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Meta-analysis

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Factors Affecting Mortality in People Living with HIV with Antiretroviral Therapy: A Meta-Analysis

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ABSTRACT

Background: TB is the leading cause of death among people living with HIV. In 2020, an estimated 214,000 people living with HIV died from TB. People with AIDS have a severely damaged immune system. They are increasingly suffering from severe diseases, called opportunistic infections (OI). This study aims to analyze and estimate the influence of gender, TB Coinfection, Opportunistic Infection on mortality in ODHIV with Antiretroviral Therapy.
Subjects and Method: Systematic review and meta-analysis using PRISMA flowchart and the PICO model. Population: ODHIV with ART. Intervention: Women, Co-infected TB, Opportunistic Infections. Comparison: Male, no co-infected TB, no Opportunistic Infection. Outcome: Mortality Article search using Google Scholar, PubMed and Science Direct databases. The keywods used include "HAART" or "HIV" or "HIV/AIDS" and "Gender" and "TB Coinfections" or "TB" and "Opportunistic Infections" and "Mortality" and "Antiretroviral Treatment". The 17 included articles are fulltext in English with a cohort design study from 2008 to 2023 and report on the Hazard Ratio in a multivariate analysis. Data analysis using the RevMan 5.3 application.
Results: A total of 17 cohort studies involving 23,651 research subjects from Vietnam, China, Japan, Ethiopia, and South Africa. The data collected showed that female ODHIV had a mortality risk of 0.7 times compared to male ODHIV (aHR= 0.70; CI 95%=0.60 to 0.79; p<0.001). In ODHIV with coinfected TB has a mortality risk of 1.86 times compared to ODHIV without coinfected TB (aHR= 1.89; CI 95%=1.36 to 2.61; p<0.001). ODHIV with Opportunistic Infection has a 1.90-fold risk of mortality compared to ODHIV without Opportunistic Infection (aHR= 1.90; CI 95%=1.50 to 2.42; p<0.001).
Conclusion: Female gender decreases the risk of mortality, while TB coinfection and Opportunistic infection increase the risk of mortality in ODHIV with Antiretroviral Therapy.

Keywords: HIV, ART, TB co-infection, opertunistic infection, mortality

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BACKGROUND

An estimated 39 million (33.1–45.7 million) people were living with HIV by the end of 2022. In 2022, a total of 630,000 (480,000 to 880,000) people died from HIV-related diseases globally. The global HIV epidemic

claimed 69% more lives in 2022 since its peak in 2004. HIV continues to be a major global public health problem, claiming 40.4 million (32.9–51.3 million) lives so far. Globally, 29.8 million people living with HIV receive antiretroviral therapy. Of the total number of people living with HIV in 2022, 86% (73–98) were aware of their status, 76% (65–89%) received treatment and 71% (60–83%) had successfully suppressed viral load (UNAIDS, 2023).

In most countries in the world, such as the United States, gay and bisexual men are the largest populations infected with HIV. According to data from the Centers for Disease Control and Prevention (CDC), gay, bisexual adults and adolescents who have sex with men report that male sex accounts for 71% of new HIV cases in the world (CDC, 2021b).

Every day, more than 4,100 people die from tuberculosis (TB) and nearly 30,000 people fall ill from TB disease, although the disease is preventable and treatable. TB can attack anyone and anywhere. However, the chances of developing TB disease are 18 times higher in people living with HIV. Everyone living with HIV should get TB preventive treatment. Nearly 7.5 million people living with HIV received TB preventive treatment in 2018-2020, surpassing the global target of 6 million in 2018 and 2022 previously. TB is the leading cause of death among people living with HIV and accounts for about a third of AIDS-related deaths globally. In 2020, an estimated 214,000 people living with HIV died from TB. TB is one of the single predictors of HIV exacerbation (Damtew, 2015). The global target to reduce TB deaths in people with HIV by 75% by 2020 has only been reached 62% (UNAIDS, 2022).

Opportunistic infection (OI) is a disease that causes infection in individuals with weakened immune systems, especially in people with Human Immunodeficiency Virus (ODHIV). Everyone living with HIV is susceptible to various forms of OI, although the prevalence and incidence of HIV-related OI vary widely. Despite advances in HIV diagnosis and treatment, opportunistic infections (OIs) remain a significant leading cause of illness and death among HIV/AIDS patients in low- and middle-income countries. OI is classified according to its severity as WHO clinical stage I to IV. More severe infections are thought to be associated with a poor disease prognosis, and their severity depends on the condition of pathogen exposure, pathogen virulence, and immune system status (Sutini., et al, 2022). HIV weakens the immune system and causes the risk of developing opportunistic infections that can accelerate the development and transmission of HIV. The most frequent occurrence of OI differs between low-income countries. Common OIs include: Candidiasis, Cervical Cancer, Sarcoma, Pneumocystis Pneumonia (PCP), and Coccidioidomycosis (CDC, 2021a).

This study aims to analyze and estimate the influence of gender, TB Coinfection, and Opportunistic Infection on mortality in ODHIV with Antiretroviral Therapy.

SUBJECTS AND METHOD

1. Study Design

This study is a systematic review and meta-analysis study. Article searches are collected from Google Scholar, PubMed and Science Direct. The keywords used are "HIV" AND "ART" AND "TB Co-Infection" AND "Opportunistic Infection" AND "Mortality" OR "death" AND "Cohort" AND "aHR". There were 17 primary studies that met the inclusion criteria of this study.

2. Step of Meta-Analysis

Meta-analysis is carried out in 5 stages as follows:

1) Formulate research questions using the PICO model (Population, Intervention, Comparison, Outcomes).
2) Searching for articles on electronic databases used includes Google Scholar, PubMed, and ScienceDirect.
3) Conducting screening and assessing primary studies using the critical assessment checklist for cross-sectional studies.
4) Extract data and incorporate the effect size of each major study into the RevMan 5.3 application
5) Interpreting results and concluding.

3. Inclusion Criteria

Full paper articles use a kohor design. The analysis used is multivariate with Adjusted Hazards Ratio (aHR). The study subjects were people with HIV on ARV therapy. The research interventions were gender, TB, opportunistic infections. The result of the research was death. And the exclusion criteria are non-English language articles and articles published before 2008.

4. Exclusion Criteria

The exclusion criteria in this study are RCT (randomized controlled trials) studies, quasi-experiments, research protocols, preliminary studies, and non-full text articles.

5. Operational Definition of Variable

Mortality: The permanent disappearance of all signs of life, which can occur at any time after a living birth

Gender: Socially constructed characteristics of women, men, girls, and boys. It includes the norms, behaviors, and roles associated with the existence of a woman, man, woman, or man, as well as their influence on each other.

Co-infection TB: A disease caused by infection with the bacterium Mycobacterium tuberculosis, which a person suffers while experiencing other infections at the same time.

Opportunistic Infections: The more common and more severe disease in people with HIV has a severely damaged immune system (other than TB)

6. Study Instruments

The assessment of the quality of the main article in this study uses a checklist of critical appraisal assessment of cohort studies for meta-analysis research (Murti, 2023).

7. Data Analysis

The articles in this study were collected using PRISMA diagrams and analyzed using the Review Manager 5.3 application by calculating the effect size and heterogenity (I^2) of the selected research results. The results of data analysis are presented in the form of forest plots and funnel plots.

RESULTS

The process of searching for primary articles involved exploring studies that focused on the influence of gender, TB coinfection, and opportunistic infections on mortality in individuals living with HIV (ODHIV) who were undergoing Antiretroviral Therapy (ART). This comprehensive meta-analysis was conducted by systematically searching four widely recognized journal databases, including PubMed, Google Scholar, ScienceDirect, and other relevant repositories. Through this rigorous process, a total of 17 relevant articles were identified. The review process for these articles, following established systematic review protocols, is illustrated in Figure 1, which presents the PRISMA Diagram summarizing the selection steps. These 17 articles encompass a diverse geographical range, with studies conducted across both the African and Asian continents, as highlighted in Figure 2.

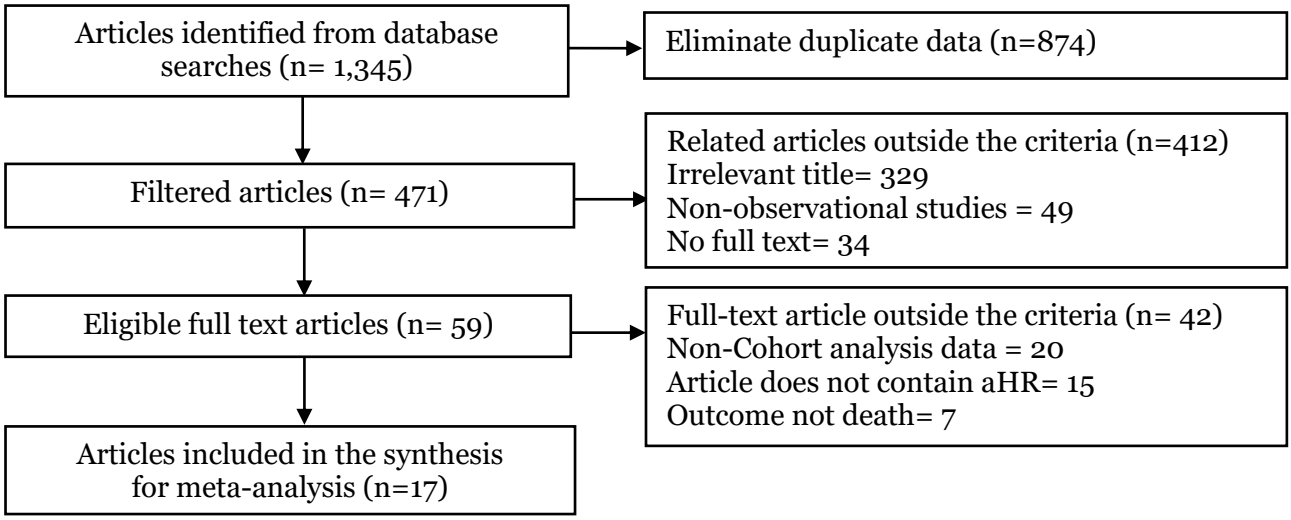

Figure 1. PRISMA flowchart article factors affecting mortality in people living with HIV with antiretroviral therapy

Figure 2. Location map of research factors affecting mortality in people living with HIV with antiretroviral therapy

Table 1. Critical appraisal for cohort study of the effect of condom use, anal bleeding, and group sex on the risk of HIV infection in men sexually engaged

Authors (Year)	Criteria														Total
	1a	1b	1c	1d	2a	2b	3a	3b	4a	4b	5	6a	6b	7	
Aemro et al. (2021)	2	2	2	2	2	2	2	1	2	2	1	2	2	1	25
Andarge et al. (2022)	2	2	2	2	2	2	2	1	2	2	2	2	2	2	27
Chen et al. (2022)	2	2	2	2	0	2	2	1	2	2	2	2	2	1	24
Cuong et al. (2012)	2	2	2	2	2	2	2	1	1	2	2	2	2	1	25
Damteu et al. (2015)	2	2	2	2	2	2	2	2	2	2	2	2	2	0	26
Fekade et al. (2017)	2	2	2	2	2	1	2	1	1	2	2	2	2	2	25
Girma et al. (2022)	2	2	2	2	2	0	2	2	2	2	2	2	2	0	24
Nigussie et al. (2020)	2	2	2	2	0	2	2	2	2	2	2	2	2	0	24

Authors (Year)	Criteria														Total
	1a	1b	1c	1d	2a	2b	3a	3b	4a	4b	5	6a	6b	7	
Nishijima et al. (2020)	2	2	2	2	2	2	2	2	2	2	2	2	2	2	28
Niu et al. (2023)	2	2	2	2	0	2	2	2	2	2	2	2	2	1	25
Ojikutu et al. (2008)	2	2	2	2	2	1	2	2	1	2	2	2	2	1	25
Setegn et al. (2015)	2	2	2	2	2	2	2	1	2	2	2	2	2	2	26
Seyoum et al. (2017)	2	2	2	2	2	0	2	2	2	2	2	2	2	0	24
Siraj et al. (2022)	2	2	2	2	0	2	2	1	2	2	2	2	2	1	24
Tachbele et al. (2016)	2	2	2	2	2	2	2	2	2	2	1	2	2	1	26
Tadesse et al., (2024)	2	2	2	2	0	2	2	2	1	2	2	2	2	1	24
Teshale et al., (2022)	2	2	2	2	2	2	2	1	2	2	1	2	2	1	25

Description of the question criteria:

1. Formulation of research questions in the acronym PICO.

a. Is the population in the primary study the same as the population in the PICO meta-analysis?

b. Is the operational definition of exposure/ intervention in the primary study the same as the definition intended in the meta-analysis?

c. Are the comparisons used in the primary study the same as those planned in the meta-analysis?

d. Are the outcome variables studied in the primary study the same as those planned in the meta-analysis?

2. Methods for selecting research subjects.

a. Descriptive cohort studies (prevalence): Were the samples randomly selected?

b. Cohort analytical studies: Are the samples randomly selected or purposive?

3. Methods for measuring interventions and outcome variables

a. Are exposures/interventions and outcome variables measured with the same instruments in all primary studies?

b. If the variables are measured on a categorical scale, are the cutoffs or categorical used the same between primary studies?

4. Design-related bias

a. What is the Response Rate?

b. Is non-response related to outcome?

5. Methods to control confounding

a. Is there any confusion in the results/ conclusions of the primary study?

b. Have primary studyused the right methods to control the effects of confusion?

6. Statistical analysis methods

a. In cohort studies, is a multivariate analysis performed? Multivariate analysis includes multiple linear regression analysis, multiple logistic regression analysis, and Cox regression analysis.

b. Do primary studies report effect measures or relationships of multivariate analysis outcomes? (for example, adjusted OR, adjusted regression coefficient).

7. Conflict of Interest

a. Is there a conflict of interest with the research sponsor?

b. If there is a conflict of interest, give it a value of "0".

c. If there is no conflict of interest, give it a grade of "2".

d. When in doubt, give it a "1".

The assessment instructions:

1. The total answer score for each question is "2".
2. If in one question all answer items are "Yes", then give a score of "2" to the question.
3. If there is one item in one question whose answer is "No", then give the question a score of "1".
4. If in one question all the answer items are "No", then give the question a score of "0".
5. If the total score = 14 then the primary study can be used in the meta-analysis.

6. If the total score is <14 then the primary study cannot be used in the meta-analysis

Table 4. PICO cohort study articles on gender influence, TB Coinfection and Opportunistic Infection with mortality in ODHIV with Antiretroviral Therapy with sample number (n=23,651)

Author (year)	Country	Sample	P	I	C	O
Andarge et al. (2022)	Ethiopia	323	ODHIV with ART	Women, Co-Infected TB, Opportunistic Infections	Male, without Co-Infected TB, and without Opportunistic Infection	Mortality
Chen et al. (2022)	China	5,557	PLHIV/AIDS on ART	PLHIV/AIDS on ART	Male	Mortality
Cuong et al. (2012)	Vietnam	640	PLHIV on ART	PLHIV on ART	Male, without TB co-infection, and without opportunistic infections	Mortality
Fekade et al. (2017)	Ethiopia	594	PLHIV adults on ART	PLHIV adults on ART	Male	Mortality
Girma et al. (2022)	Ethiopia	419	PLHIV on ART	PLHIV on ART	Male	Mortality
Nishijima et al. (2020)	Japan	165	PLHIV adults on HAART	PLHIV adults on HAART	Male	Mortality
Niu et al. (2023)	China	11,468	Adult HIV patients on ART	Adult HIV patients on ART	Male, without TB co-infection, and without opportunistic infections	Mortality
Setegn et al. (2015)	Ethiopia	120	PLHIV on ART	PLHIV on ART	Male, without TB co-infection, and without opportunistic infections	Mortality
Seyoum et al. (2017)	Ethiopia	456	PLHIV on ART	PLHIV on ART	Male, and without TB co-infection	Mortality
Tadesse et al. (2014)	Ethiopia	520	PLHIV adults on HAART	PLHIV adults on HAART	Male and without opportunistic infections	Mortality
Teshale et al. (2022)	Ethiopia	475	Adult HIV patients on ART	Adult HIV patients on ART	No TB co-infection	Mortality
Aemro et al. (2021)	Ethiopia	514	PLHIV on ART	PLHIV on ART	No TB co-infection	Mortality
Damtew et al. (2015)	Ethiopia	784	PLHIV on ART	PLHIV on ART	No TB co-infection and no opportunistic infections	Mortality
Nigussie et al., (2020)	Ethiopia	447	PLHIV on ART	PLHIV on ART	No TB co-infection	Mortality
Tachbele et al (2016)	Ethiopia	350	PLHIV/AIDS on ART	PLHIV/AIDS on ART	No opportunistic infections	Mortality
Ojikutu et al. (2008)	South Africa	309	PLHIV on ART	PLHIV on ART	No opportunistic infections	Mortality
Siraj et al. (2022)	Ethiopia	510	PLHIV on ART	PLHIV on ART	Male	Mortality
Andarge et al. (2022)	Ethiopia	323	ODHIV with ART	Women, Co-Infected TB, Opportunistic Infections	Male, without Co-Infected TB, and without opportunistic Infection	Mortality
Chen et al. (2022)	China	5,557	PLHIV/AIDS on ART	PLHIV/AIDS on ART	Male	Mortality

Table 3. Data on adjusted hazard ratio (aHR) and 95% (95% CI) confidence interval of gender effect on mortality in ODHIV with antiretroviral therapy with sample size (n=20,737)

Author (Year)	aHR	CI 95%	
		Lower Limit	Upper Limit
Andarge et al. (2022)	0.79	0.22	2.85
Chen et al. (2022)	0.77	0.59	0.99
Cuong et al. (2012)	1.90	0.70	5.30
Fekade et al. (2017)	1.01	0.65	1.56
Girma et al. (2022)	0.83	0.62	1.12
Nishijima et al. (2020)	0.43	0.20	0.93
Niu et al. (2023)	0.62	0.47	0.83
Setegn et al. (2015)	0.37	0.24	0.57
Seyoum et al. (2017)	0.70	0.40	1.23
Tadesse et al. (2024)	0.53	0.28	1.00
Teshale et al. (2022)	0.73	0.30	1.75

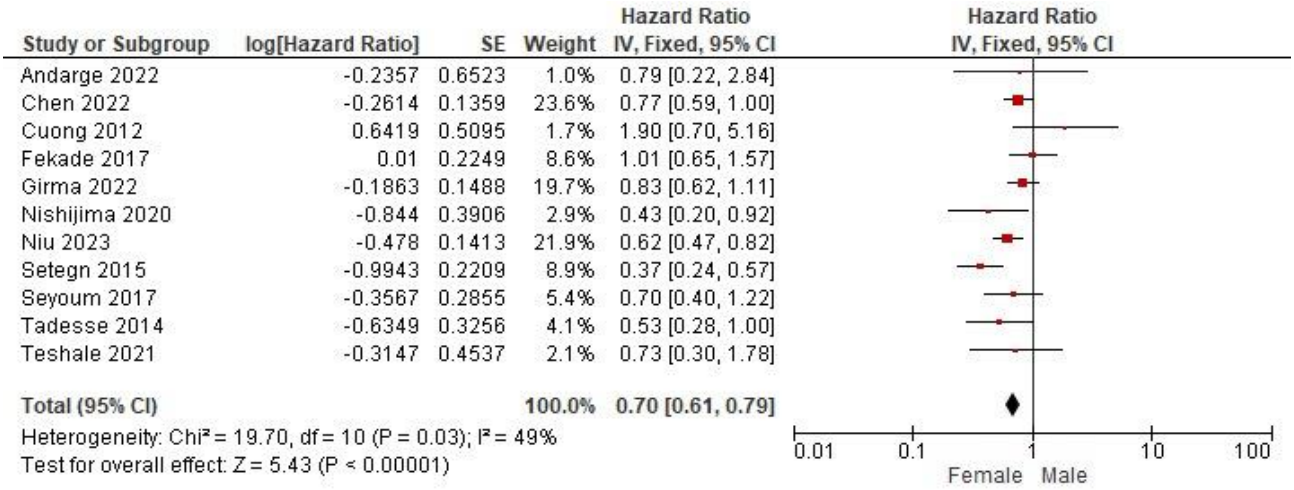

Figure 3. Forest plot of gender influence on mortality in ODHIV with antiretroviral therapy

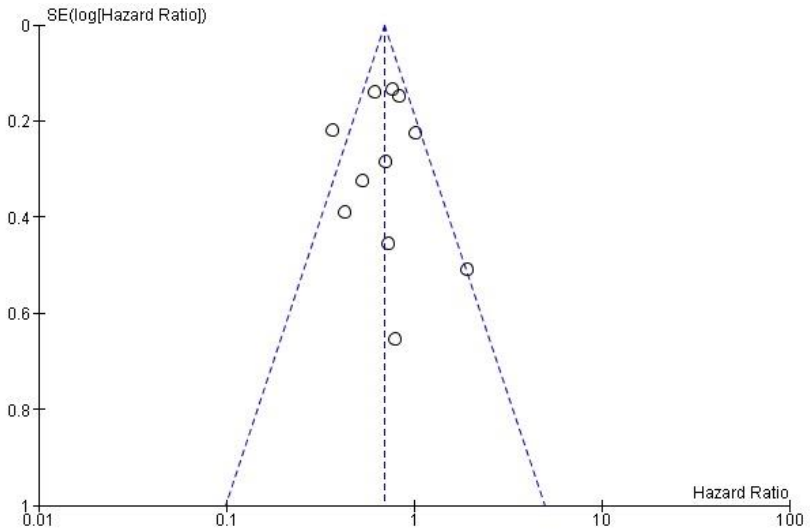

Figure 4. Plot funnel of gender influence with mortality in ODHIV with antiretroviral therapy

Table 3 presents the adjusted hazard ratio (aHR) and 95% (95%CI) confidence interval of gender influence with mortality from each primary study conducted meta-analysis. Sample size from this meta-analysis (n)= 20,737 in ODHIV with antiretroviral therapy.

The forest plot in Figure 3 shows that there is an influence of gender on the risk of mortality in people with HIV who receive antiretroviral therapy and is statistically significant. In ODHIV the female sex has a mortality risk of 0.7 times compared to the male ODHIV (aHR = 0.70; CI 95%=0.61 to 0.79; p<0.001). The forest plot also showed low heterogeneity (I^2= 49%). Thus, the average calculation of effect estimation uses the fixed effect model approach.

The funnel plot in Figure 4 shows that the distribution of the estimated effect is the same between the section on the right and the left of the vertical line of the average estimate. Thus, the plot funnel does not indicate publication bias.

Table 4. Data on adjusted hazard ratio (aHR) and 95% (95%CI) confidence interval of the effect of TB coinfection with mortality in ODHIV with antiretroviral therapy with sample size (n=4.154)

Author (Year)	aHR	CI 95%	
		Lower Limit	Upper Limit
Aemro et al. (2021)	1.73	0.66	4.55
Andarge et al. (2022)	3.07	0.76	12.36
Cuong et al. (2012)	0.70	0.30	1.70
Damteu et al. (2015)	1.81	1.24	2.65
Nigussie et al. (2020)	1.65	0.85	3.19
Setegn et al. (2015)	4.51	2.86	7.11
Seyoum et al. (2017)	1.28	0.74	2.15
Tachbele et al. (2016)	1.82	1.41	3.51
Tadesse et al. (2014)	2.62	0.91	7.50

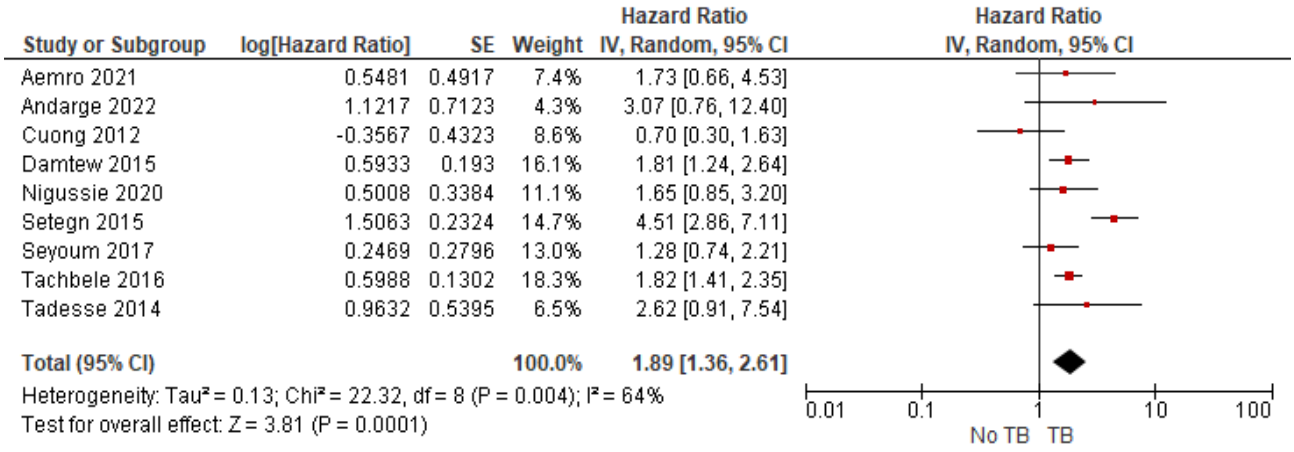

Figure 5. Forest plot of the effect of TB coinfection on mortality in ODHIV with antiretroviral therapy

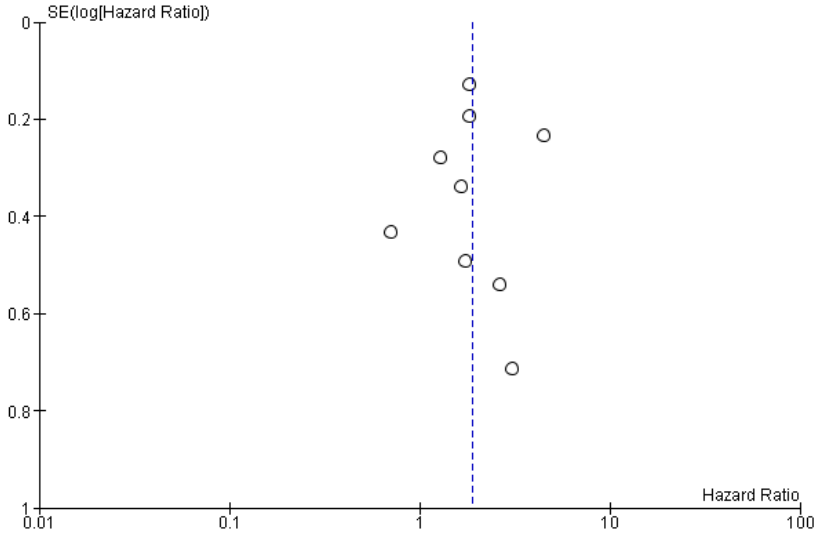

Figure 6. Funnel plot of the effect of TB coinfection on mortality in ODHIV with antiretroviral therapy

Table 4 presents the adjusted hazard ratio (aHR) and the 95% confidence interval of the effect of TB coinfection with mortality from each primary study conducted meta-analysis. Sample size from this meta-analysis (n)= 4,154 in ODHIV with antiretroviral therapy.

The forest plot in Figure 5 shows that there is an effect of TB co-infection on the risk of mortality in ODHIV receiving antiretroviral therapy and is statistically significant. ODHIV with coinfected TB has a mortality risk of 1.86 times compared to ODHIV without coinfected TB (aHR= 1.89; CI 95%=1.36 to 2.61; p<0.001). The forest plot also shows high heterogeneity (I2 = 64%). Therefore, the model used is a random effect model.

The funnel plot in Figure 6 shows that the distribution of the estimated effect is not equal between the right and left parts with more left parts. Thus the plot funnel indicates publication bias. Because the distribution of the effect estimate in the plot funnel is more on the left which is different from the location of the diamond shape which is to the right of the zero hypotheses vertical line in the forest plot image, the publication bias tends to over estimate the actual effect.

Table 5. Data on adjusted hazard ratio (aHR) and 95% confidence interval (95%CI) of the effect of opportunistic infection with mortality in ODHIV with antiretroviral therapy with sample size (n=3,280)

Author (Year)	aHR	CI 95%	
		Lower Limit	Upper Limit
Andarge et al. (2022)	4.59	1.17	18.07
Cuong et al. (2012)	1.30	0.70	2.40
Nigussie et al. (2020)	1.86	1.05	3.33
Ojikutu et al. (2008)	2.58	1.37	4.88
Setegn et al. (2015)	2.51	1.46	4.31
Seyoum et al. (2017)	1.38	0.78	2.43
Siraj et al. (2022)	4.58	1.20	5.65
Teshale et al. (2022)	1.25	0.54	1.86

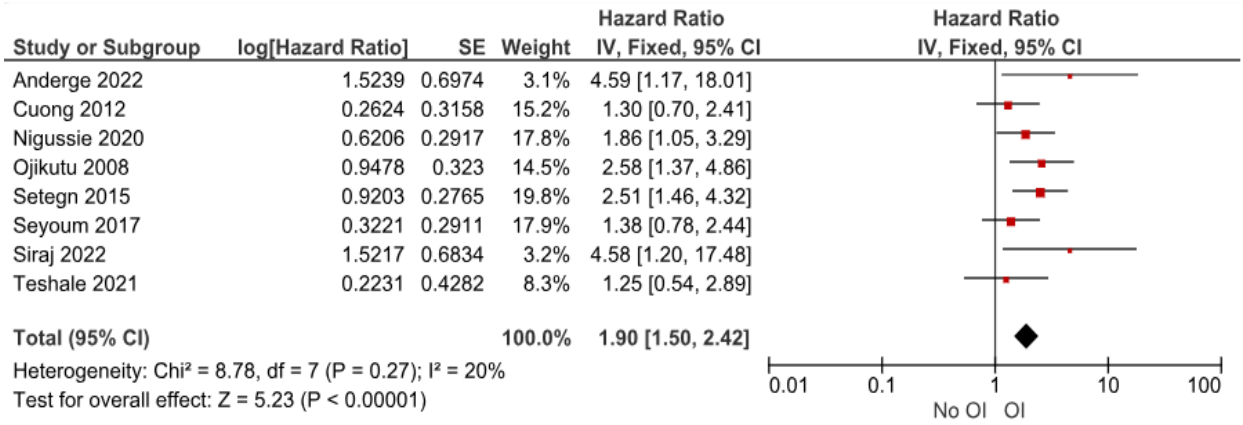

Figure 7. Forest plot of the effect of opportunistic infection with mortality in ODHIV with antiretroviral therapy

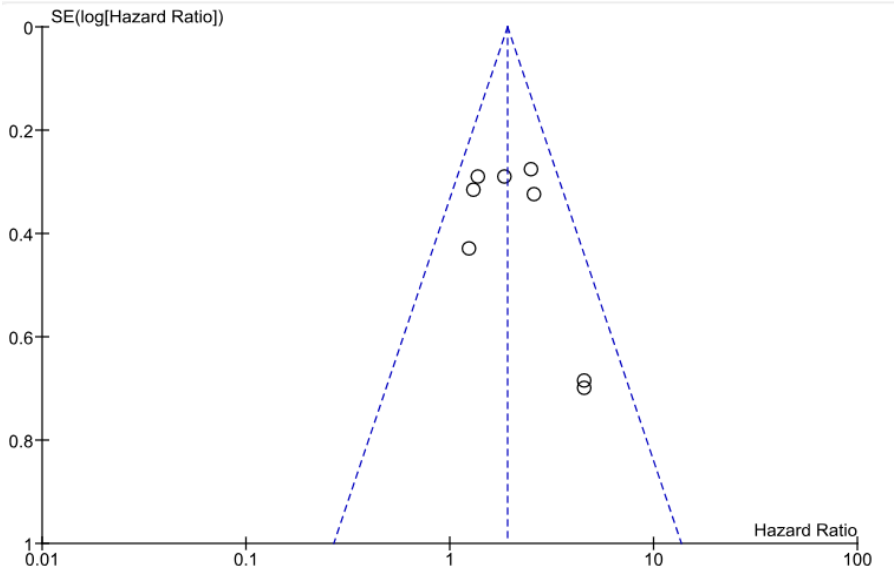

Figure 8. Funnel plot of the effect of Opportunistic infection with mortality in ODHIV with antiretroviral therapy

Table 6 presents the adjusted hazard ratio (aHR) and 95% (95%CI) confidence interval of gender influence with mortality from each primary study conducted meta-analysis. Sample size from this meta-analysis (n)= 3,280 in ODHIV with antiretroviral therapy.

The forest plot in Figure 7 shows that there is an effect of opportunistic infection on the risk of mortality in people with HIV who receive antiretroviral therapy and is statistically significant. ODHIV with opportunistic infection has a risk of mortality 1.9 times compared to ODHIV without opportunistic infection (aHR= 1.90; CI 95%=1.50 to 2.42; p<0.001). The forest plot shows low heterogeneity (I^2= 20%). Thus, the average calculation of effect estimation uses the fixed effect model approach.

The funnel plot in Figure 8 shows that the distribution of the estimated effect is evenly distributed to the right and left of the vertical line of the average estimate. Thus, the plot funnel does not indicate publication bias.

DISCUSSION

1. Effect of gender on mortality in ODHIV with antiretroviral therapy

The results of the meta-analysis of these 11 primary studies revealed that female ODHIV had an increased risk of mortality by 0.7 times compared to male ODHIV (aHR= 0.70; CI95%=0.61 to 0.79; p<0.001). Women lower the risk of mortality in ODHIV with antiretroviral therapy.

The largest contributor to HIV is men because each year accounts for around 66% of HIV infection cases in gay and bisexual ODHIV (CDCb, 2021). Men have higher mobility than women, so they are more at risk of getting HIV even after taking antiretroviral therapy. Antiretroviral therapy works by stopping the reproduction of the HIV. However, if HIV levels are still detected due to non-compliance with therapy carried out by gays and bisexuals, then antiretroviral therapy does not work optimally, resulting in mortality (Cleveland, 2024).

In countries on the African continent, patients who have received ART, although through the treatment can suppress the spread of the virus, there is still a higher risk of mortality, especially in the male sex. This is also related to the amount of CD4 in the body of men less than women (Maskew et al, 2013).

2. Effect of TB coinfection on mortality in ODHIV with antiretroviral therapy

Through analysis of meta-results from 9 primary studies, it was found that in ODHIV with co-infected TB, the risk of mortality increased by 1.86 times compared to ODHIV without co-infected TB (aHR= 1.89; CI95%= 1.36 to 2.61; p<0.001). Reduced access to TB diagnosis and treatment has resulted in an increase in TB deaths. The forecast for 2020 is 214,000 deaths in people with HIV (up from 209,000 in 2019). Of the TB deaths among people living with HIV, 50% were men, 40% were women, and 9.8% were children. Among all episodes of TB incidence, 8% of them are people living with HIV (WHO, 2022). The highest proportion of TB episodes of HIV co-infection occurs in countries in the African region included in the WHO, exceeding 50% in some parts of southern Africa. Nearly 12 million TB-related HIV deaths could have been prevented in the 2000-2020 period thanks to TB/HIV-related interventions (Goletti, 2023).

Global HIV testing coverage in people diagnosed with TB remained high in 2020 at 73% (up from 70% in 2019). However, the absolute number of people diagnosed with TB who know their HIV status fell from 4.8 million in 2019 to 4.2 million in 2020 (a decrease of 15%). In 87 countries and regions, at least 90% of people diagnosed with TB are aware of their HIV status (Shapiro et al, 2012)

Antiretroviral Therapy coverage in people diagnosed with TB and known to be HIV positive was 88% in 2020, the same as in 2019. The success rate of treatment in people with HIV is still lower (77% globally in 2019), although there has been a steady improvement over time. The global number of people living with HIV annually receiving TB preventive treatment increased from less than 30,000 in 2005 to 3.0 million in 2019, with a decrease of 23% between 2019 and 2020, to 2.7 million (Nyasulu et al, 2022).

At least 6 million people living with HIV have received TB preventive treatment by 2022. The future target is to ensure that 90% of people living with HIV receive TB preventive treatment by 2025 and reduce TB-related deaths among people living with HIV by 80% by 2025 (compared to baseline data in 2010). Everyone living with HIV should be tested for TB and everyone with TB should be screened for HIV. This is key

to preventing TB-related deaths in people living with HIV (WHO, 2023).

3. Effect of opportunistic Infection on Mortality in ODHIV with antiretroviral therapy

Through the analysis of meta-results data from these 8 primary studies, it was revealed that in ODHIV with opportunistic infection, the risk of mortality increased by 1.9 times compared to ODHIV without opportunistic infection (aHR= 1.90; CI 95%=1.50 to 2.42; p<0.001). People with AIDS have a severely damaged immune system. They are increasingly suffering from severe diseases, called opportunistic infections (OI). Causes of people with HIV suffering from IO include WHO clinical, CD4 count, and compliance with the use of ART drugs. Malnutrition is also a determining factor in the findings of IO in adults (Woldegeorgis et al, 2023).

Diagnosis and treatment related to opportunistic infections have been widely carried out, but opportunistic infections require a thorough understanding of the environment and determinants, especially in young people because clinical detection alone is not enough (Wondifraw., et al, 2022).

Some of the reasons why ODHIV still experience opportunistic infections are because they do not know that they have HIV so they do not undergo treatment, they know that they are ODHIV but do not regularly use ART therapy, and they have had HIV for a long time before being diagnosed so that their immunity has weakened and the ART used has not reached viral suppression (HIV.gov, 2024).

AUTHOR CONTRIBUTION

Fauziah Shinta Anindita and Fenita Indriani are researchers who choose topics, search and collect articles, analyze data and write scripts. Bhisma Murti and Nindita Arum Veibiani helped analyze the data and review the research documents.

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CONFLICT OF INTEREST

There are no conflicts of interest.

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