asia.
– Case reports and series with < 10 participants.
– Animal studies.
– In Vitro studies.
– Studies where baseline anemia was treated before assessment.
– Review articles, editorials, or conference abstracts.

Study outcome

The outcome variable in this systematic review and meta-analysis was the prevalence of Anemia Among People Living with HIV/AIDS in Southeast Asia. Anemia was defined as a haemoglobin level Children (6–59 months): < 11.0 g/dL Children (5–11 years): < 11.5 g/dL Children (12–14 years): < 12.0 g/dL. Adults: Men (15 years and above): < 13.0 g/dL, Women (non-pregnant, 15 years and above): < 12.0 g/dL, Pregnant Women: < 11.0 g/dL [16, 17, 22].

Information sources

We systematically searched four major databases: PubMed/MEDLINE, Embase, Scopus, and Web of Science from 2000 until November 2024. The search strategy combined Medical Subject Headings (MeSH) terms and free-text keywords related to"Anemia,""HIV","AIDS","PLHIV,"and"Southeast Asian countries,". The complete search strategy for each database is provided in Supplementary Table 1. Additional relevant studies were identified by manually searching reference lists [18]. The literature search was initiated from 2000 onwards to capture studies reflecting modern HIV care practices. This timeframe was chosen because it coincides with several crucial developments: the widespread implementation of highly active antiretroviral therapy (HAART) as the standard of care (2000), the introduction of WHO's standardised criteria for anemia definition and severity classification in HIV patients (2002), and the establishment of systematic HIV treatment monitoring protocols in Southeast Asia. Additionally, this period marked significant improvements in research methodology and reporting standards, particularly for observational studies in resource-limited settings, ensuring the inclusion of methodologically robust and clinically relevant evidence.

Study selection and quality assessment

To gather and arrange search results and eliminate duplicate articles, the retrieved articles from this systematic review and meta-analysis were imported into Rayyan. The articles were then independently screened by two reviewers (V.S. and A.R.) based on their titles and abstracts. The two reviewers engaged in lively debates and reached a consensus. (Y.M) was a third reviewer who was involved in cases of disagreement. Using the critical appraisal tools developed by the Joanna Briggs Institute (JBI) [19], the reviewers evaluated the included studies methodological quality. The instruments include items for evaluating both external and internal validity.

Each study was assigned a number between 1 and 0 based on the JBI critical appraisal tools. Elements that are explicitly stated in the research's method section were given a value of 1, whereas items that are not explicitly expressed in the method section were given a value of zero (0). Lastly, the total score was used to assess the included studies'overall methodological quality. Articles with methodological quality scores of 0–3 out of 9 were deemed low quality, those with scores of 4–6 were deemed moderate, and those with scores of 7 or more were deemed high quality.

Data extraction

After assessing methodological quality, articles that satisfied eligibility requirements were extracted by two reviewers using a predefined data extraction sheet. The data extraction phase involved two researchers (V.S. and A.R.) using Excel tables independently to extract data. The primary contents of the extraction are as follows: (1) The articles contain basic information such as the first author, publication year, country, study design, population, ART status, income category, sample size, and so on. (2) Determine the prevalence of Anemia among people living with HIV and associated risk factor data; (3) Identify key information for biased risk assessment and (4) Quality indicators. After the data have been extracted, it have been summarized, shared, and reviewed. If there is a dispute, it is forwarded to the third researcher (Y.M.) for review.

Statistical analysis

We used R Software version 4.4.2 with the'meta'and'metafor'packages to statistically evaluate data on the prevalence rate and risk factors of Anemia Among People Living with HIV/AIDS in Southeast Asia, as well as the I2 value to assess the study heterogeneity. If I2 > 50% and p < 0.1, it indicates a high heterogeneity among studies, Due to anticipated heterogeneity, we used: Random-effects models with Freeman-Tukey double arcsine transformation for prevalence data, over fixed effects as it accounts for both within-study sampling error and between-study variation, providing more conservative estimates that better reflect the true uncertainty

in our findings. This approach is particularly appropriate for observational studies with diverse populations and settings, as confirmed by significant Q-statistics and tau^2 values indicating meaningful between-study variance Otherwise, for statistical purposes, the fixed effect model was adopted.

If the variability among the included study results is high, The subgroup analysis approach is used to attempt to identify the obvious causes of heterogeneity, but additional examination of the sources of heterogeneity is required. This article's subgroups are as follows: Country, Population, Study category, Study design, ART status, Publication year, Income category, and Pregnancy status. In every statistical analysis, the p-value is fixed at 0.05. Sensitivity analyses & Influence diagnostics have been performed to deal with High heterogeneity among the included studies. To check for publication bias, we opted for funnel plots, and an Egger test was used. A P-value <0.05 in the Egger test indicated statistically significant publication bias. The'metafor'tool in R (version 4.4.2) was used to meta-regress subgroup analyses using a random-effects model. Sample sizes were used to determine variance and proportions of anemia prevalence in HIV were used to calculate effect sizes. I^2 statistics were generated to evaluate residual heterogeneity, and R^2 values were derived for each moderator to quantify the percentage of heterogeneity explained. At $p < 0.05$, the significance level was established. A 95% confidence interval (CI) was computed for each effect estimate. Several techniques, such as bootstrap confidence intervals with 1000 iterations, were employed to confirm the robustness of the R^2 value.

Results

Literature search and identified results

A database literature search, along with a manual search, revealed a total of 1872 studies. After removing duplicate and irrelevant research [20], there were 1220 studies. Then, 1220 articles were examined. 1172 studies were eliminated based on their titles & abstracts. 2 records from the remaining 48 research could not be retrieved, and 7 studies were excluded because 6 did not utilize WHO criteria for Anemia definition, and 1 had poor data reporting. After removing irrelevant publications, 39 full-text studies were discovered and used for the final quantitative analysis (Fig. 1).

Features of the included research

This systematic review and meta-analysis included 39 publications [21]. The study includes 29 articles from India, 6 from Indonesia, 2 from Nepal, and 2 from Thailand. The sample size for the included studies ranged from HIV infections ranged from 42 to 6996. The selected studies were divided into 27 cross-sectional studies, 11 cohort studies, and 1 case–control study. The 39 studies involved 21,427 HIV-infected persons, with 31 from low-income countries and 8 from high-income countries (Table 1).

The prevalence of anemia among people living with HIV/AIDS in Southeast Asia

The random effects model, which accounts for heterogeneity among studies, results in a pooled prevalence of 0.50 (95% CI: 0.43–0.57). The heterogeneity statistics ($I^2 = 99.6\%$, $\tau^2 = 0.0613$, $p = 0.00$) indicate substantial variability among the studies (Fig. 2).

Subgroup analysis of the prevalence of anemia among people living with HIV/AIDS in Southeast Asia

Meta-analysis of the prevalence of Anemia Among People Living with HIV/AIDS suggests that there is high heterogeneity among studies. To try to pinpoint the cause of heterogeneity, we plan to do a subgroup analysis. This study's subgroups comprised: Study design (Cross-sectional; Cohort; Case–Control), Study Category (Cross-sectional; Follow-up study), ART Status (Naïve; Mixed; On ART), Study year (2000–2015; 2016–2024), Country (India; Indonesia; Nepal; Thailand), Population (Adults; Children; Pregnant women; Adult + Adolescents). Here all studies have used a random effect model except in pregnant women were used a common effect model ($I^2 = 0\%$, $p < 0.001$). The results of the subgroup analysis are shown in Table 2.

Subgroup analysis for country

A subgroup analysis by Country showed that the prevalence of Anemia among People Living with HIV/AIDS in India was 50% [95% CI: 38–61%], whereas the prevalence in Nepal was 61% [95% CI:53–58%], and in Indonesia was 45% [95%CI:36–55%], and in Thailand was 23% [95% CI:8–49%] (supplementary Fig. 1).

Subgroup analysis for ART status

The prevalence of Anemia among ART-naive HIV/AIDS patients was 58% [95% CI:27–83%], according to a subgroup analysis by ART status. In contrast, 48% of ART users reported using it [95% CI: 39–57%]. and 54% [95% CI:46–62%] of ART mixed patients had this condition. (Supplementary Fig. 2).

Subgroup analysis for population characteristics

According to a subgroup analysis by the study population, the prevalence of Anemia was 49% [95% CI: 40–58%] among adults, 52% [95% CI: 37–68%] among children, and 37% [95% CI: 23–52%] among pregnant women. (supplementary Fig. 3).

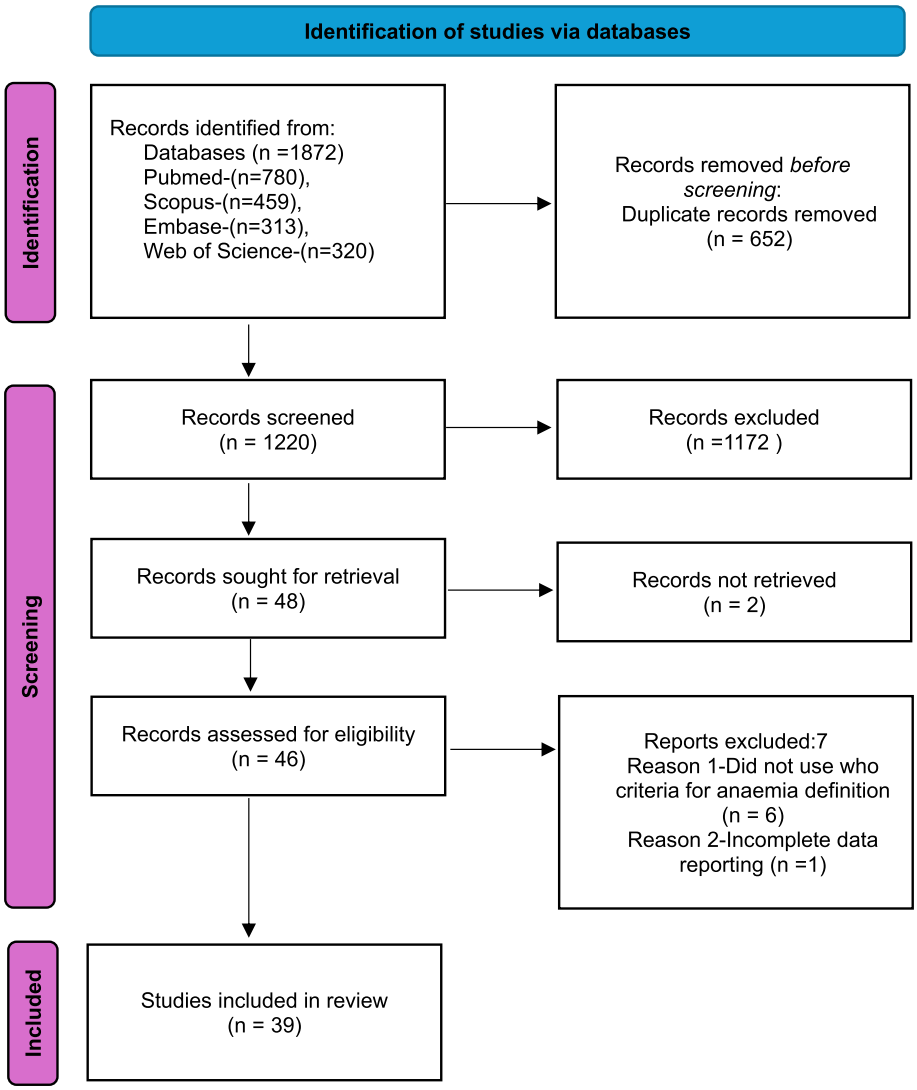

Fig. 1 Flowchart of the selection of studies for the systematic review and meta-analysis on the prevalence of Anemia among People Living with HIV/AIDS in Southeast Asia HIV = Human immunodeficiency virus

Subgroup analysis for world bank country classifications

A subgroup analysis by Income showed that the prevalence of Anemia among HIV/AIDS patients in the lower middle country was 50% [95% CI: 39–61%], whereas in the upper middle country was 39% [95% CI: 25–54%] (supplementary Fig. 4).

Subgroup analysis for study design

A subgroup analysis by the Study Design showed that the prevalence of Anemia among HIV/AIDS patients in a cross-sectional study was 50% [95% CI: 41–59%], whereas in the prospective cohort was also 48%. (supplementary Fig. 5).

Subgroup analysis for study category

A subgroup analysis by the Study Category showed that the prevalence of Anemia among people with HIV/AIDS in a cross-sectional study was 50% [95%CI: 39–61%], whereas in a follow-up study was 49%. (supplementary Fig. 6).

Subgroup analysis for study year

A subgroup analysis by the Study Year showed that the prevalence of Anemia among HIV/AIDS patients from 2000 to 2015 was 46% [95% CI: 36–56%], whereas in 2016–2024 was 50% [95% CI: 39–61%] (supplementary Fig. 7).

Table 1 Features of the articles selected as part of the meta-analysis and systematic review

Sr No	Author(s)	Country	Income Category	Study Design	Population	Publication Year	Anemia Definition	ART_Regimen	ART Status	Sample Size	Prevalence (%)	Quality Score
1	Shah et al. [23]	India	Lower-middle	Cross-sectional	Children	2005	WHO Classification	Not Specified	Naive	42	52.4	4
2	Gita Sinha et al. [24]	India	Lower-middle	Cross-sectional	Pregnant Women	2007	WHO Classification	ZDV-based ART	Both	906	37.1	8
3	Kumarasamy et al. [25]	India	Lower-middle	Cross-sectional	Adults	2008	Not Specified	HAART	Experienced	3154	5.4	6
4	Anita Shet et al. [26]	India	Lower-middle	Cross-sectional	Children	2009	WHO Classification	Not Specified	Both	248	66.0	7
5	Ramnath Subbaraman et al. [27]	India	Lower-middle	Cross-sectional	Adults	2009	WHO Classification	Not Specified	Naive	6996	41.0	8
6	Dikshit et al. [28]	India	Lower-middle	Cross-sectional	Adults	2009	WHO Classification	Not Specified	Both	200	65.5	7
7	Agarwal et al. [29]	India	Lower-middle	Cross-sectional	Adults	2010	WHO Classification	ZDV-based ART	Experienced	1256	16.2	7
8	Wisaksana et al. [30]	Indonesia	Upper-middle	Cross-sectional	Adults	2011	WHO Classification	HAART	Both	869	39.1	8
9	Shet et al. [31]	India	Lower-middle	Cross-sectional	Children	2011	Not Specified	ZDV-based ART	Both	80	52.5	6
10	Anwikar et al. [32]	India	Lower-middle	Retrospective cohort	Adults	2011	Not Specified	HAART	Experienced	1844	2.8	8
11	Kapavarapu et al. [33]	India	Lower-middle	Prospective cohort	Children	2012	WHO Classification	Not Specified	Both	85	40.0	7
12	Parinitha et al. [34]	India	Lower-middle	Cross-sectional	Adults	2012	Not Specified	Not Specified	Naive	250	84.0	6
13	Wisaksana et al. [35]	Indonesia	Upper-middle	Prospective cohort	Adults	2013	WHO Classification	HAART	Both	127	63.4	7
14	Mathews et al. [36]	India	Lower-middle	Cross-sectional	Adults	2013	Not Specified	ZDV-based ART	Both	187	40.1	6
15	Chowta et al. [37]	India	Lower-middle	Retrospective cohort	Adults	2013	Not Specified	HAART	Experienced	99	58.6	5
16	Yapan et al. [38]	Thailand	Upper-middle	Cross-sectional	Pregnant Women	2014	WHO Classification	HAART	Both	105	41.0	9
17	Singh et al. [39]	India	Lower-middle	Prospective cohort	Children	2014	WHO Classification	ZDV-based ART	Experienced	70	75.0	6
18	Martin et al. [40]	Nepal	Lower-middle	Cross-sectional	Adults	2014	WHO Classification	HAART	Both	319	55.8	9
19	Verma et al. [41]	India	Lower-middle	Cross-sectional	Children	2014	WHO Classification	HAART	Experienced	55	36.4	8
20	Kuwalairat et al. [42]	Thailand	Upper-middle	Cross-sectional	Adults	2014	WHO Classification	ZDV-based ART	Experienced	303	11.2	9

Table 1 (continued)

Sr No	Author(s)	Country	Income Category	Study Design	Population	Publication Year	Anemia Definition	ART_Regimen	ART Status	Sample Size	Prevalence (%)	Quality Score
21	Kulkarni et al. [43]	India	Lower-middle	Cross-sectional	Adults	2015	Not Specified	Not Specified	Both	200	77.5	6
22	Shet et al. [44]	India	Lower-middle	Prospective cohort	Children	2015	WHO Classification	HAART	Both	241	47.1	9
23	Patil et al. [45]	India	Lower-middle	Cross-sectional	Adults	2016	Not Specified	Not Specified	Experienced	111	14.4	5
24	Raman et al. [46]	India	Lower-middle	Cross-sectional	Adults	2016	Not Specified	Not Specified	Both	120	77.0	6
25	Wahyuwibowo et al. [47]	Indonesia	Upper-middle	Cross-sectional	Adults	2018	WHO Classification	ZDV-based ART	Experienced	54	38.9	8
26	Aithal et al. [48]	India	Lower-middle	Cross-sectional	Adults	2018	WHO Classification	Not Specified	Experienced	228	62.2	7
27	Bhagrati et al. [49]	India	Lower-middle	Prospective cohort	Children	2019	WHO Classification	HAART	Both	489	17.6	7
28	Pertiwi et al. [50]	Indonesia	Upper-middle	Case–control	Adults	2020	WHO Classification	ZDV-based ART	Experienced	503	29.4	8
29	Bhardwaj et al. [51]	India	Lower-middle	Cross-sectional	Adults	2020	Not Specified	HAART	Both	120	69.17	4
30	Sah et al. [52]	Nepal	Lower-middle	Cross-sectional	Adults	2020	Not Specified	Not Specified	Both	210	66.7	8
31	Sunita P et al. [53]	India	Lower-middle	Retrospective cohort	Adults	2020	Not Specified	HAART	Experienced	100	54.0	7
32	Suja et al. [54]	India	Lower-middle	Cross-sectional	Adults	2020	Not Specified	HAART	Both	100	47.0	4
33	Mahajan et al. [55]	India	Lower-middle	Mixed cohort	Adults	2020	Not Specified	HAART	Experienced	400	61.5	8
34	Aryastuti et al. [56]	Indonesia	Upper-middle	Cross-sectional	Adults	2021	WHO Classification	Not Specified	Both	243	54.7	8
35	Chitralekha et al. [57]	India	Lower-middle	Retrospective cohort	Adults	2021	Not Specified	HAART	Experienced	211	66.4	7
36	Mungal et al. [58]	India	Lower-middle	Cross-sectional	Adults	2021	WHO Classification	HAART	Both	200	70.4	6
37	Kumar Pushkar et al. [59]	India	Lower-middle	Cross-sectional	Children	2022	Not Specified	Not Specified	Experienced	106	84.0	5
38	Mahajan et al. [60]	India	Lower-middle	Retrospective cohort	Adults & children	2023	WHO Classification	HAART	Experienced	513	77.7	9
39	Wiraguna et al. [61]	Indonesia	Upper-middle	Cross-sectional	Adults	2024	Not Specified	Not Specified	Naive	83	47.0	8

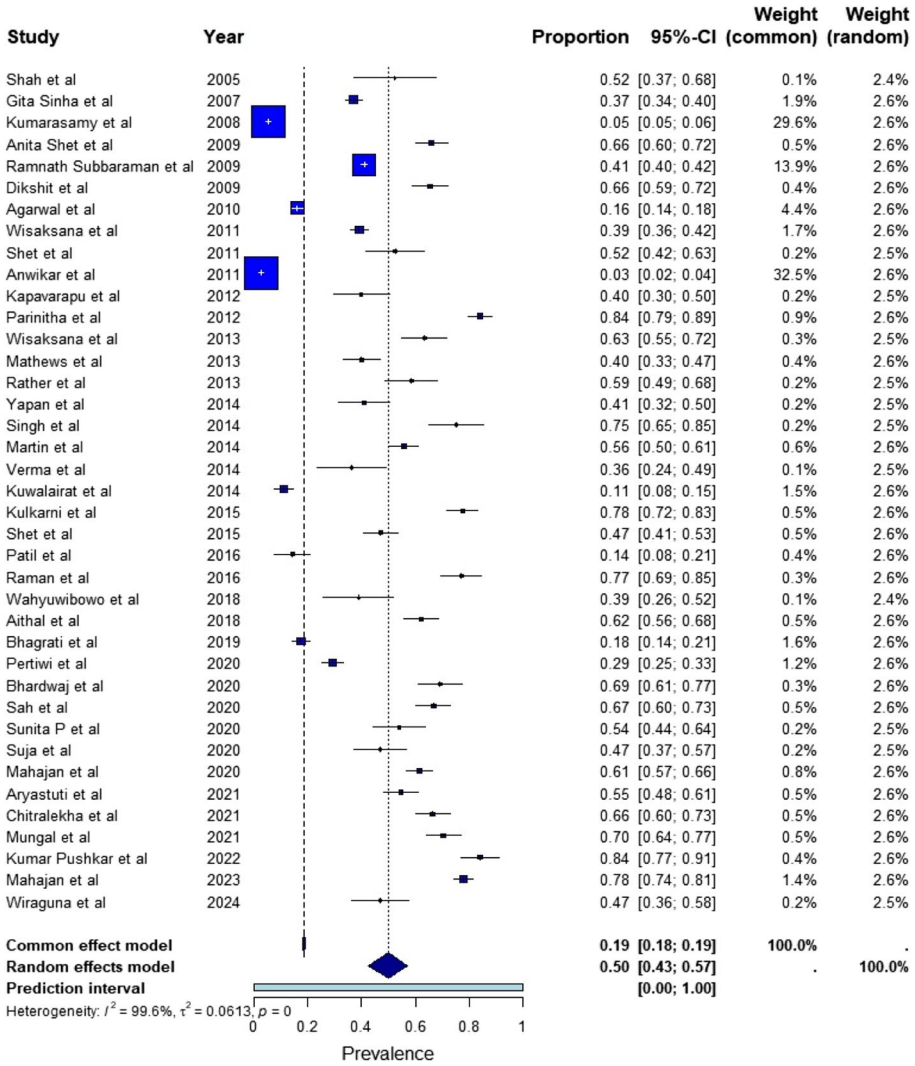

Fig. 2 Meta-analysis forest figure of the prevalence of Among People Living with HIV/AIDS in Southeast Asia

Subgroup analysis for pregnancy status

A subgroup analysis by the Pregnancy status showed that the prevalence of Anemia among HIV/AIDS in Pregnant women was 37% [95% CI: 35–41%], whereas in nonpregnant was 48% [95% CI: 39–58%] (supplementary Fig. 8).

Subgroup analysis for ART regimen

The subgroup analysis across ART regimens reveals significant heterogeneity in anemia prevalence. For patients on HAART (Highly Active Antiretroviral Therapy), the pooled prevalence was 44% (95% CI: 30–59%), with substantial between-study heterogeneity (I^2 = 99.2%). Studies, where the ART regimen was not specified, showed the highest prevalence at 61% (95% CI: 40–71%), suggesting that undefined treatment protocols may be associated with poorer hematological outcomes. Notably, ZDV-based ART demonstrated the lowest pooled prevalence at 35% (95% CI: 22–50%), though this finding should be interpreted cautiously given the known hematological toxicity of zidovudine. The overall heterogeneity across all subgroups (I^2 = 98.8%, τ^2 = 1.2977) indicates substantial variability in anemia prevalence that cannot be explained by ART regimen alone. The significant test for subgroup differences (χ^2 = 877.76, df = 2, p < 0.0001) suggests that the type of ART regimen meaningfully influences anemia risk. These findings emphasize the importance of considering individual patient factors when selecting ART regimens and implementing regular monitoring protocols, particularly in settings where specific regimens are associated with higher anemia prevalence (supplementary Fig. 11).

Table 2 summary table of meta-analysis results of prevalence of among people living with hiv/aids in southeast asia

Subgroup	Number of Studies	Heterogeneity	Effect Model	Prevalence % [95% CI]
ART Status	39	$I^2 = 98.8\%, p < 0.001$	Random effect	0.48[0.39–0.57]
ART-naive	4	$I^2 = 97.8\%, p < 0.001$	Random effect	0.58[0.27–0.83]
On ART	16	$I^2 = 99.3\%, p < 0.001$	Random effect	0.38[0.22–0.58]
Mixed	19	$I^2 = 96.3\%, p < 0.001$	Random effect	0.54[0.46–0.62]
Country	39	$I^2 = 98.8\%, p < 0.001$	Random effect	0.48[0.39–0.57]
India	29	$I^2 = 99\%, p < 0.001$	Random effect	0.50[0.38–0.61]
Indonesia	6	$I^2 = 93.2\%, p < 0.001$	Random effect	0.45[0.36–0.55]
Thailand	2	$I^2 = 97.5\%, p < 0.001$	Random effect	0.23[0.08–0.49]
Nepal	2	$I^2 = 83.9\%, p = 0.0128$	Random effect	0.61[0.53–0.68]
Study Design	39	$I^2 = 98.8\%, p < 0.001$	Random effect	0.48[0.39–0.57]
Cross-sectional	27	$I^2 = 99.6\%, p < 0.001$	Random effect	0.50[0.41–0.59]
Retrospective cohort	5	$I^2 = 99.8\%, p < 0.001$	Random effect	0.52[0.16- 0.88]
Prospective cohort	5	$I^2 = 98.1\%, p < 0.001$	Random effect	0.48[0.21–0.76]
Mixed cohort	1	NA	NA	0.61[0.57–0.66]
Case–control	1	NA	NA	0.29[0.25–0.34]
Income Level	39	$I^2 = 98.8\%, p < 0.001$	Random effect	0.48[0.39–0.57]
Lower-middle	31	$I^2 = 99.0\%, p < 0.001$	Random effect	0.50[0.39–0.61]
Upper-middle	8	$I^2 = 95.5\%, p < 0.001$	Random effect	0.39[0.25–0.54]
Population Group	39	$I 2 = 99.6\%, p < 0.001$	Random effect	0.50[0.43–0.57]
Children	9	$I^2 = 98.2\%, p < 0.001$	Random effect	0.52[0.37–0.68]
Pregnant women	2	$I^2 = 0\%, p < 0.001$	Common effect	0.42[0.39–0.44]
Adults + Children	1	NA	NA	0.78[0.74–0.81]
Adults	27	$I^2 = 99.7\%, p < 0.001$	Random effect	0.49[0.40–0.58]
Pregnancy Status	39	$I 2 = 98.8\%, p < 0.001$	Random effect	0.48[0.39- 0.57]
Non-pregnant	37	$I^2 = 98.9\%, p < 0.001$	Random effect	0.48[0.39–0.58]
Pregnant	2	$I^2 = 0, p < 0.001$	Common effect	0.37[0.35–0.41]
Publication Year	39	$I 2 = 99.6\%, p < 0.001$	Random effect	0.50[0.43- 0.57]
2000–2015	22	$I^2 = 99.7\%, p < 0.001$	Random effect	0.46[0.36–0.56]
2016–2024	17	$I^2 = 98.5\%, p < 0.001$	Random effect	0.55[0.45–0.66]
Study Category	39	$I 2 = 99.6\%, p < 0.001$	Random effect	0.50[0.43- 0.57]
Cross-sectional	27	$I 2 = 99.6\%, p < 0.001$	Random effect	0.50[0.43- 0.57]
Follow up study	12	$I 2 = 99.7\%, p < 0.001$	Random effect	0.49[0.40–0.58]
ART Regimen	39	$I 2 = 98.8\%, p < 0.001$	Random effect	0.48[0.39–0.57]
ZDV based	8	$I 2 = 97.2\%, p < 0.001$	Random effect	0.35[0.22–0.50]
HAART	17	$I 2 = 99.2\%, p < 0.001$	Random effect	0.44[0.30–0.59]
Not Specified	14	$I 2 = 97.4\%, p < 0.001$	Random effect	0.61[0.49–0.71]
Anemia Definition	39	$I 2 = 98.8\%, p < 0.001$	Random effect	0.48[0.39–0.57]
WHO	22	$I 2 = 98\%, p < 0.001$	Random effect	0.48[0.39–0.57]
Other	17	$I 2 = 99.3\%, p < 0.001$	Random effect	0.48[0.32–0.66]

Subgroup analysis for anemia definition

When comparing the WHO classification versus other definitions for anemia diagnosis, both analyses showed substantial heterogeneity ($I^2 > 98\%$). Studies using the WHO classification yielded random effects pooled prevalence of 48% (95% CI: 39–57%) with a total sample size of 14,172 participants. In contrast, studies using other classification methods showed the same random effects prevalence of 48% (95% CI: 32–66%) but with a smaller sample size of 7,255 participants. While the point estimates were identical, studies using non-WHO definitions showed wider confidence intervals, suggesting less precision. The common effect model estimates differed (41% vs 22%), indicating that the choice of anemia definition may influence prevalence estimates. However, given the high heterogeneity in both groups, the random

effects model provides more reliable estimates. This suggests that despite different diagnostic criteria, the overall burden of anemia in HIV patients remains consistent at around 48%, though standardisation of diagnostic criteria would improve estimate precision (Supplementary Fig. 12).

Sensitivity analysis

The sensitivity analysis, conducted using a leave-one-out approach across all 39 studies, demonstrated the overall robustness of our meta-analysis findings. The impact of removing individual studies on the pooled prevalence estimate ranged from − 0.12 to 0.00, indicating relatively stable results. Examining the specific data, the removal of individual studies showed varying effects on the pooled prevalence: Kumarasamy et al. (49.80%, 95% CI: 41.38–58.23%), Anwikar et al. (50.22%, 95% CI: 42.21–58.23%), and Patil et al. (49.03%, 95% CI: 40.15–57.98%) demonstrated the most notable changes in pooled estimates. The highest pooled prevalence was observed after removing Anwikar et al. (50.22%), while the lowest was seen after removing Kumar Pushkar et al. (46.81%). The heterogeneity remained consistently high across all analyses (I^2 ranging from 98.27% to 98.83%), with minimal variation regardless of which study was removed. Particularly, when Kumarasamy et al.'s study was removed, the I^2 value decreased to 98.26%, while the removal of Bhagrati et al.'s study resulted in an I^2 of 98.79%. The narrow range of changes in both pooled prevalence estimates (46.81% to 50.22%) and confidence intervals across all iterations suggests that our meta-analysis findings are robust and not substantially influenced by any single study. This consistency reinforces the reliability of our findings regarding anemia prevalence among PLHIV in Southeast Asia (Supplementary Table 2. Sensitivity Analysis) (Supplementary Fig. 9).

Heterogeneity and publication bias

The analysis of publication bias and heterogeneity for the meta-analysis of anemia prevalence among HIV-infected patients reveals several important findings. The original pooled prevalence estimate was 49.84%, which was only slightly adjusted to 47.76% after the trim-and-fill analysis, suggesting minimal publication bias impact. This small adjustment, requiring only 2 additional imputed studies, indicates the relatively symmetric distribution of study effects. Egger's test ($p = 0.206$) and Begg's test ($p = 0.894$, $z = 0.13$) both failed to detect significant publication bias, as their p-values are well above the conventional significance level of 0.05. However, there is substantial heterogeneity among the studies, as evidenced by the very high I-squared value of 98.80%, indicating that approximately 98.80% of the variability in effect estimates is due to true heterogeneity rather than sampling error. This heterogeneity is further quantified by a tau-squared value of 1.29, representing the between-study variance. The Begg's test bias estimate of 11 (SE = 11.66) has a small standard error, suggesting considerable uncertainty in this estimate. The funnel plot visually supports these findings, showing a relatively symmetric distribution of studies around the pooled estimate, with some scatter that reflects the high heterogeneity. The small number of imputed studies (2) visible as open circles in the funnel plot further confirms the minimal publication bias in this meta-analysis (Fig. 3 & Supplementary Table 4).

Meta-regression

The meta-regression analysis revealed complex patterns across multiple dimensions of anemia prevalence among PLHIV in Southeast Asia. ART status emerged as a significant predictor, with experienced users showing a protective effect ($\beta = -0.113$, adjusted $R^2 = 42.8\%$) compared to both naïve and mixed groups ($\beta = 0.072$ and $\beta = 0.083$ respectively). The income category demonstrated substantial explanatory power, with lower-middle income countries showing increased risk ($\beta = 0.118$, adjusted $R^2 = 52.4\%$) compared to upper-middle income countries ($\beta = -0.118$, adjusted $R^2 = 38.6\%$), suggesting socioeconomic factors play a crucial role in anemia prevalence.

Publication year analysis indicated temporal trends, with studies from 2016–2024 showing a positive association ($\beta = 0.096$, adjusted $R^2 = 46.7\%$) compared to earlier studies (2000–2015, $\beta = -0.096$, adjusted $R^2 = 48.3\%$), suggesting possible changes in detection or reporting practices over time. Population group analysis revealed varying associations, with adults and children combined showing the strongest positive association ($\beta = 0.286$), though the small sample size ($n = 1$) limited its explanatory power (adjusted $R^2 = 0\%$). Study design categories showed minimal associations, with cross-sectional studies ($\beta = 0.008$), retrospective cohort ($\beta = 0.022$), and prospective cohort ($\beta = -0.017$) all demonstrating adjusted R^2 values of 0%, suggesting study methodology had limited impact on reported prevalence.

Country-specific analysis showed notable variations, with Thailand demonstrating the strongest negative association ($\beta = -0.253$) and Nepal the strongest positive association ($\beta = 0.120$), though small sample sizes (n = 2 each) resulted in adjusted R^2 values of 0%. Pregnancy status analysis showed identical but opposite associations for pregnant and non-pregnant groups ($\beta = \pm 0.114$), though limited sample sizes affected their explanatory power (adjusted $R^2 = 0\%$). Notably, all subgroup analyses demonstrated very high heterogeneity ($I^2 > 99\%$), indicating substantial unexplained variation across studies.

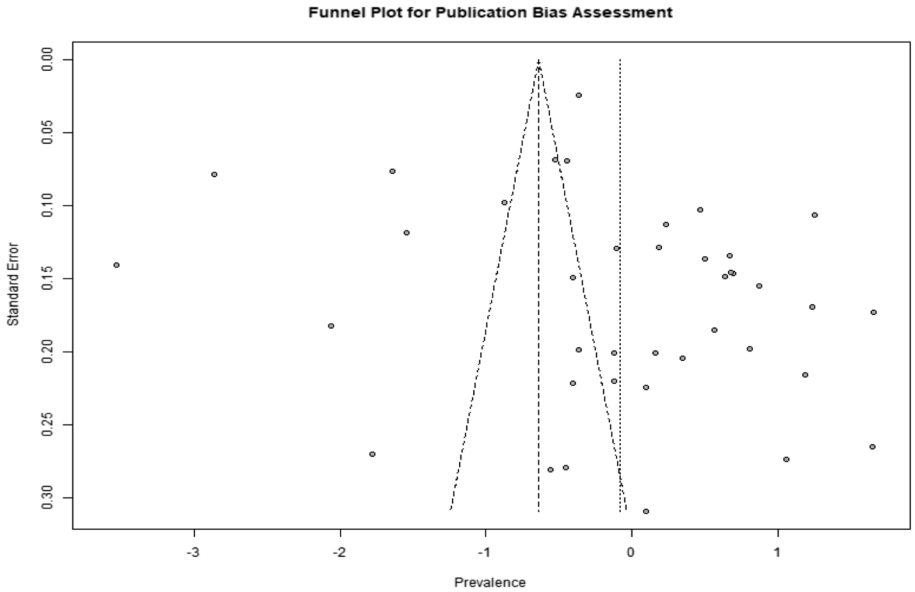

Fig. 3 The pooled prevalence of Anemia among people with HIV has been estimated applying a funnel plot of the included studies

Subgroup analysis of Anemia definitions and ART regimens revealed consistent patterns across categories. WHO classification showed a stronger negative association (β = − 20.16) compared to non-specified definitions (β = − 17.42), while among ART regimens, non-specified treatments showed positive association (β = 10.29) contrasting with the protective effects of both ZDV-based ART (β = − 9.69) and HAART (β = − 10.19). All subgroups maintained identical explanatory power (Adjusted R^2 = 6.45%) and high heterogeneity (I^2 > 97%) with no statistical significance, suggesting that neither anemia definition nor ART regimen type alone substantially explains variance in anemia prevalence among PLHIV in Southeast Asia.

These findings suggest that while certain factors, particularly ART status, income level, and publication period, explain meaningful portions of the variance in anemia prevalence, the relationship between these variables and anemia risk is complex and likely influenced by multiple interacting factors. The consistently high I^2 values across all analyses emphasize the need for careful consideration of local contexts and multiple risk factors when developing interventions to address anemia in PLHIV populations.

Meta-regression analysis revealed important patterns in the relationship between ART status, country income levels, and anemia prevalence among PLHIV in Southeast Asia. For ART status, we observed notable differences in the direction and magnitude of associations. ART-experienced individuals showed a protective effect (β = − 0.113, CI: − 0.252 to 0.026), with an adjusted R^2 of 42.8%, suggesting that ART experience explains a substantial portion of the variance in anemia prevalence. Conversely, both ART-naïve and mixed experience groups showed positive associations (β = 0.072 and β = 0.083 respectively), with the mixed experience group demonstrating a slightly higher explanatory power (adjusted R^2 = 45.2%). While these associations did not reach statistical significance (p > 0.05), the substantial adjusted R^2 values suggest clinically meaningful relationships between ART status and anemia prevalence.

The analysis of country income levels revealed particularly striking socioeconomic disparities. Lower-middle income countries showed a positive association with anemia prevalence (β = 0.118, CI: − 0.054 to 0.289), with an adjusted R^2 of 52.4%—the highest among all analyzed factors. Upper-middle income countries showed an inverse relationship of equal magnitude (β = − 0.118), though with a lower adjusted R^2 of 38.6%. This pattern suggests that socioeconomic factors substantially influence anemia risk, with lower-middle-income countries facing a greater burden. The high I^2 values (> 99%) across both ART status and income level analyses indicate substantial heterogeneity, suggesting that these relationships are complex and likely influenced by multiple interacting factors.

At the country level, while Thailand showed the strongest negative association (β = − 0.253) and Nepal the strongest positive association (β = 0.120), the small sample sizes (n = 2 for each) resulted in adjusted R^2 values of 0%, limiting the reliability of these specific country-level findings. India, with the largest sample size (n = 29),

showed a modest positive association (β = 0.069) but also with an adjusted R^2 of 0%, suggesting that country-specific effects may be confounded by other factors such as healthcare system capabilities and access to treatment.

These findings have important implications for clinical practice and public health policy:

1. The substantial explanatory power of ART status suggests that optimizing antiretroviral therapy could be crucial in managing anemia risk among PLHIV.
2. The strong influence of country income levels indicates that addressing socioeconomic disparities should be a key component of strategies to reduce anemia burden in this population.
3. The high heterogeneity across analyses suggests that interventions may need to be tailored to specific contexts, considering both treatment access and socioeconomic circumstances.
4. The varying effects across countries highlight the need for nation-specific approaches while considering broader regional patterns in healthcare delivery and economic resources.

This analysis underscores the complex interplay between clinical management (ART status) and structural factors (country income levels) in determining anemia risk among PLHIV in Southeast Asia. Future research should focus on understanding the mechanisms behind these associations and developing targeted interventions that account for both treatment and socioeconomic factors. (Supplementary Table 2).

The risk factors of anemia in people living with HIV

Our meta-analysis systematically evaluated potential risk factors for anemia among PLHIV in Southeast Asia, revealing several significant associations with varying degrees of strength and precision. The findings can be categorized into treatment-related, immunological, demographic, and clinical factors:

Treatment-related factors

Zidovudine use showed a strong association with anemia(OR = 9.28, 95% CI: 1.18–73, $p < 0.05$), though the wide confidence interval suggests considerable uncertainty in the effect size. This association, derived from two studies with moderate heterogeneity ($I^2 = 85.5\%$), underscores the importance of careful monitoring during zidovudine therapy. The timing of ART initiation also proved significant, with ART-naïve status showing increased risk (OR = 2.67, 95% CI: 1.17–6.12, $p < 0.05$), though heterogeneity was substantial ($I^2 = 72.7\%$).

Immunological and clinical factors

Low CD4 count demonstrated a robust association (OR = 3.56, 95% CI: 2.59–4.9, $p < 0.001$), supported by the largest evidence base (8 studies) with moderate heterogeneity ($I^2 = 45\%$). Opportunistic infections showed a significant but modest association (OR = 2.19, 95% CI: 1.07–4.5, $p < 0.05$) with moderate heterogeneity ($I^2 = 46\%$). Surprisingly, the advanced HIV stage (3 & 4) showed no significant association (OR = 1.42, 95% CI: 0.64–3.15), though this finding was based on only two studies with minimal heterogeneity ($I^2 = 0\%$).

Nutritional and demographic factors

Underweight BMI showed a strong association (OR = 4.75, 95% CI: 3.57–6.33, $p < 0.05$) with remarkable precision and no heterogeneity ($I^2 = 0\%$). Female gender demonstrated a consistent association (OR = 3.06, 95% CI: 2.71–3.45, $p < 0.05$) across four studies with minimal heterogeneity ($I^2 = 11\%$). Stunting in pediatric populations showed a significant association (OR = 2.36, 95% CI: 1.54–3.62, $p < 0.001$) with low heterogeneity ($I^2 = 30.3\%$).

Laboratory parameters

Viral load showed moderate association (OR = 2.86, 95% CI: 1.47–5.58, $p < 0.05$) with no heterogeneity ($I^2 = 0\%$), while low WBC count showed a trend toward association but missed statistical significance (OR = 3.67, 95% CI: 0.92–14.63, $p = 0.0531$).

Behavioural factors

Neither alcohol consumption (OR = 0.85, 95% CI: 0.47–1.56) nor smoking (OR = 0.99, 95% CI: 0.44–2.22) showed significant associations, with minimal to moderate heterogeneity ($I^2 = 0\%$ and 41% respectively).

Environmental factors

Rural residence showed no significant association (OR = 3.1, 95% CI: 0.22–43.64, $p = 0.401$), though high heterogeneity ($I^2 = 96.4\%$) suggests potential unmeasured confounding factors (Table 3).

These findings underscore the multifactorial nature of anemia risk in PLHIV and highlight the importance of comprehensive patient assessment, particularly regarding medication choice, immunological status, and nutritional support. The strong associations with modifiable factors such as BMI and ART status suggest potential targets for intervention, while the consistent gender disparity indicates the need for sex-specific monitoring approaches.

Table 3 The risk factors of Anemia in people living with HIV

Risk factor	Number of included literature	Results of heterogeneity test	Effect model	Result	
		I2		OR (95%CI)	*p*
Zidovudine (2,10)	2	85.5%	Random effect model	9.28 [1.18–73]	< 0.05*
Stunting (4,22)	2	30.3%	Random effect model	2.36 (1.54–3.62)	< 0.001*
Rural (4,38)	2	96.4%	Random effect model	3.1 (0.22–43.64)	0.401
Low CD4 Count (2,5,19,20,22,26,30,38)	8	45%	Random effect model	3.56 (2.59–4.9)	< 0.001*
Underweight BMI (5,26)	2	0%	Fixed effect model	4.75 [3.57–6.33]	< 0.05*
Female Gender (5,20,28,30)	4	11%	Fixed effect model	3.06 (2.71- 3.45)	< 0.05*
Viral Load (16, 22)	2	0.0%	Fixed effect model	2.86 (1.47–5.58)	< 0.05*
Low WBC (25, 38)	2	0%	Fixed effect model	3.67 (0.92–14.63)	0.0531
Before ART_ (30,38)	2	72.7%	Random effect model	2.67 (1.17–6.12)	< 0.05*
HIV Stage 3 & 4	2	0%	Fixed effect model	1.42(0.64–3.15)	0.376
Alcohol	2	0%	Fixed effect model	0.85(0.47–1.56)	0.605
Smoking	2	41%	Random effect model	0.99(0.44–2.22)	0.995
Opportunistic Infections	4	46%	Random effect model	2.19(1.07–4.5)	< 0.05*

Time trend analysis

The scatter plot with regression line shows an upward trend in anemia prevalence over the 19 years. The data points exhibit considerable variability, with prevalence rates ranging from approximately 3% to 84%. The blue regression line indicates a positive slope, suggesting an overall increasing trend in prevalence over time. The grey shaded area represents the 95% confidence interval, which widens towards both ends of the period, indicating greater uncertainty in the estimates at the temporal extremes.

Statistically, the Mann–Kendall test reveals a significant monotonic trend (Tau = 0.2463, $p = 0.0314$), confirming that the observed increase in prevalence is not due to chance. The linear regression analysis suggests an average increase in prevalence of 1.39% per year, though this trend is marginally significant ($p = 0.0544$) with a relatively low R-squared value of 0.0964, indicating substantial variability in the data not explained by time alone.

The wide confidence intervals in both the regression estimates (− 2.73% to 279.76% annual change) and total change over the study period (− 51.84% to 5315.39%) reflect high heterogeneity in reported prevalence rates. This heterogeneity is visually apparent in the scatter plot, where clusters of studies from similar periods report widely varying prevalence rates. This suggests that while there is a general increasing trend in anemia prevalence over time, other factors beyond temporal changes (such as study population characteristics, geographical location, or methodological differences) likely play important roles in determining prevalence rates.

The visualization also reveals potential outliers, particularly studies reporting very low (< 10%) or very high (> 80%) prevalence rates, which contribute to the wide confidence intervals and moderate statistical significance. Despite this variability, the consistent positive trend supported by both parametric (linear regression) and non-parametric (Mann–Kendall) tests suggests a concerning pattern of increasing anemia burden among HIV/AIDS patients over the study period (Fig. 4 & Supplementary Table 5).

Influence diagnostic analysis

Based on the influence diagnostic plots analysis, the meta-analysis appears methodologically sound with no severe influential cases. The DFFITS values are generally small and consistent, with most studies falling within ± 1, though a few studies show moderate influence with values around 2–3. Cook's Distance measures similarly show low influence for most studies, with only occasional peaks. The Covariance Ratio indicates generally stable precision estimates, ranging from 28–36, while the change in tau^2 values (1.05–1.35) demonstrates consistent heterogeneity across studies without substantial individual study impacts. Both Hat Values (0.026–0.030) and study weights (2.6–3.2%) show remarkably uniform distributions, indicating balanced contributions from all studies with no single study dominating the analysis. Overall, these diagnostics suggest a robust meta-analysis where heterogeneity is well-distributed rather than driven by individual studies, supporting the reliability of the pooled estimates (supplementary Fig. 10).

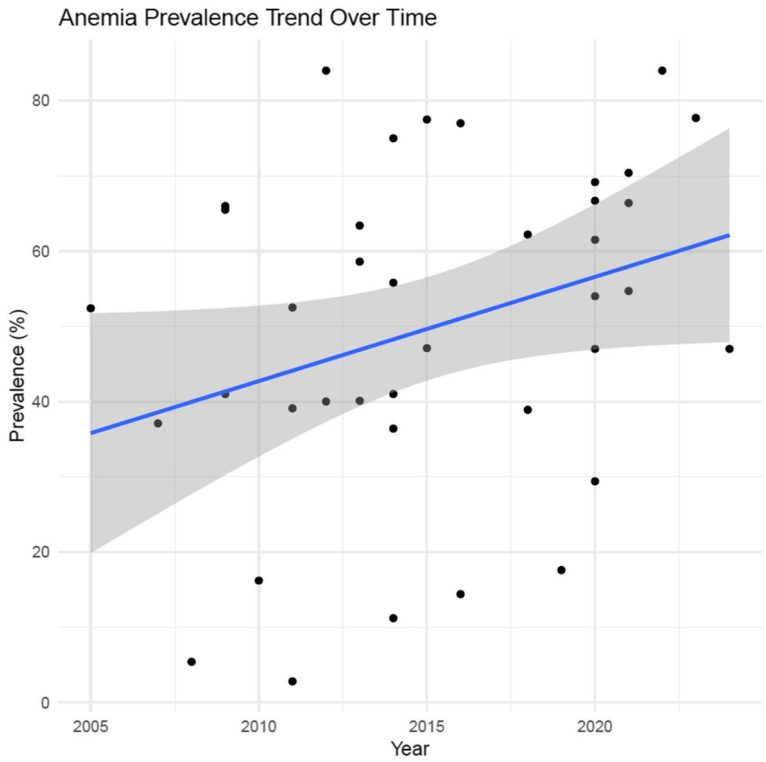

Fig. 4 Time Trend Analysis

Discussion

Anemia is the most frequent hematological abnormality among people with HIV/AIDS. Anemia in those living with HIV/AIDS can be triggered by opportunistic infections, cancer, or therapeutic adverse effects. Thirty-nine studies with a total of 21,427 PLHIV were included. The pooled prevalence of Anemia was 50% (95% CI: 43–57%) & Furthermore The pooled prevalence of Anemia was 39.7% (95% CI: 31.4%– 48.0%) for children living with HIV aged < 15 years, 46.6% (95% CI: 41.9%– 51.4%) for adults (men and non-pregnant women) living with HIV aged ≥ 15 years, and 48.6% (95% CI: 41.6%– 55.6%) for pregnant women living with HIV in systematic review and meta-analysis by Cao G, et al. in China [62]· The overall prevalence of 27.8% of HAART initiated and 45.5% of HAART naive pediatric HIV/AIDS patients were infected in Ethiopia by Mengist et al. [63]·

Subgroup analysis revealed higher prevalence in ART-naïve individuals (58%) compared to those on ART (38%), children (52%) compared to adults (49%) and pregnant women (37%), and those from lower-middle-income countries (50%) versus upper-middle-income countries (39%) and Nepal have a higher prevalence (61%) while Thailand has (23%). Furthermore, A subgroup analysis by highly active antiretroviral therapy (HAART) status showed that the prevalence of Anemia among HAART naive HIV/AIDS patients was 39.11% (95% CI: 29.28–48.93%) whereas the prevalence among HAART experienced was 36.72% (95% CI: 31.22–42.22%) in East Africa: A systematic review and meta-analysis by Getu et al. [64].

The high prevalence of anemia among PLHIV in Southeast Asia (pooled prevalence 48%, 95% CI: 39–57%) underscores the critical need for comprehensive screening and intervention protocols, particularly in resource-limited settings. Persistent anemia can accelerate HIV disease progression, particularly in patients with low CD4 counts (OR = 3.56, 95% CI: 2.59–4.9), and is associated with an increased risk of opportunistic infections and reduced quality of life. The lower anemia prevalence in ART-experienced individuals (38%) compared to ART-naïve (58%) suggests that early ART initiation, combined with regular hemoglobin monitoring, could improve long-term outcomes. Our findings reveal several key factors that should inform clinical practice: First, ART-naïve individuals showed markedly higher anemia prevalence (58%, 95% CI: 27–83%) compared to those on ART (38%, 95% CI: 22–58%), emphasizing the importance of early ART initiation. Second, the strong association between low CD4 counts and anemia risk (OR = 3.56, 95% CI: 2.59–4.9, $p < 0.001$) suggests that regular hemoglobin monitoring should be intensified in patients with immunological deterioration.

Our findings highlight distinct vulnerability patterns among specific subgroups, necessitating targeted intervention strategies. Women demonstrated significantly higher anemia risk (OR = 3.06, 95% CI: 2.71–3.45, $p < 0.05$), suggesting the need for gender-sensitive care approaches including regular screening during pregnancy and menstruation cycles. The strong association between underweight BMI and anemia (OR = 4.75, 95% CI: 3.57–6.33, $p < 0.05$) emphasizes the importance of comprehensive nutritional support, including routine anthropometric monitoring and targeted supplementation programs. Children, showing higher prevalence rates (52%, 95% CI: 37–68%) compared to adults (49%, 95% CI: 40–58%), require age-appropriate interventions including growth monitoring, micronutrient supplementation, and careful ART regimen selection. For these vulnerable populations, we recommend implementing integrated care packages that combine regular anemia screening, nutritional support, and optimized ART regimens, with particular attention to avoiding high-risk medications like zidovudine (OR = 9.28, 95% CI: 1.18–73) in those with multiple risk factors. These targeted approaches should be prioritized especially in lower-middle-income countries where our analysis showed higher overall anemia prevalence. Notably, the higher prevalence in lower-middle-income countries (50%, 95% CI: 39–61%) compared to upper-middle-income countries (39%, 95% CI: 25–54%) suggests that resource allocation and healthcare system strengthening should prioritize these regions. We recommend implementing standardized screening protocols that include regular hemoglobin monitoring, particularly for high-risk groups such as ART-naïve patients, those with low CD4 counts, and undernourished individuals.

Additionally, the significant association with zidovudine use (OR = 9.28, 95% CI: 1.18–73, $p < 0.05$) suggests careful monitoring is needed when this medication is prescribed, with consideration of alternative regimens for high-risk patients. We recommend implementing structured monitoring protocols, particularly during the initial months of zidovudine therapy, with increased vigilance in patients with additional risk factors such as low CD4 counts or underweight BMI. In cases of moderate to severe anemia, clinicians should consider dose adjustments or switch to alternative antiretroviral medications like tenofovir, especially in settings with limited monitoring capabilities. Preventive measures should include routine iron status assessment and supplementation where indicated. For resource-limited settings where zidovudine remains widely used, we recommend developing standardized clinical algorithms that specify hemoglobin thresholds for dose modification or drug substitution, thereby facilitating consistent care across different healthcare settings in Southeast Asia.

While we used the validated JBI critical appraisal tools for quality assessment, it should be noted that the categorization of scores into low, moderate, and high-quality groups was based on score distribution rather than established cutoff points, as JBI does not specify thresholds for quality categorization.

Our meta-analysis revealed substantial statistical heterogeneity ($I^2 = 99.6\%$, $\tau^2 = 0.0613$, $p < 0.001$) across studies, which warrants careful interpretation of the pooled estimates. This heterogeneity likely stems from multiple sources: methodological differences (varying study designs and anemia definitions), clinical factors (different ART regimens, disease stages, and comorbidities), and population characteristics (demographic variations, nutritional status, and healthcare access across Southeast Asian countries). Subgroup analyses revealed that heterogeneity was lower in certain populations, particularly among pregnant women ($I^2 = 0\%$) and studies from Nepal ($I^2 = 83.9\%$), suggesting more consistent estimates in homogeneous populations. While this heterogeneity reflects the complex reality of anemia in HIV/AIDS across diverse settings, the consistency of findings across sensitivity analyses and subgroups supports the robustness of our main conclusions. However, clinicians should consider local contexts and population-specific factors when applying these findings to practice.

Our meta-analysis revealed a striking overall anemia prevalence of 50% (95% CI: 43–57%) among PLHIV in Southeast Asia, which is substantially higher than rates reported in the general population across the region. In India, which contributed the majority of studies to our analysis ($n = 29$), the general population anemia prevalence ranges from 22.7% to 39.4% in adult males and 53.1% to 59.8% in adult females according to the National Family Health Survey- 5 (2019–21) [65], with an overall prevalence of approximately 35.7% across all age groups. This represents a substantial disparity compared to our findings of 50.0% (95% CI: 38–61%) among Indian PLHIV. Similarly, in Indonesia, general population anemia rates of 32.9% stand in contrast to the 45.0% (95% CI: 36–55%) [66] we observed among Indonesian PLHIV.

This comparative disparity extends to specific vulnerable populations. Among children, our analysis showed an anemia prevalence of 52.3% (95% CI: 37–68%) in HIV-infected children, compared to general population rates of 39.5% in India [65] and 33.2% in Indonesia [66]. For pregnant women, we found anemia prevalence of 37.0% (95% CI: 35–41%) among those with HIV, which aligns more closely with general population rates of 40–45% in pregnant women across Southeast Asia [67, 68],

suggesting that pregnancy-related anemia risk may partially overshadow HIV-specific factors in this subgroup.

The risk factor profile also reveals important distinctions. While certain risk factors for anemia such as female gender (OR = 3.06, 95% CI: 2.71–3.45) and underweight/malnutrition (OR = 4.75, 95% CI: 3.57–6.33) are shared between PLHIV and the general population, their impact appears amplified in the HIV-infected population. For instance, the gender disparity in anemia risk is approximately 1.5–2 times higher in the general population [69, 70] but reaches threefold in our PLHIV analysis.

Moreover, several risk factors identified in our study are specific to or markedly intensified in PLHIV populations, including low CD4 count (OR = 3.56, 95% CI: 2.59–4.9), zidovudine use (OR = 9.28, 95% CI: 1.18–73), and opportunistic infections (OR = 2.19, 95% CI: 1.07–4.5). These HIV-specific risk factors contribute substantially to the elevated anemia burden and require targeted interventions that extend beyond general population anemia control strategies [71, 72].

Socioeconomic disparities appear to influence anemia risk in both populations but with different magnitudes. Our finding of higher anemia prevalence in lower-middle-income countries (50%, 95% CI: 39–61%) compared to upper-middle-income countries (39%, 95% CI: 25–54%) mirrors general population trends, where economic status correlates inversely with anemia risk [71, 73]. However, the impact of socioeconomic factors appears more pronounced in PLHIV, likely due to compounded effects of limited healthcare access, nutritional deficiencies, and delayed diagnosis of both HIV and anemia.

The trends over time also present an interesting contrast. While our analysis showed an increasing trend in anemia prevalence among PLHIV over the study period (2005–2024), general population anemia rates in Southeast Asia have shown modest declines during similar timeframes according to WHO global anemia estimates [74, 75]. This divergence suggests that despite improved HIV treatment access, anemia management among PLHIV may not have received proportionate attention in clinical protocols and public health initiatives.

These comparative insights have important implications for clinical practice and public health programming. The substantially higher anemia burden in PLHIV calls for integration of routine anemia screening and management into HIV care protocols, which should extend beyond the general population approaches. Additionally, the identified HIV-specific risk factors, particularly those related to immunosuppression and treatment, require specialized monitoring and intervention strategies that would not be captured in general population anemia control programs [72, 76].

Furthermore, the socioeconomic gradient observed in both populations but more pronounced in PLHIV suggests that interventions should prioritize resource-limited settings and incorporate both medical and social support mechanisms [71, 73]. The needs of vulnerable subgroups, particularly children and women with HIV, require particular attention given their disproportionate anemia burden compared to their counterparts in the general population [77, 78].

The strengths of our analysis include comprehensive database coverage, robust statistical methodology including sensitivity analyses, extensive subgroup and meta-regression analyses, assessment of temporal trends, and rigorous quality assessment of included studies. However, we acknowledge limitations including high statistical heterogeneity despite subgroup analyses and Potential exclusion of non-English language studies, Potential geographic or cultural research biases, and Pooled results that might not directly translate to individual patient scenarios.

Conclusion

This systematic review and meta-analysis represent the first comprehensive assessment of anemia prevalence among PLHIV in Southeast Asia. The study reveals that anemia remains a significant health challenge in this population, particularly affecting ART-naïve individuals, children, and those in lower-middle-income countries. These findings underscore both a public health challenge and a health equity issue that requires urgent attention. Healthcare systems should implement enhanced screening protocols and early interventions, with a particular focus on high-risk groups. Future interventions should be targeted and culturally sensitive, addressing both immediate clinical needs and underlying socioeconomic determinants of health.

Supplementary Information

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Supplementary Material 1.

Supplementary Material 2.

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Authors' contributions

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Data availability
The datasets generated and/or analyzed during the current study are not publicly available to protect the privacy of the study participants but are available from the corresponding author upon reasonable request.

Declarations

Ethics approval and consent to participate
This systematic review and meta-analysis were based on previously published studies and did not involve direct human participants, interventions, or collection of primary data. Therefore, ethical approval and individual patient consent were not required.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

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