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Prevalence of Opportunistic Infections and Determinants Among HIV-Positive Patients in Ethiopia: A Systematic Review and Meta-Analysis

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ABSTRACT

Background and Aims: Opportunistic infections (OIs) associated with HIV are the primary cause of morbidity and mortality among individuals living with HIV/AIDS. Evaluating the extent of OIs at the national level is essential for developing targeted interventions and effective control measures. Therefore, the aim of this study was to evaluate the pooled prevalence and identify the associated factors of OIs among HIV-positive individuals across all age groups.

Methods: This systematic review and meta-analysis was conducted following the PRISMA guidelines. It included studies published in English, research articles conducted in Ethiopia, and articles released between 2013 and 2023. A systematic search of articles on the prevalence and determinants of OIs among patients living with HIV in Ethiopia was conducted across four databases (PubMed, ScienceDirect, Scopus, and the Cochrane Library). To evaluate heterogeneity and publication bias, the study employed Cochran's Q, inverse variance (I^2), sensitivity analysis, funnel plots, and Begg and Egger regression tests. The meta-analysis was executed using STATA software, version 14.

Results: Of the 207 articles examined, only 26 met the inclusion requirements. The overall prevalence of OIs among HIV-positive patients was 42.71% (95% CI: 36.87–48.56). OIs among HIV-positive individuals were significantly associated with baseline WHO clinical stage II and above (OR: 2.83; 95% CI: 1.93–3.73), khat chewers (OR: 1.94; 95% CI: 1.21–2.66), poor adherence to ART (OR: 2.32; 95% CI: 1.51–3.13), and individuals with an initial CD4 number less than 200 cells/mm^3 (OR: 2.32; 95% CI: 1.55–3.09).

Conclusion: Chewing khat, poor adherence, low CD4 count, and WHO stage II and above were found to be predictors of OIs. A constant state of awareness is required for healthcare providers to improve decisions about the proper diagnosis and management of OIs among HIV-positive individuals.

Abbreviations: AOR, adjusted odds ratio; CI, confidence interval; GRADE, grading of recommendations assessment, development and evaluation; OIs, opportunistic infections; PLHIV, people living with human immunodeficiency virus; PRISMA, preferred reporting items for systematic reviews and meta-analyses; SNNPR, Southern Nations, Nationalities, and Peoples Region.

1 | Introduction

Opportunistic infections (OIs) are infections that occur in individuals with weakened immune systems [1]. Patients with HIV who have fewer than 200 CD4+ T cells per microliter are at a higher risk for experiencing these infections. HIV attacks and destroys human CD4 cells, leading to a reduced immune response against OIs, including bacterial, fungal, parasitic, viral infections, and certain types of cancer [2]. More than 90% of people with OIs play a role in the development of morbidity and mortality associated with AIDS [3]. Nevertheless, the widespread use of highly active antiretroviral therapy (HAART) and chemotherapy has had the most significant impact on decreasing mortality related to OIs [4].

More than 38 million people worldwide live with HIV/AIDS, with nearly 650,000 deaths in 2021 [5], including 1.7 million children (under 15 years of age) [6], and according to a 2019 report, almost 95,000 children with HIV-related deaths occurred mainly due to OIs [7]. Africa has the highest prevalence of HIV and the largest number of individuals living with the virus, exceeding 25 million [8]. Despite Africa comprising 14% of the global population, sub-Saharan Africa (SSA) is the region that is most heavily impacted by this epidemic [9]. Prevalence rates of OIs among HIV-positive patients vary considerably across different African countries. For example, research shows prevalence rates of 35.0% in Tanzania, 37.1% in Somalia, 51.9% in Cameroon, 61.7% in Nigeria, and 78.8% in Kenya [10–14].

Morbidity and mortality related to HIV are primarily due to the underlying immunosuppression caused by the virus, which results in life-threatening OIs as the disease progresses [15]. The ongoing spread of the AIDS pandemic has led to the emergence of new opportunistic diseases that exploit the immunocompromised condition of individuals infected with human immunodeficiency virus type 1 (HIV-1) [16, 17]. HIV-1 affects the medical, biological, and pharmacological dimensions of leishmaniasis, while the presence of Leishmania further complicates HIV-1 infection. This dual burden hinders effective treatment strategies and decreases the life expectancy of patients with AIDS [16, 17]. In vitro studies show that HIV-1 infection of monocyte-derived macrophages (MDMs) typically hinders their phagocytic abilities [18] and triggers a cytokine response that results in the release of tumor necrosis factor-alpha (TNF-α), interleukin-1 (IL-1), IL-6, and IL-8, among others [18]. The presence of these cytokines significantly influences the infection and replication of *Leishmania* during co-infections [18].

Reduced access to effective HIV treatment, difficulties adhering to ART, and inadequate medical care are the main causes of rising OIs rate among HIV-positive children in developing nations [19]. Lower technological applications for early detection, treatment, and prevention of OIs, as well as inadequate safety measures [20]. In patients living with HIV, OIs can create potential risks and influence the patient's response to ART therapy. If not identified and treated promptly, these effects can lead to a reduced quality of life, accelerated disease progression, heightened healthcare costs, and an increased likelihood of treatment failure [21]. The risk factors for developing OIs in patients with HIV are influenced by exposure to potential pathogens, the virulence of those pathogens, the level of host immunity, and the use of antimicrobial prophylaxis. Many of these OIs are linked to a greater risk of mortality among HIV patients [22]. Furthermore, individuals suffering from complications due to opportunistic diseases may experience interruptions in their ART, which can result in a more rapid progression of HIV disease [23].

In Ethiopia, there are 37,186 people living with HIV. The HIV prevalence rates in Gambella, Addis Ababa, Dire Dawa, and Harari are 48%, 34%, 25%, and 24%, respectively [24]. The prevalence of OIs is regarded as minor infections until they present with life-threatening complications [25]. Some regional studies have reported a prevalence ranging from 19% to 48%, despite this in Ethiopia there is lack of nationally representative and comprehensive data on the extent of OIs and associated factors [26]. At Debre Markos Referral Hospital, located in East Gojjam, Ethiopia, the prevalence of OIs among HIV patients on ART remains high, with oral candidiasis at 11.8%, chronic diarrhea at 9.9%, and tuberculosis at 9.7% [22]. It was associated with age, WHO stages III and IV, chewing khat, adhering to an ART regimen, having low hemoglobin levels, and recent weight [27].

According to Woldegeorgis et al. [28], oral candidiasis (25.31%), pulmonary tuberculosis (22.04%), herpes zoster (14.95%), bacterial pneumonia (12.50%), chronic diarrhea (6.66%), and extrapulmonary tuberculosis (5.49%) were the six most frequent OIs noted in Ethiopia. Ethiopia's geographical location, climate, and unique biological and cultural characteristics create an environment conducive to the prevalence of various infections, including OIs [29]. A wealth of studies have examined OIs in HIV-positive individuals in Ethiopia, including one systematic review and meta-analysis focused exclusively on adults [28]. However, there has yet to be a comprehensive study that systematically analyzes data across all age groups. Thus, the purpose of this study is to compile and provide summary estimates of the available data on OIs and associated factors among HIV-positive patients of all age groups in Ethiopia.

2 | Methods

2.1 | Country Profile

Ethiopia spans a total area of 1,000,000 km^2 (386,102 sq. miles) in the Horn of Africa. It shares borders with five countries: Sudan and South Sudan to the west, Kenya to the south, Djibouti and Somalia to the east, and Eritrea to the north [30]. As of October 21, 2024, Ethiopia's population is estimated at 133,093,561, based on the latest United Nations data compiled by Worldometer. This figure represents 1.62% of the global population, positioning Ethiopia as the eleventh most populous country in the world [31]. The country has a population density of 132 individuals per km^2, with approximately 22.1% of its inhabitants (29,204,015 people in 2024) living in urban areas. The average age in Ethiopia is 18.9 years [31].

2.2 | Search Strategy

This systematic review and meta-analysis adhered to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses

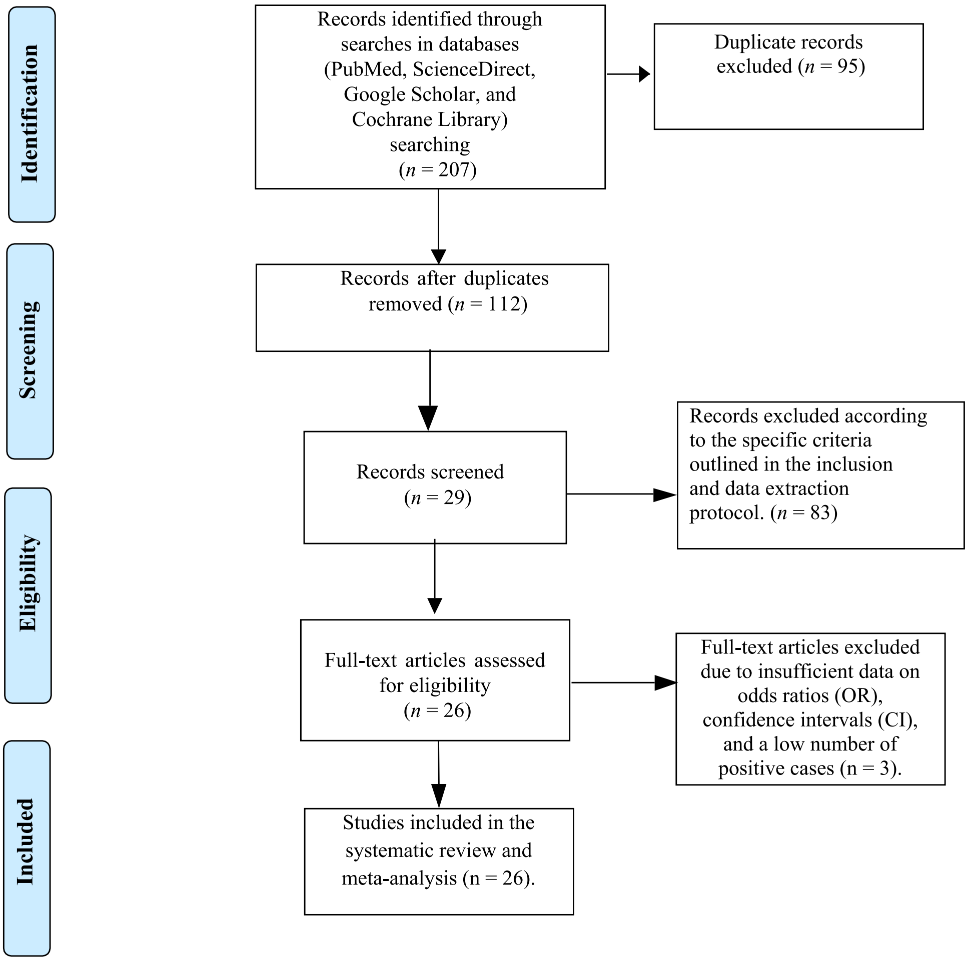

FIGURE 1 | PRISMA flow diagram showing the eligible studies.

(PRISMA) guidelines [32]. A systematic search was performed across various databases, including PubMed, Scopus, ScienceDirect, and the Cochrane Library. Key search terms with Boolean operations (AND or OR) used were "Prevalence," "magnitude," "epidemiology," "opportunistic infections," "risk factors," "predictors," "determinants," "individuals living with HIV," "people with HIV," "HIV-positive patients," "HIV" "HIV/AIDS" and "Ethiopia." Study selection was limited to those that provided clear information on sample sizes, positive sample counts, study locations, and associated risk factors. Language and time restrictions were not taken during the search for studies, and all published and unpublished studies up to September 1, 2023 were included. This method was in line with the study's aim to evaluate the prevalence and distribution of OIs among HIV-positive patients in Ethiopia.

2.3 | Criteria for Inclusion and Exclusion of Studies

2.3.1 | Inclusion Criteria

In this systematic review and meta-analysis all studies are observational encompassed 14 cross-sectional studies, one case-control study, and 11 cohort studies. A total of 26 studies were reviewed, focusing on HIV-positive individuals in Ethiopia to examine the prevalence of OIs and associated risk factors. The included sources comprised reports published exclusively in English and primary studies conducted in Ethiopia. The analysis covered findings from 11 years of research on OIs and their contributing factors in HIV-positive patients, with articles published between 2013 and 2023.

2.3.2 | Exclusion Criteria

This review excluded studies that lacked full-text access, duplicate publications, and extensions of analyses from original research. Additionally, articles with insufficient information, those based on personal opinions, reports that did not align with the desired outcomes, qualitative study designs, case reports, unpublished data, and previous systematic reviews were also omitted.

2.4 | Data Extraction

Data from studies that meet the required criteria were extracted and recorded in an Excel spreadsheet (Microsoft, Redmond, Washington, USA). The data extraction protocol includes the name of the first author, publication year, study setting, sample size, number of positive cases, prevalence of OIs, and associated risk factors. If the research was conducted over multiple years in a single location, the most recent year within that range was selected for analysis.

TABLE 1 | List and characteristics of 26 eligible studies conducted from 2013–2023 among people living with HIV in Ethiopia.

Author	Publication year	Region	Study design	Sample size	Case (*n*)	Prevalence (%)	Quality
Damtie et al.	2013 [34]	Amhara	Cross-sectional	360	71	19.7	6
Misker et al.	2014 [35]	SNNPR	Cohort	464	177	38.2	5
Moges & Kassa	2014 [27]	Amhara	Cross-sectional	423	181	42.8	6
Mitiku et al.	2015 [36]	Oromia	Cohort	358	172	48.0	4
Alemayehu et al.	2017 [37]	SNNPR	Cross-sectional	362	164	45.3	6
Deribe & Estifanos	2018 [38]	A/Ababa	Cohort	315	264	83.8	6
Solomon et al.	2018 [39]	SNNPR	Cohort	744	658	88.4	5
Urgessa et al.	2018 [40]	Oromia	Cross-sectional	418	219	52.4	5
Agezew et al.	2019 [41]	Amhara	Cross-sectional	315	69	21.9	6
Dereje et al.	2019 [42]	A/Ababa	Cross-sectional	384	130	33.6	5
Hailu et al.	2020 [43]	Tigray	Cross-sectional	394	205	52.0	4
Melkamu et al.	2020 [44]	Amhara	Cohort	408	111	34.6	5
Wachamo & Bonja	2020 [45]	SNNPR	Cross-sectional	420	166	39.6	6
Weldearegawi	2020 [46]	Tigray	Cohort	400	195	48.8	5
Fite & Aga	2020 [47]	Oromia	Cross-sectional	497	310	62.3	5
Chanie et al.	2021 [48]	Amhara	Cohort	349	86	24.9	5
Dembelu & Wosenelh	2021 [49]	SNNPR	Cross-sectional	450	119	26.4	5
Getachew et al.	2021 [50]	Amhara	Cross-sectional	304	71	23.4	5
Tewachew et al.	2021 [51]	Amhara	Case-control	339	113	33.3	4
Kebede et al.	2022 [52]	Amhara	Cross-sectional	405	171	42.2	4
Mequanente et al.	2022 [53]	Amhara	Cross-sectional	389	218	56.2	5
Tegegne et al.	2022 [54]	Amhara	Cohort	354	114	32.2	5
Wondifraw et al.	2022 [55]	Amhara	Cohort	354	135	38.1	6
Birmeka	2023 [56]	Oromia	Cross-sectional	1448	572	39.2	6
Dagnaw et al.	2023 [57]	Amhara	Cohort	715	543	75.9	5
Mekonnen et al.	2023 [58]	Amhara	Cohort	452	120	26.6	5

Abbreviation: SNNPR, Southern Nations, Nationalities, and Peoples Region.

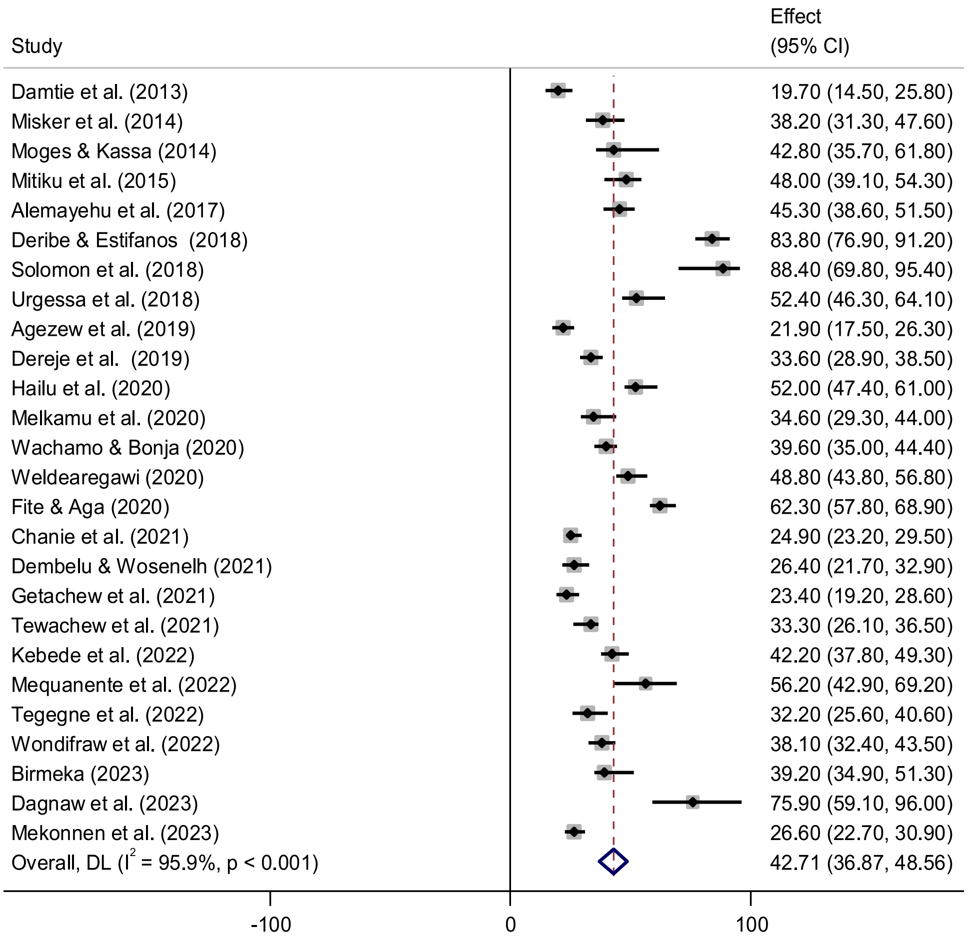

FIGURE 2 | Pooled prevalence of OIs among people with HIV in Ethiopia.

2.5 | Quality Assessment of Individual Studies

The overall quality of the evidence was assessed using the GRADE approach (Grading of Recommendations Assessment, Development, and Evaluation) [33]. Three primary evaluation methods, each rated at 2 points, were employed to determine each study's quality: methodological quality, comparability, and outcome and statistical analysis. Studies receiving a total score of 5–6 points were classified as high quality, 4 points as moderate quality, and 0–3 points as low quality [33].

2.6 | Data Analysis

The pooled effect size was determined using a random effects model due to the significant heterogeneity observed among the included studies. To investigate the sources of this heterogeneity, we performed a subgroup analysis based on sample size, region, study design, and publication year. We assessed statistical heterogeneity and variability with Cochran's Q statistic and I^2, while funnel plot symmetry was utilized to identify publication bias. Begg's and Egger's tests were conducted to estimate publication bias at a significance level of 5%, with a *p*-value of 0.05 indicating its presence. For I^2, heterogeneity is categorized as high when it exceeds 75%, substantial between 50% and 75%, moderate between 25% and 50%, and low when below 25%. The association between OIs and risk factors was evaluated using a log odds ratio (OR) and a 95% confidence interval (CI). In meta-analysis, if the CI does not include 1 for ratios (odds ratio, risk ratio) or does not include 0 for differences (e.g., mean difference), the risk factor is significantly associated with the outcome. Furthermore, in pooled risk factors, I^2 value indicates the degree of heterogeneity and the I^2 *p*-value tests the heterogeneity's significance association. All analysis was performed as per the SAMPL guidelines and using STATA software version 14 (StataCorp LLC 4905 Lakeway Drive College Station, Texas 77845-4512, USA) with two-sided tests.

3 | Results

A total of 207 articles were identified on the prevalence and determinants of OIs among HIV-positive patients in Ethiopia. After removing 95 duplicates, 112 articles remained. Of these, 83 were excluded after eligibility assessment based on the inclusion and exclusion criteria. From the remaining 29 articles, 3 were excluded for various reasons, including the absence of ORs, CI, and data on the number of positive cases. Therefore, 26 studies met the eligibility criteria and were included in the final systematic review and meta-analysis (Figure 1).

3.1 | Characteristics of the Eligible Studies

The characteristics of the studies included in the meta-analysis are summarized in Table 1. A total of 26 studies met the eligibility criteria and were included in the analysis. These studies

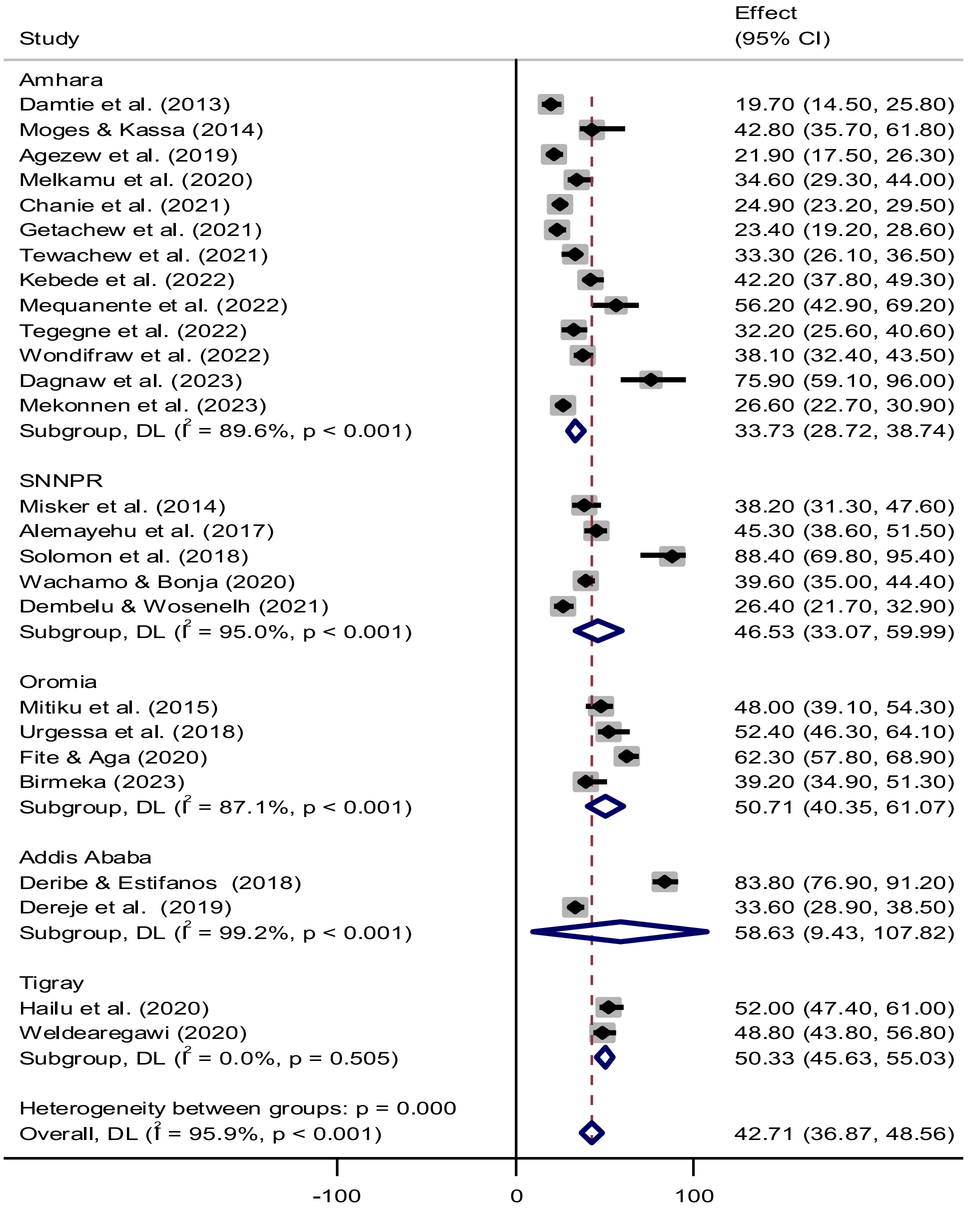

FIGURE 3 | Pooled prevalence of OIs by regions among people with HIV in Ethiopia.

were conducted between 2013 and 2023 and featured cross-sectional, cohort, and case-control designs. Eight studies were conducted from 2013 to 2018, seven studies between 2019 and 2020, and eleven studies from 2021 to 2023. The meta-analysis encompassed five regions: Addis Ababa (2 studies), Amhara (13 studies), Oromia (4 studies), SNNPR (5 studies), and Tigray (2 studies). The prevalence of OIs reported across the eligible studies ranged from 19.7% to 88.4% (see Table 1).

3.2 | Pooled Prevalence of OIs

The pooled prevalence of OIs among HIV-positive individuals in Ethiopia was calculated using a random-effects model. The analysis found an overall national prevalence of 42.71% (95% CI: 36.87–48.56). Additionally, the I^2 statistic demonstrated a high level of heterogeneity among the included studies, with an I^2 value of 95.9%, indicating considerable variability in the research outcomes (Figure 2).

3.3 | Subgroup Analysis

A high pooled prevalence of OIs among HIV-positive patients in Ethiopia was reported in Addis Ababa with 58.63% (95% CI: 9.43–107.82), followed by the Oromia region with 50.71% (95% CI: 40.35–61.07) and the Tigray region with 50.33% (95% CI: 45.63–55.03), SNNPR 46.53% (95% CI: 33.07–59.99), while the lowest prevalence of OIs were observed in Amhara at 33.73% (95% CI: 28.72–38.74) (Figure 3).

According to the study design, the cohort studies produced the highest pooled prevalence estimate of 48.21% (95% CI: 37.02–59.39), followed by the cross-sectional (39.42%; 95% CI: 32.20–46.65), and case-control studies (33.30%; 95% CI: 28.10–38.50, see Figure 4).

Throughout the study period, the highest pooled prevalence estimate was observed between 2013 and 2018, at 52.13% (95% CI: 35.71–68.55). This was followed by the period from 2019 to

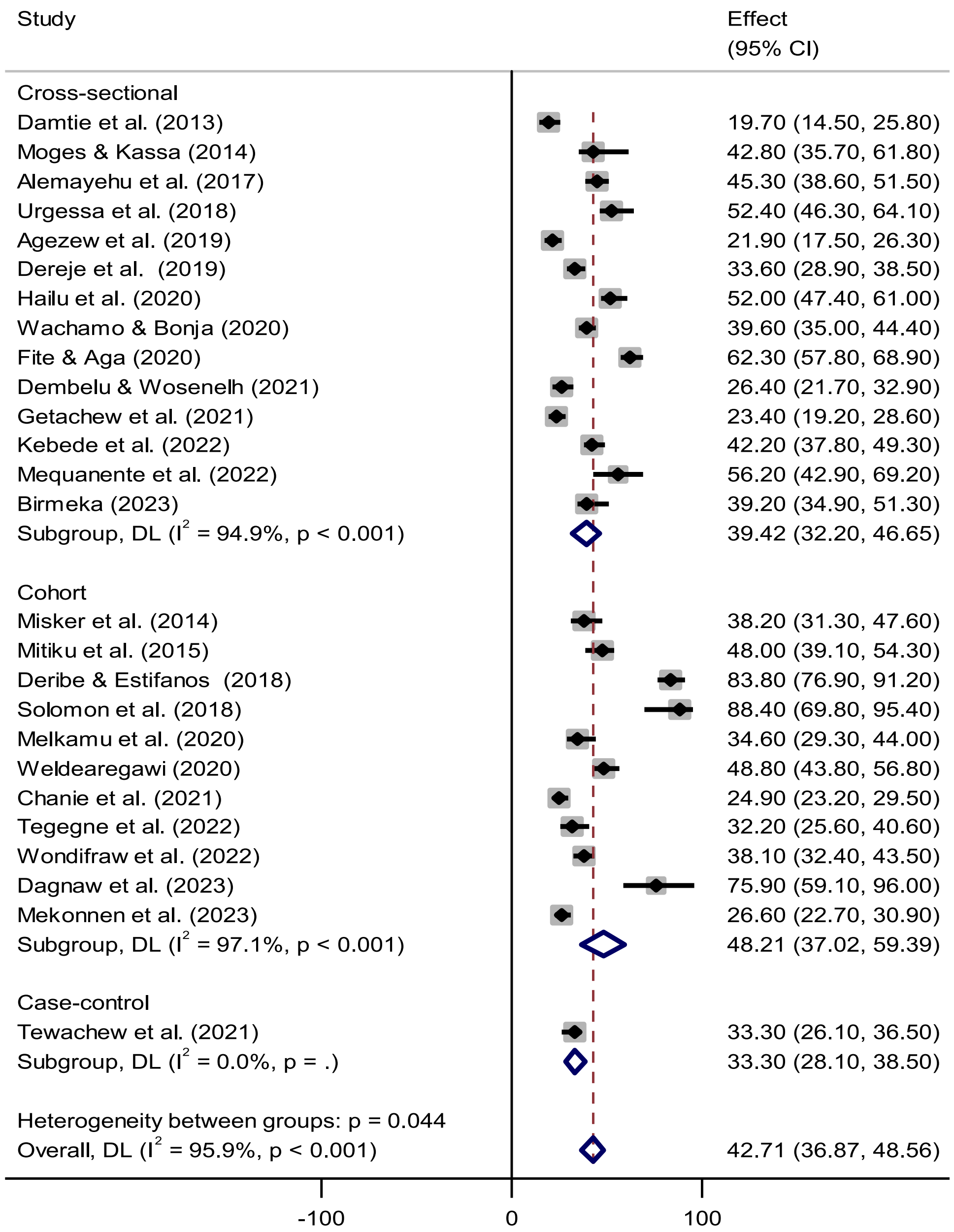

FIGURE 4 | Pooled prevalence of OIs by study design among people with HIV in Ethiopia.

2020, which had a pooled prevalence estimate of 41.76% (95% CI: 31.18–52.33). The lowest prevalence was recorded in the period from 2021 to 2023, at 35.32% (95% CI: 30.00–40.65) (see Figure 5).

The sample size distribution showed that authors utilized 384 and above sample sizes had the highest pooled prevalence estimate, 45.81% (95% CI: 38.83–52.79), followed by sample sizes below 384, 38.44% (95% CI: 28.94–47.94) (Figure 6).

3.4 | Factors Associated With OIs in Ethiopia

This systematic review and meta-analysis investigated various potential risk factors linked to the prevalence of OIs among individuals with HIV in Ethiopia such as a baseline CD4 count of less than 200 cells/mm^3, khat chewing, older age, lower educational attainment, and inadequate adherence to ART.

The relationship between OIs and WHO baseline stages II and above was examined in 11 studies. Findings indicate that individuals with WHO stage II and above face a 2.83-fold increased risk (95% CI: 1.93–3.73) of developing OIs compared to their counterparts. Figure 7 highlights a significant association between OIs and WHO stages II and higher.

The association between khat chewing and OIs were examined in four studies. The risk of OIs was 1.94 times higher (95% CI: 1.21–2.66) in khat chewers compared to nonchewers. This factor was also significantly associated with OIs among HIV-positive patients (Figure 8).

The association between OI and aging was examined in seven studies. Older adults had a 1.16-fold increased risk (95% CI: 0.59–1.72) of developing OIs compared to younger people. Even if, in this study, there was no significant association between OI and people older than 75 years (Figure 9).

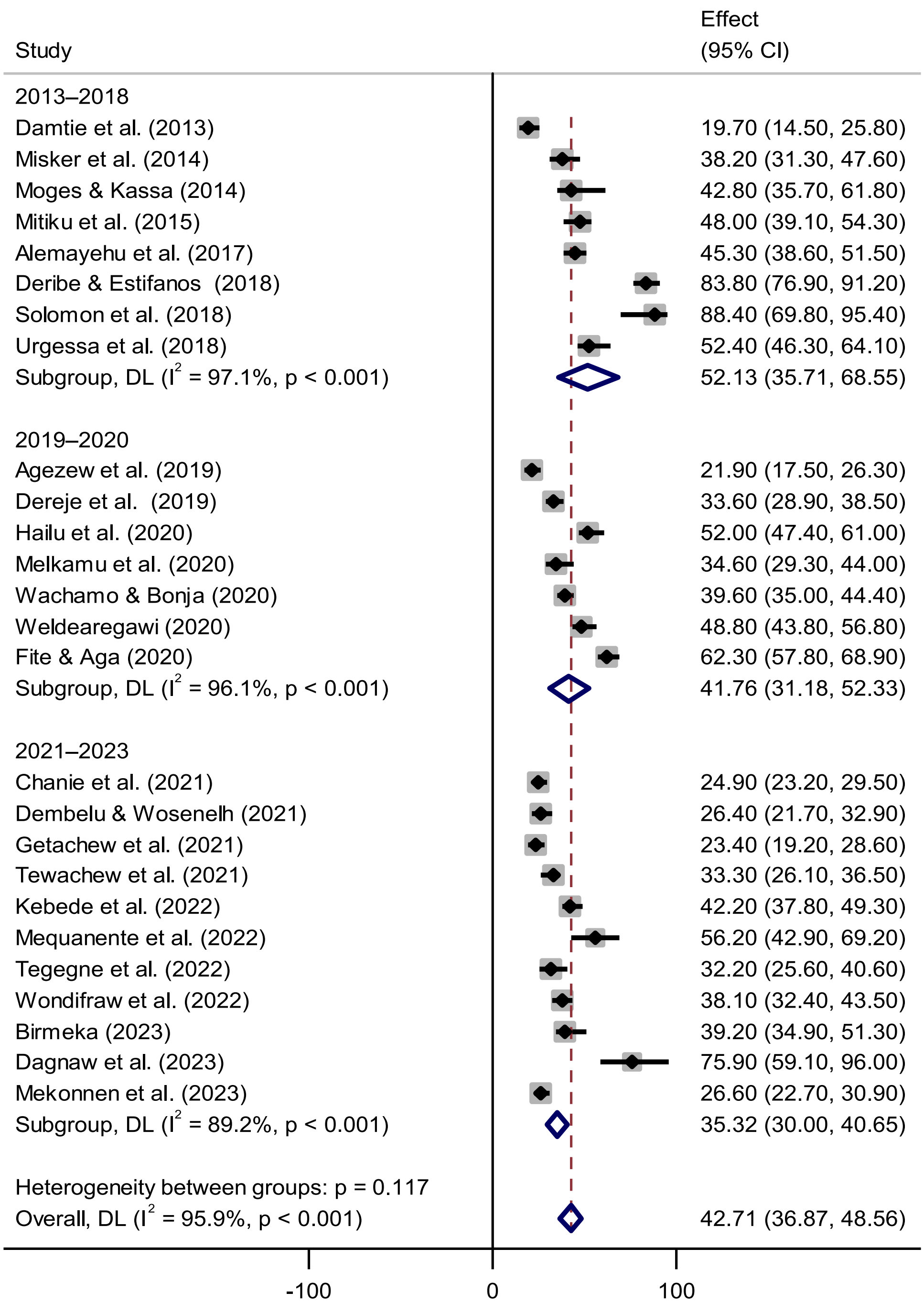

FIGURE 5 | Pooled prevalence of OIs by publication year among people with HIV in Ethiopia.

The association between OIs and educational status was analyzed through an analysis of five studies. People with lower education had a 0.76-fold greater threat (95% CI: 0.05–1.48) to develop OIs compared to educated people. However, there was no significant association between OIs and lower educational status (Figure 10).

The association between OIs and the initial CD4 count less than 200 cells/mm^3 per microliter was computed from 15 studies. People who had an initial CD4 number less than 200 cells/mm^3 had a 2.32 times greater chance (95% CI: 1.55–3.09) of developing OIs than those who had a CD4 number greater than 200 cells/mm^3. This factor was significantly associated with OIs (Figure 11).

Six studies showed that low adherence to ART was linked to an increased risk of OIs. Individuals with poor adherence to their ART regimen had a 2.32-fold higher risk (95% CI: 1.51–3.13) of contracting OIs compared to those who adhered well. Furthermore, the relationship between OIs and poor adherence to ART was found statistically significant (Figure 12).

3.5 | Heterogeneity, Publication Bias, and Sensitivity Analysis

Heterogeneity and publication bias were observed in the studies included in the analysis. There was a significant degree of

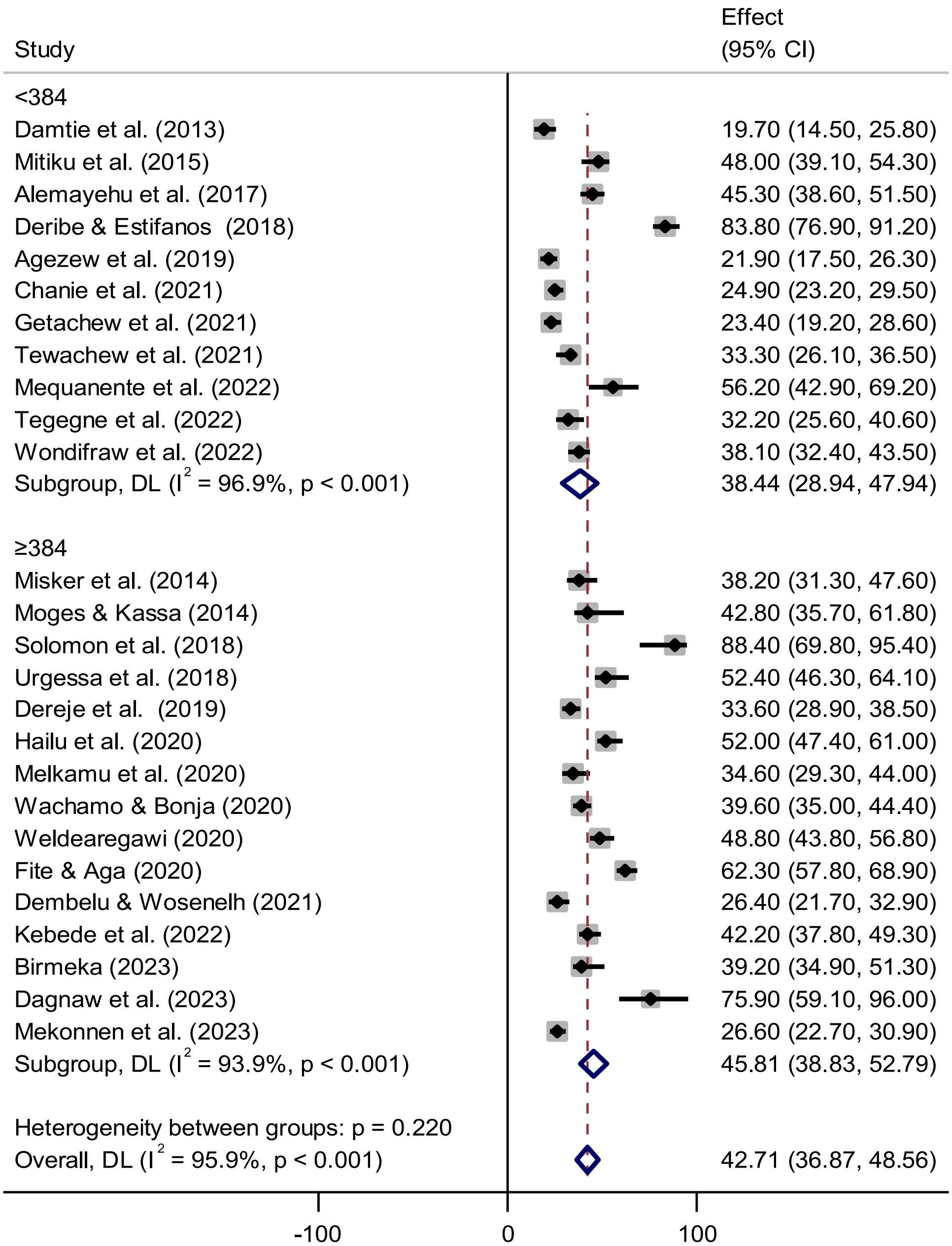

FIGURE 6 | Pooled prevalence of OIs by sample size among people with HIV in Ethiopia.

heterogeneity among the studies, with an I^2 value of 95.9% ($p < 0.001$). The funnel plot presented in Figure 13a showed a symmetrical distribution. Furtherore, the results from the Egger test (Figure 13b) and the Begg test (Figure 13c) indicated no significant evidence of publication bias ($p > 0.05$). A sensitivity analysis was also performed by sequentially excluding each study to assess the influence of individual studies on the overall effect size. This analysis revealed that four studies—Deribe & Estifanos, Agezew and colleagues, Fite & Aga, and Chanie and colleagues—significantly affected the overall prevalence of OIs among individuals living with HIV/AIDS in Ethiopia. The effect size estimates after the removal of each study were 34.82 (33.65–36.00), 37.16 (35.96–38.36), 34.91 (33.73–36.10), and 37.85 (36.61–39.10), corresponding to the studies of Deribe & Estifanos, Agezew and colleagues, Fite & Aga, and Chanie and colleagues. Upon the complete exclusion of these four studies, the overall estimate adjusted to 36.25 (34.89–37.61) (Figure 13d).

4 | Discussion

Opportunistic infections (OIs) are more prevalent and often more severe in individuals with compromised immune systems, such as PLHIV [59]. This meta-analysis sought to identify the prevalence and predictors of OIs among HIV-infected patients in Ethiopia. The studies revealed several factors associated with OIs, including baseline WHO stage II or higher, khat chewing, age, education level, a CD4 count below 200 cells per mm^3, and poor adherence to ART.

In this meta-analysis, the overall pooled prevalence of OIs was 42.71%. This finding is consistent with studies conducted in Taiwan (47.6%) [60], and Uganda (43%) [61]. However, this result is notably higher than the 22.4% prevalence reported in Nigeria [62] and the 27.4% found in New York City [63]. However, this finding is lower than the results of previous studies conducted in India (53.4%) [64],

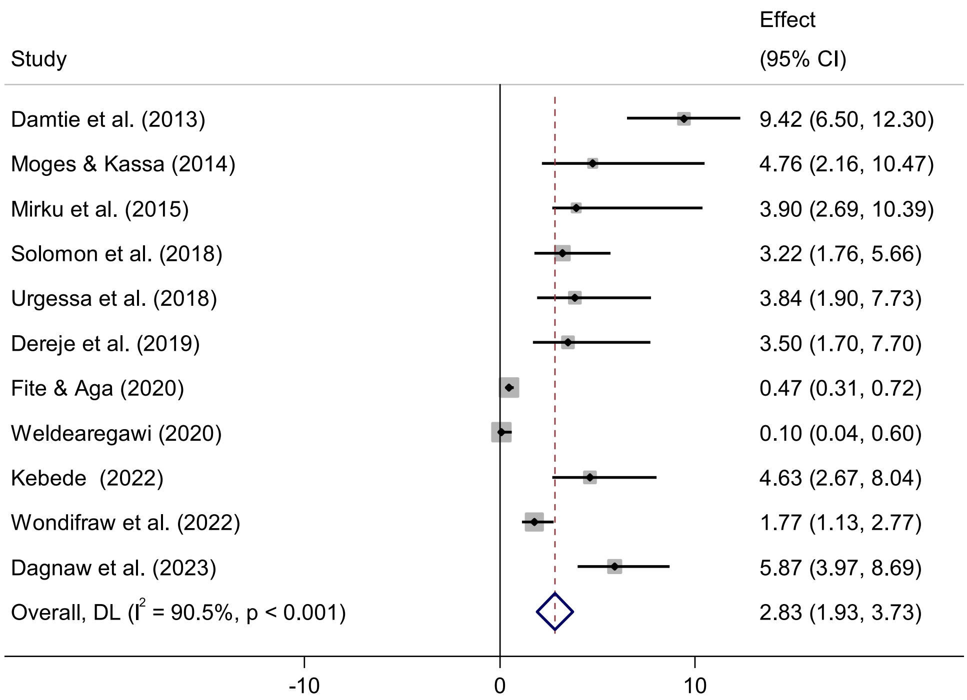

FIGURE 7 | Baseline WHO stage II and above as risk factor for OIs among people with HIV in Ethiopia.

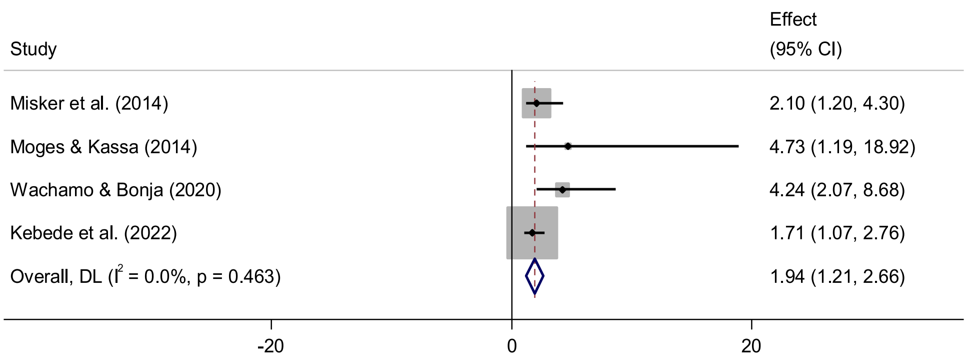

FIGURE 8 | Chewing khat as risk factor for OIs among people with HIV in Ethiopia.

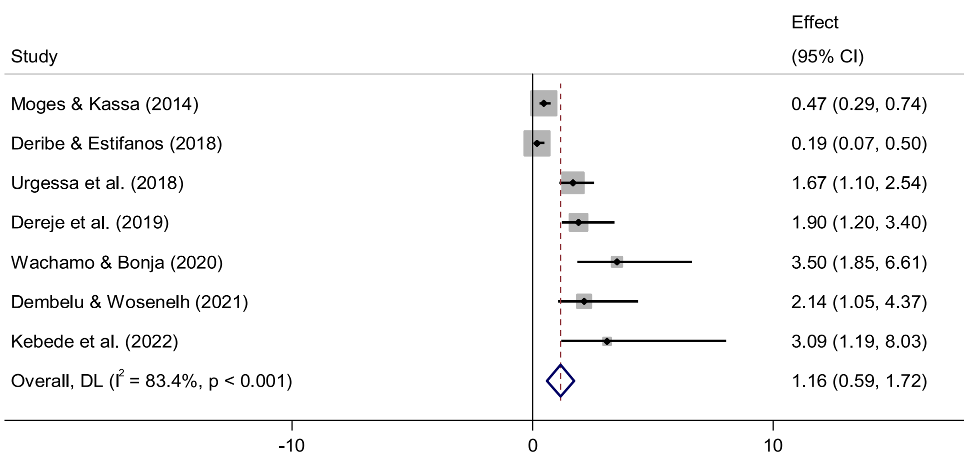

FIGURE 9 | Older age as risk factor for OIs among people with HIV in Ethiopia.

Nigeria (61.7%) [65], Bahir Dar (88.9%) [66] and Mekele (57.1%) [67]. This variation may be due to differences in CD4 position, differences in duration of HAART, differences in host immunity of study subjects, differences in methodology, and sample sizes.

Thus, to combat the high pooled prevalence of OIs among HIV/AIDS patients in Ethiopia, targeted healthcare policies and strategies are needed. These include improving ART access, strengthening screening and early detection, integrating preventive

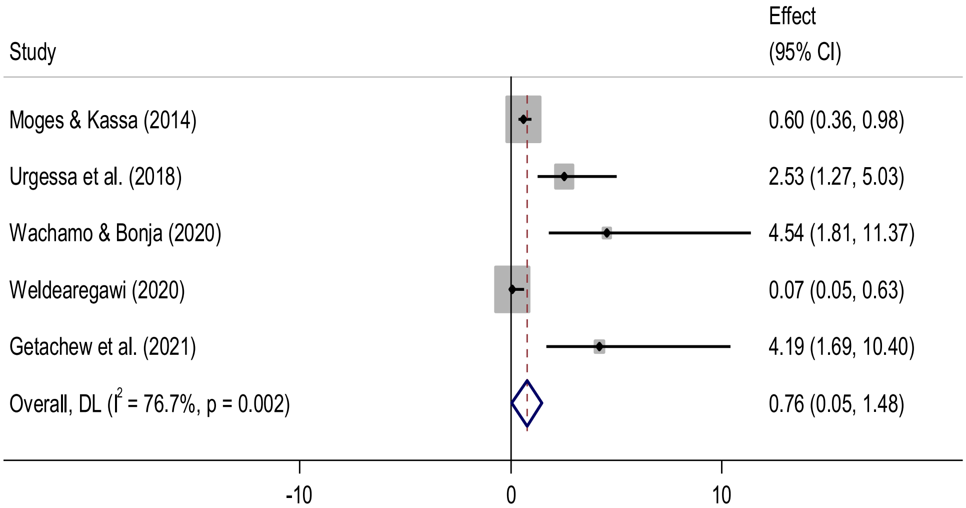

FIGURE 10 | Lower educational statuses as risk factor for OIs among people with HIV in Ethiopia.

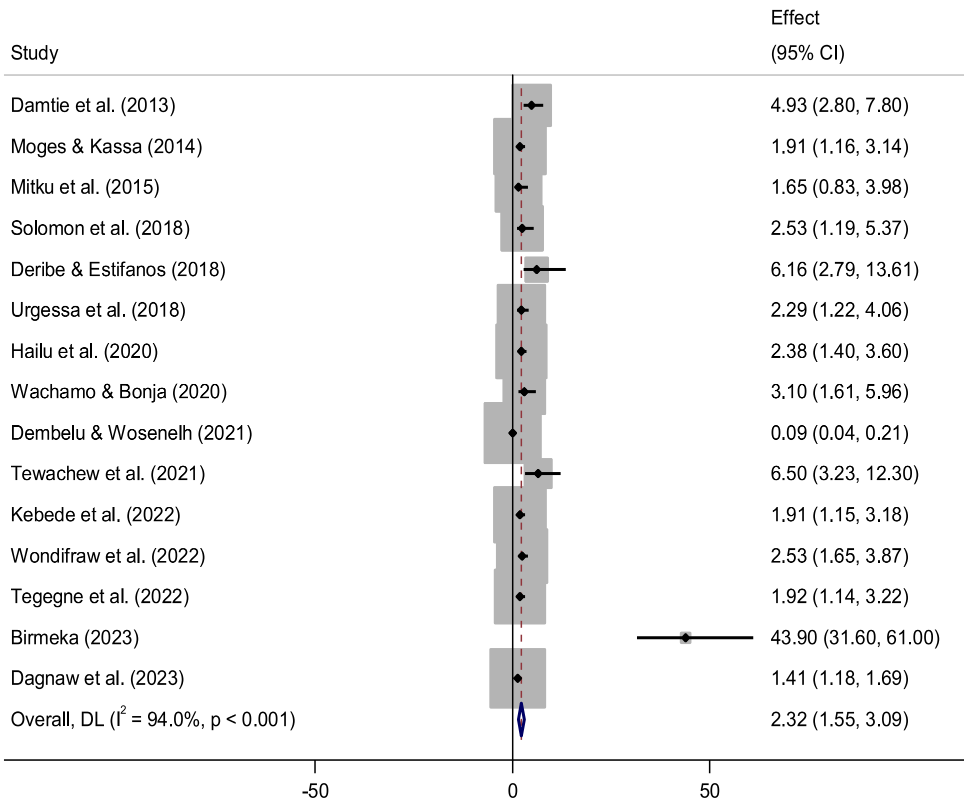

FIGURE 11 | Initial CD4 count less than 200 cells/mm^3 as risk factor for OIs among people with HIV in Ethiopia.

strategies, improving healthcare infrastructure, training healthcare providers, raising public awareness, enhancing laboratory services, promoting multidisciplinary care, supporting mental health services, strengthening data collection and research, and partnering with NGOs and community organizations. These strategies aim to improve treatment outcomes, reduce the risk of OIs, and ensure comprehensive care for HIV patients.

Regionally, the highest estimated pooled prevalence of OIs was reported in Addis Ababa, the capital city of Ethiopia, at 58.63%. This figure, however, is significantly lower than the 78.8% prevalence found in research conducted in Kenya [14]. The findings of this meta-analysis indicate that the New York City Department of Health and Mental Hygiene reports a higher prevalence of OIs among newly diagnosed adult AIDS cases than the previously stated figure of 27.4% [63]. The high prevalence of OIs in the area might be due to overcrowding of people and a lack of sanitation that can expose them to different infections. We suggest policy and healthcare practitioners to intervene OIs burden in urban areas like Addis Ababa. These include tailored programs, community-based approaches, integrated care models, resource allocation, data-driven decision-making, cross-regional collaboration, and public health education. These interventions should focus on strengthening healthcare

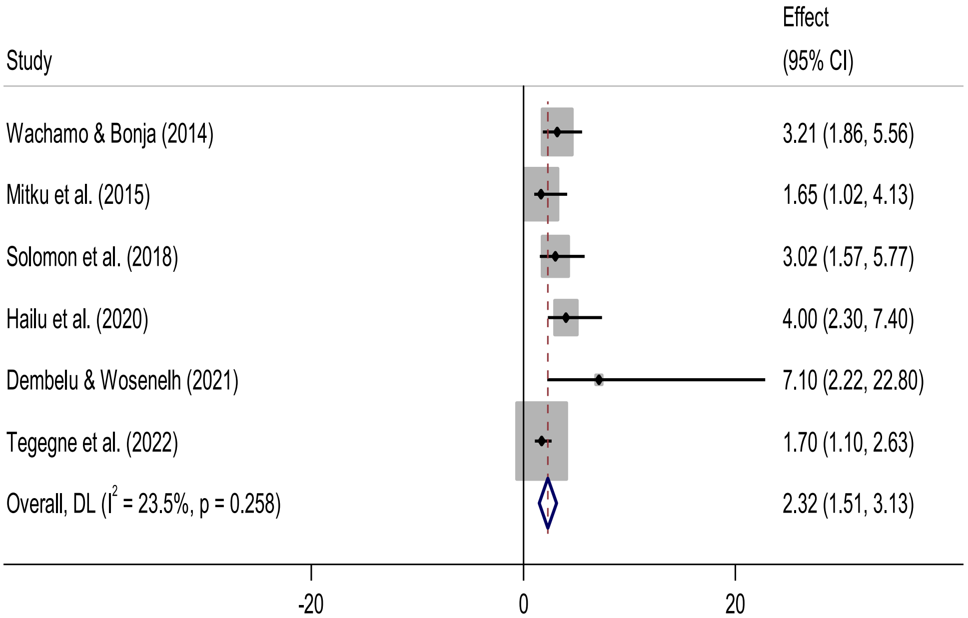

FIGURE 12 | Poor adherences to ART as risk factor for OIs among people with HIV in Ethiopia.

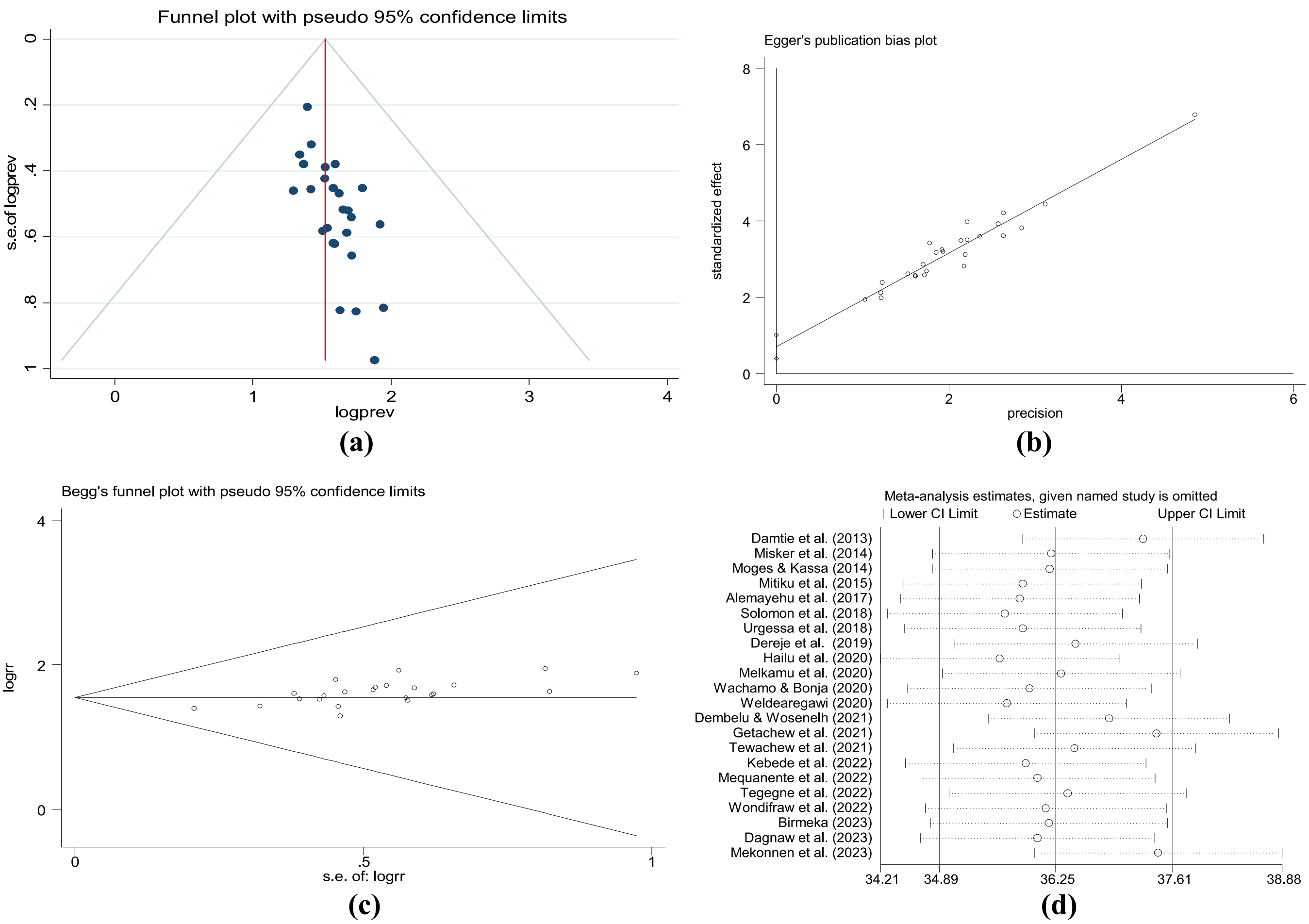

FIGURE 13 | (a) The funnel plot illustrates publication bias among the studies in this meta-analysis, (b) The Egger publication bias plot, (c) Begg's publication bias test, (d) Sensitivity analysis.

systems, leveraging successful models, and ensuring adequate funding for prevention and treatment programs.

The lowest prevalence of OI was observed in Amhara at 33.73% that can be attributed to factors such as access to healthcare services, quality of care, cultural practices, socioeconomic factors, education levels, and epidemiological factors. Rural areas may benefit from community-based healthcare initiatives, while urban areas may benefit from such initiatives. Strong community support and health education can also contribute to better health outcomes. Regional health initiatives targeting TB and other OIs may be more effective.

The largest estimated pooled prevalence for the study period was 52.13%, which was recorded between 2013 and 2018. But the study period that spanned 2019 and 2020 yielded a pooled prevalence estimate of 41.76%, and the study period that spanned 2021 and 2023 yielded the lowest prevalence, 35.32%. Similar findings were reported in Uganda, where the annual prevalence of OIs were 57.6% in 2004 and decreased to 27.5% in 2013 [68]. The decrease in prevalence of OIs from year to year is interpreted as possibly due to increased awareness and improved HIV management.

In this meta-analysis, the AOR of WHO baseline II and higher is linked to OIs; among HIV-positive individuals, it is 2.83 times more probable to develop OIs than for WHO baseline I. This result is consistent with studies conducted elsewhere [14, 65, 69, 70]. Given that the WHO staging is greater, further increasing the risk of OIs, this could be the result of decreased immunity. Most patients initiate treatment at an advanced stage of AIDS, which complicates the effectiveness of medication in reversing the condition.

In this study, patients with poor adherence to ART were found to have 2.32 times higher risk of experiencing OIs compared to their counterparts. This finding aligns with results from surveillance studies conducted in Ethiopia [71], Nigeria [65], and South Africa [72]. This can be attributed to the fact that poor adherence leads to a decline in CD4 count, which is directly associated with the development of OIs.

The current pooled systematic review and meta-analysis study revealed that individuals who chew khat while taking ART medications are 1.94 times more likely to develop OIs compared to those who do not use khat. This finding is in agreement with results from single surveillance study [52]. This may be attributed to several factors. Chewing khat can lead to malnutrition due to reduced appetite and may impair health-seeking behavior by providing a temporary sense of relief. Additionally, khat is often harvested in unsanitary conditions, exposing users to contaminants from environments with poor hygiene, such as areas with open defecation, which increases the risk of OIs. Furthermore, the habit of chewing khat can result in financial strain, as it requires significant time and money, potentially limiting access to nutritious food and other healthcare resources. These findings highlight the need for health officials and healthcare providers to implement targeted strategies to mitigate the risks and consequences of OIs among HIV-positive adults [45].

In this meta-analysis, the AOR for individuals with an initial CD4 count of less than 200 cells/mm^3 was 2.32 times higher in acquiring OIs than the counterparts. This outcome aligns with studies from Cape Town, South Africa [73] and Bangladesh [74] which indicated that OIs are more prevalent in patients with a baseline CD4 count of fewer than 200 cells/mm^3. Simultaneously, research from Asia [75], India [76], and Latin America [77, 78] revealed that low CD4 counts at the time of enrollment in ART significantly increased the chance of acquiring OIs. This could be attributed to the weakened immune response that predisposes individuals to OIs. Since CD4 cells play a crucial role in the body's cellular and hormonal immune responses to infections, this finding is consistent with the expected outcome. Thus, a low CD4 count may be due to an increased susceptibility to OIs.

5 | Limitation of the Study

A notable drawback of meta-analysis involving observational data is the impact of residual confounding. Additionally, another limitation of this review is that it included only publications and reports in English. Similarly, there is a lack of data to examine the prevalence of OIs among HIV-positive individuals by age and gender. Another limitation of this study is that the OIs from the included studies were not collected and reported as a subgroup analysis. The lack of regional diversity can also influence the interpretation of results, potentially skewing policy recommendations or practical applications.

6 | Conclusions

In Ethiopia, the overall prevalence of OIs among HIV-positive patients has decreased, from 52.13% in 2013–2018 to 35.32% in 2021–2023. In the current study, baseline WHO II and above, baseline CD4 count less than 20 cells/mm^3, khat chewing, and poor adherence to HAART were significantly associated with OIs among people with HIV. This study suggests that further research is needed to cover all regions of Ethiopia and explore the impact of age, gender, and other factors on OIs among HIV-positive individuals, in order to enhance our understanding of this complication and its management.

Author Contributions

Aleka Aemiro: conceptualization, methodology, data curation, resources, visualization, validation, investigation, writing–original draft. **Abayeneh Girma:** conceptualization, data curation, software, formal analysis, project administration, supervision, investigation, validation, visualization, writing–review and editing. **Demsew Beletew:** resources, writing–original draft, data curation, investigation, validation, visualization.

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The authors have nothing to report.

Ethics Statement

This article does not contain any studies with human participants or animals performed by any of the authors.

Consent

For this type of study consent for publication is not required.

Conflicts of Interest

The authors declare no conflicts of interest.

Data Availability Statement

The authors confirm that the data supporting the findings of this study are available within the article [and/or] its supplementary materials. The data that support the findings of this study are available from the corresponding author upon reasonable request.

Transparency Statement

The lead author Abayeneh Girma affirms that this manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned (and, if relevant, registered) have been explained.

References

1. P. Gona, R. B. Van Dyke, P. L. Williams, et al., "Incidence of Opportunistic and Other Infections in HIV-Infected Children in the HAART era," *Journal of the American Medical Association (Chicago, IL)* 296, no. 3 (2006): 292–300.

2. J. R. N. Nansseu and J. J. R. Bigna, "Antiretroviral Therapy Related Adverse Effects: Can Sub-Saharan Africa Cope With the New 'Test and Treat' Policy of the World Health Organization?," *Infectious Diseases of Poverty* 6 (2017): 1–5.

3. G. C. Cook and A. Zumla, *Manson's Tropical Diseases* (Elsevier Health Sciences, 2009).

4. R. P. Walensky, A. D. Paltiel, E. Losina, et al., "The Survival Benefits of AIDS Treatment in the United States," *Journal of Infectious Diseases* 194, no. 1 (2006): 11–19.

5. World Health Organization (WHO). HIV/AIDS Epidemiology, accessed 13 March, 2023, https://www.afro.who.int/health-topics/hivaids.

6. UNIAS: Global HIV and AIDS statistics 2019 fact sheet, accessed 11 March, 2023. https://www.unaids.org/en/resources/fact-sheet.

7. H. Global, *AIDS Statistics–2018 fact sheet* (Geneva: Joint United Nations Programme on HIV, AIDS, 2018).

8. W. H. Organization, *Annual Report of the Regional Director on the Work of WHO in the African Region, World Health Organization* (Regional Office for Africa, 2022).

9. A. a. h. f. u. o. e. m. u. c. d. f. F. e. p. UNAIDS (2014). Fact Sheet, accessed 10 March.

10. C. F. Kibwengo, T. K. Kabalimu, and E. E. Sungwa, "Opportunistic Infections and Associated Factors Among HIV Infected Patients on Anti-Retroviral Treatment at Bombo Hospital in Tanga Region, Tanzania," *African Journal of Health Sciences* 35, no. 3 (2022): 252–262.

11. A. K. Mohamud, O. A. Ahmed, A. A. Mohamud, and N. I. Dirie, "Magnitude of Opportunistic Infections and Associated Factors Among Adult People Living With Human Immune Deficient Virus on Art at Selected Public Hospital, Mogadishu Somalia: Cross-Sectional Study," *Annals of Medicine & Surgery* 85, no. 7 (2023): 3364–3371.

12. E. N. Tufon, A. D. Bih, and M. Alice, "Occurrence and Risk Factors for Opportunistic Infections in HIV Patients Attending the Bamenda Regional Hospital, Cameroon," *Prevalence* 118 (2014): 73.7.

13. A. Saidu, M. Bunza, U. Abubakar, T. Adamu, M. Ladan, and S. Fana, "A Survey of Opportunistic Infections in HIV Seropositive Patients Attending Major Hospitals of Kebbi State, Nigeria," *Bayero Journal of Pure and Applied Sciences* 2, no. 1 (2009): 70–74.

14. G. K Chepkondol, P. E Jolly, N. Yatich, O. Mbowe, and W. G Jaoko, "Types and Prevalence of HIV-Related Opportunistic Infections/Conditions Among HIV-Positive Patients Attending Kenyatta National Hospital in Nairobi, Kenya," *African Health Sciences* 20, no. 2 (2020): 615–624.

15. K. Ranganathan and K. M. R. Umadevi, "Common Oral Opportunistic Infections in Human Immunodeficiency Virus Infection/Acquired Immunodeficiency Syndrome: Changing Epidemiology; Diagnostic Criteria and Methods; Management Protocols," *Periodontology 2000* 80, no. 1 (2019): 177–188.

16. J. Alvar, P. Aparicio, A. Aseffa, et al., "The Relationship Between Leishmaniasis and Aids: The Second 10 Years," *Clinical Microbiology Reviews* 21, no. 2 (2008): 334–359.

17. I. Cruz, J. Nieto, J. Moreno, C. Cañavate, P. Desjeux, and J. Alvar, "Leishmania/HIV Co-Infections in the Second Decade," *Indian Journal of Medical Research* 123, no. 3 (2006): 357–388.

18. R. Lodge, M. Ouellet, C. Barat, G. Andreani, P. Kumar, and M. J. Tremblay, "HIV-1 Promotes Intake of Leishmania Parasites by Enhancing Phosphatidylserine-Mediated, CD91/LRP-1-Dependent Phagocytosis in Human Macrophages," *PLoS One* 7, no. 3 (2012): e32761.

19. L. M. Mofenson, M. T. Brady, S. P. Danner, et al., "Guidelines for the Prevention and Treatment of Opportunistic Infections Among HIV-Exposed and Hiv-Infected Children: Recommendations from CDC, the National Institutes of Health, the HIV Medicine Association of the Infectious Diseases Society of America, the Pediatric Infectious Diseases Society, and the American Academy of Pediatrics," *MMWR: Recommendations and Reports* 58, no. RR–11 (2009): 1–166.

20. S. A. Iacob, D. G. Iacob, and G. Jugulete, "Improving the Adherence to Antiretroviral Therapy, a Difficult but Essential Task for a Successful HIV Treatment—Clinical Points of View and Practical Considerations," *Frontiers in Pharmacology* 8 (2017): 831.

21. G. M. Belay, E. H. Engeda, and A. D. Ayele, "Late Antiretroviral Therapy Initiation and Associated Factors Among Children on Antiretroviral Therapy at University of Gondar Comprehensive Specialized Hospital, Gondar, Northwest Ethiopia: A Cross-Sectional Study," *BMC Research Notes* 12 (2019): 255.

22. R. E. Chaisson and R. D. Moore, "Prevention of Opportunistic Infections in the Era of Improved Antiretroviral Therapy," *Journal of Acquired Immune Deficiency Syndromes & Human Retrovirology* 16 (1997): S14–S22.

23. M. J. Glesby, D. R. Hoover, H. Farzadegan, J. B. Margolick, and A. J. Saah, "The Effect of Influenza Vaccination on Human Immunodeficiency Virus Type 1 Load: A Randomized, Double-Blind, Placebo-Controlled Study," *Journal of Infectious Diseases* 174, no. 6 (1996): 1332–1336.

24. Y. Berhane, Y. Mekonnen, E. Seyoum, L. Gelmon, and D. Wilson, "HIV/AIDS in Ethiopia: An Epidemiological Synthesis," in *Ethiopia HIV/AIDS Prevention & Control Office (HAPCO) and Global AIDS Monitoring & Evaluation Team (GAMET)*, 2008.

25. H. Ephi, "Related Estimates and Projections for Ethiopia–2017," Ethiopian Public Health Institute, 2017.

26. E. Kindie, Z. Alamrew Anteneh, and E. Worku, "Time to Development of Adverse Drug Reactions and Associated Factors Among Adult HIV Positive Patients on Antiretroviral Treatment in Bahir Dar City, Northwest Ethiopia," *PLoS One* 12, no. 12 (2017): e0189322.

27. N. Moges and G. Kassa, "Prevalence of Opportunistic Infections and Associated Factors Among Hiv Positive Patients Taking Anti-Retroviral Therapy in Debremarkos Referral Hospital, Northwest Ethiopia," *Journal of AIDS and Clinical Research* 5, no. 5 (2014): 1–300.

28. B. Z. Woldegeorgis, Z. Zekarias, B. G. Adem, M. S. Obsa, and A. A. Kerbo, "Prevalence and Determinants of Opportunistic Infections Among HIV-Infected Adults Receiving Antiretroviral Therapy in Ethiopia: A Systematic Review and Meta-Analysis," *Frontiers in Medicine* 10 (2023): 1087086.

29. A. Girma and A. Genet, "Magnitude and Determinants of Intestinal Parasites Among Children Under Five in Ethiopia During 2010–2023: A Systematic Review and Meta-Analysis," *Fetal and Pediatric Pathology* 43, no. 1 (2024): 47–65.

30. A. Genet and A. Girma, "Magnitude, Associated Risk Factors, and Trend Comparisons of Identified Tuberculosis Types Among Prisons in Ethiopia: A Systematic Review and Meta-Analysis," *Health Science Reports* 7, no. 1 (2024): e1789.

31. Worldometer. Current World Population, 2024. https://www.worldometers.info/world-population/ethiopia-population/.

32. D. Moher, A. Liberati, J. Tetzlaff, D. G. Altman, and PRISMA Group, "Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement," *Annals of Internal Medicine* 151, no. 4 (2009): 264–269.

33. D. Atkins, M. Eccles, S. Flottorp, et al., "Systems for Grading the Quality of Evidence and the Strength of Recommendations I: Critical Appraisal of Existing Approaches The GRADE Working Group," *BMC Health Services Research* 4 (2004): 1–7.

34. D. Damtie, G. Yismaw, D. Woldeyohannes, and B. Anagaw, "Common Opportunistic Infections and Their CD4 Cell Correlates Among HIV-Infected Patients Attending at Antiretroviral Therapy Clinic of Gondar University Hospital, Northwest Ethiopia," *BMC Research Notes* 6 (2013): 1–7.

35. D. M. Direslgne Misker, M. D. Meaza Demissie, and H. M. Habtamu Mellie, "Effect of Highly Active Antiretroviral Therapy on Incidence of Opportunistic Infections Among HIV Positive Adults in Public Health Facilities of Arba Minch Town, South Ethiopia: Retrospective Cohort Study," *Journal of AIDS and Clinical Research* 5 (2014): 1–6.

36. H. Mitiku, z Teklemariam, and F. Weldegebreal, "Magnitude of Opportunistic Infections and Associated Factors in HIV-Infected Adults on Antiretroviral Therapy in Eastern Ethiopia," *HIV/AIDS-Research and Palliative Care* 7 (2015): 137–144.

37. M. Alemayehu, Y. Yisehak, W. Alaro, and B. Alemayehu, "Opportunistic Infections Among HIV/AIDS Patients Taking Ante-Retroviral Therapy at Tertiary Care Hospital in Wolaita Zone, Southern Ethiopia," *Journal of AIDS and Clinical Research* 8, no. 2 (2017): 1–4.

38. A. Deribe and W. Estifanos, "Magnitude and Determinants of Opportunistic Infections Among HIV/AIDS Patients in Sphmmc, Addis Ababa, Ethiopia, Retrospective Study," *JOJ Public Health* 4 (2018): 555627.

39. F. B. Solomon, B. N. Angore, H. C. Koyra, E. G. Tufa, T. M. Berheto, and M. Admasu, "Spectrum of Opportunistic Infections and Associated Factors Among People Living With HIV/AIDS in the Era of Highly Active Anti-Retroviral Treatment in Dawro Zone Hospital: A Retrospective Study," *BMC Research Notes* 11 (2018): 1–7.

40. F. Urgessa, A. Ararsa, and Z. Ataro, "Prevalence and Associated Risk Factors of Opportunistic Infections Among Anti-Retro Viral Treatment Naive HIV/AIDS Infected Patients," *Journal of AIDS and Clinical Research* 09, no. 03 (2018): 1000763.

41. T. Agezew, A. Tadesse, L. Derseh, M. Yimer, and G. Fetene, "Magnitude and Predictor Factors of Opportunistic Infections Among Adult Treatment Users at Universty of Gondar, 2019," 2022.

42. N. Dereje, K. Moges, Y. Nigatu, and R. Holland, "Prevalence and Predictors of Opportunistic Infections Among HIV Positive Adults on Antiretroviral Therapy (On-ART) Versus Pre-ART In Addis Ababa, Ethiopia: A Comparative Cross-Sectional Study," *HIV/AIDS-Research and Palliative Care* 11 (2019): 229–237.

43. T. Hailu, H. Hagos, K. Gemechu, H. Tesfay, and B. Tadesse, "Prevalence of Opportunistic Infections and Associated Factors Among HIV-Infected Patients on Antiretroviral Therapy in Eastern Zone of Tigray, Ethiopia: A Cross-sectional Study," *Journal of AIDS and Clinical Research* (2020), https://doi.org/10.21203/rs.3.rs-52785/v1.

44. M. W. Melkamu, M. T. Gebeyehu, A. D. Afenigus, et al., "Incidence of Common Opportunistic Infections Among HIV-Infected Children on ART at Debre Markos Referral Hospital, Northwest Ethiopia: A Retrospective Cohort Study," *BMC Infectious Diseases* 20 (2020): 1–12.

45. D. Wachamo and F. Bonja, "Magnitude of Opportunistic Infections and Associated Factors Among HIV-Positive Adults on ART at Selected Public Hospitals in Sidama National Regional State, Southern Ethiopia," *HIV/AIDS-Research and Palliative Care* 12 (2020): 479–487.

46. T. Z. Weldearegawi, H. Gerensea, H. Berihu, G. Gidey, and M. Z. Welearegay, "The Magnitude of Opportunistic Infections and Associated Factors in HIV-Infected Adults on Antiretroviral Therapy in Southern Zone Tigray, Ethiopia: A Cross-Sectional Study," *Pan African Medical Journal* 35, no. 1 (2020): 126.

47. M. B. Fite and D. J. Aga, "Spectrum of Opportunistic Disease and Associated Factors Among Patients Attending ART Clinic, Nekemte Specialized Hospital, Western Ethiopia," *bioRxiv* (2020), https://doi.org/10.1101/2020.10.06.327668.

48. E. S. Chanie, W. A. Bayih, B. M. Birhan, et al., "Incidence of Advanced Opportunistic Infection and Its Predictors Among HIV Infected Children at Debre Tabor Referral Hospital and University of Gondar Compressive Specialized Hospitals, Northwest Ethiopia, 2020: A Multicenter Retrospective Follow-Up Study," *Heliyon* 7, no. 4 (2021): e06745.

49. M. Dembelu, M. Kote, G. Gilano, and T. Mohammed, "Incidence and Predictors of Reoccurrence of Opportunistic Infection Among Adult HIV/AIDS Patients Attending ART Clinic at Public Health Facilities in Arba Minch Town, Southern Ethiopia: A Retrospective Cohort Study," *PLoS One* 16, no. 12 (2021): e0261454.

50. T. Getachew, T. Hailu, and M. Alemu, "Prevalence of Opportunistic Intestinal Parasitic Infections Among HIV/AIDS Patients Before and After Commencement of Antiretroviral Treatment at Felege Hiwot Referral Hospital: A Follow-Up Study," *HIV/AIDS-Research and Palliative Care* 13 (2021): 767–774.

51. A. S. Tewachew, W. N. Mekonnen, A. D. Mekuria, and Y. E. Amare, "Determinants of Opportunistic Infections Among HIV-Positive Patients on HAART in Debre Berhan Referral Hospital, North Shoa Zone, Ethiopia, 2020: A Case–Control Study," *HIV/AIDS-Research and Palliative Care* 13 (2021): 337–347.

52. N. Kebede, T. Ambaye, and G. W. Bazie, "Opportunistic Infections and Associated Factors Among HIV-Infected Adults on Antiretroviral Therapy Attending Health Facilities in North Wollo, Ethiopia," 2023.

53. D. A. Mequanente, P. Srinivasan, G. Mallika, P. M. T. Ansari, and M. Wale, "Incidence of Opportunistic Infections Among HIV-Infected Children on ART at Gondar University Specialized Hospital, Ethiopia," *Indian Journal of Science and Technology* 15, no. 34 (2022): 1675–1682.

54. K. Dagnaw Tegegne, N. Cherie, F. Tadese, L. Tilahun, M. W. Kassaw, and G. Biset, "Incidence and Predictors of Opportunistic Infections Among Adult HIV Infected Patients on Anti-Retroviral Therapy at Dessie Comprehensive Specialized Hospital, Ethiopia: A Retrospective Follow-Up Study," *HIV/AIDS-Research and Palliative Care* 14 (2022): 195–206.

55. E. B. Wondifraw, B. D. Tefera, M. Zeleke, S. Nebyu, L. Tilahun, and Z. Tefera, "Incidence and Predictors of Common Opportunistic Infection Among HIV-Infected Children Attending Antiretroviral Treatment Clinic at Northeast Ethiopia, Public Hospitals 2022: A Multicenter Retrospective Follow-Up Study," *Annals of Medicine and Surgery* 84 (2022): 104910.

56. M. Birmeka, "Distribution Pattern and Prevalence of Opportunistic Infections and Their Possible Reciprocal Effects Among HIV Patients, Burayu Health Centers, Ethiopia," *Journal of Infection in Developing Countries* 17, no. 07 (2023): 1022–1029.

57. M. Dagnaw, H. Fekadu, A. Gebre Egziabher, T. Yesfue, M. Indracanti, and A. Tebeje, "Incidence of Opportunistic Infections and Its Predictors Among HIV/AIDS Patients on Antiretroviral Therapy in Gondar University Comprehensive and Specialized Hospital, Ethiopia," *HIV Research & Clinical Practice* 24, no. 1 (2023): 2187013.

58. G. B. Mekonnen, B. M. Birhane, M. T. Engdaw, W. Kindie, A. D. Ayele, and A. Wondim, "Predictors of a High Incidence of Opportunistic Infections Among HIV-Infected Children Receiving Antiretroviral Therapy at Amhara Regional State Comprehensive Specialized Hospitals, Ethiopia: A Multicenter Institution-Based Retrospective Follow-Up Study," *Frontiers in Pediatrics* 11 (2023): 1107321.

59. H. Masur, J. T. Brooks, C. A. Benson, K. K. Holmes, A. K. Pau, and J. E. Kaplan, "Prevention and Treatment of Opportunistic Infections in HIV-Infected Adults and Adolescents: Updated Guidelines From the Centers for Disease Control and Prevention, National Institutes of Health, and HIV Medicine Association of the Infectious Diseases Society of America," *Clinical Infectious Diseases* 58, no. 9 (2014): 1308–1311.

60. H.-Y. Sun, M.-Y. Chen, S.-M. Hsieh, et al., "Changes in the Clinical Spectrum of Opportunistic Illnesses in Persons With HIV Infection in Taiwan in the Era of Highly Active Antiretroviral Therapy," *Japanese Journal of Infectious Diseases* 59, no. 5 (2006): 311–316.

61. J. Rubaihayo, N. M. Tumwesigye, and J. Konde-Lule, "Trends in Prevalence of Selected Opportunistic Infections Associated With HIV/AIDS in Uganda," *BMC Infectious Diseases* 15 (2015): 1–15.

62. A. Ayyagari, A. Sharma, K. Prasad, T. Dhole, J. Kishore, and G. Chaudhary, "Spectrum of Opportunistic Infections in HIV Infected Cases in a Tertiary Care Hospital," *Indian Journal of Medical Microbiology* 17 (1999): 78–80.

63. D. B. Hanna, L. S. Gupta, L. E. Jones, D. M. Thompson, S. E. Kellerman, and J. E. Sackoff, "AIDS-Defining Opportunistic Illnesses in the HAART era in New York City," *AIDS Care* 19, no. 2 (2007): 264–272.

64. K. Saha, R. Firdaus, P. Santra, et al., "Recent Pattern of Co-Infection Amongst HIV Seropositive Individuals in Tertiary Care Hospital, Kolkata," *Virology Journal* 8 (2011): 116.

65. M. O. Iroezindu, E. O. Ofondu, H. Hausler, and B. V. Wyk, "Prevalence and Risk Factors for Opportunistic Infections in HIV Patients Receiving Antiretroviral Therapy in a Resource-Limited Setting in Nigeria," 2013.

66. B. Abera, F. Walle, T. Tewabe, A. Alem, and M. Yessin, "ART-Naive HIV Patients at Feleg-Hiwot Referral Hospital Northwest, Ethiopia," *Ethiopian Journal of Health Development* 24, no. 1 (2010): 62939.

67. Z. G. Arefaine, S. Abebe, E. Bekele, et al., "Incidence and Predictors of HIV Related Opportunistic Infections After Initiation of Highly Active Antiretroviral Therapy at Ayder Referral Hospital, Mekelle, Ethiopia: A Retrospective Single Centered Cohort Study," *PLoS One* 15, no. 4 (2020): e0229757.

68. J. Rubaihayo, N. M. Tumwesigye, J. Konde-Lule, and F. Makumbi, "Forecast Analysis of Any Opportunistic Infection Among HIV Positive Individuals on Antiretroviral Therapy in Uganda," *BMC Public Health* 16 (2016): 766.

69. P. Indira, P. M. Kumar, S. Shalini, and K. Vaman, "Opportunistic Infections Among People Living With HIV (PLHIV) With Diabetes Mellitus (DM) Attending a Tertiary Care Hospital in Coastal City of South India," *PLoS One* 10, no. 8 (2015): e0136280.

70. M. Badri, D. Wilson, and R. Wood, "Effect of Highly Active Antiretroviral Therapy on Incidence of Tuberculosis in South Africa: A Cohort Study," *Lancet* 359, no. 9323 (2002): 2059–2064.

71. M. Dalbo, and A. Tamiso, "Incidence and Predictors of Tuberculosis Among HIV/AIDS Infected Patients: A Five-Year Retrospective Follow-up Study," *Advances in Infectious Diseases* 6, no. 2 (2016): 70.

72. S. D. Lawn, L. Myer, R. Wood, L.-G. Bekker, and R. Wood, "Burden of Tuberculosis in an Antiretroviral Treatment Programme in Sub-Saharan Africa: Impact on Treatment Outcomes and Implications for Tuberculosis Control," *Aids* 20, no. 12 (2006): 1605–1612.

73. C. B. Holmes, R. Wood, M. Badri, et al., "CD4 Decline and Incidence of Opportunistic Infections in Cape Town, South Africa: Implications for Prophylaxis and Treatment," *JAIDS Journal of Acquired Immune Deficiency Syndromes* 42, no. 4 (2006): 464–469.

74. R. Noor, M. Morsalin, and B. Chakraborty, "Reduction of CD4 Count Induces Opportunistic Infections in People Living With HIV (PLHIV)," *Bangladesh Journal of Medical Science* 13, no. 3 (2014): 285–291.

75. W. Prasitsuebsai, A. Kariminia, T. Puthanakit, et al., "Impact of Antiretroviral Therapy on Opportunistic Infections of HIV-Infected Children in the Therapeutic Research, Education and AIDS Training Asia Pediatric HIV Observational Database," *Pediatric Infectious Disease Journal* 33, no. 7 (2014): 747–752.

76. N. Ylitalo, S. Brogly, M. D. Hughes, et al., Pediatric AIDS Clincial Trials Group Protocol, "Risk Factors for Opportunistic Illnesses in Children With Human Immunodeficiency Virus in the Era of Highly Active Antiretroviral Therapy," *Archives of Pediatrics & Adolescent Medicine* 160, no. 8 (2006): 778–787.

77. S. R. Nesheim, B. G. Kapogiannis, M. M. Soe, et al., "Trends in Opportunistic Infections in the Pre–and Post–Highly Active Antiretroviral Therapy Eras Among HIV-Infected Children in the Perinatal AIDS Collaborative Transmission Study, 1986–2004," *Pediatrics* 120, no. 1 (2007): 100–109.

78. M. Borle and Y. Sunkoj, "Opportunistic Infection Among HIV Infected Children and Their CD4 Cell Correlates," *IOSR Journal of Dental and Medical Sciences* 15, no. 3 (2016): 584.