Effect of Body Mass Index on Mortality in Patients with Tuberculosis and HIV Co-Infection within the Scope of Asia Africa: A Systematic Review and Meta-Analysis

Mufti As Siddiq M Irzal, Tri Yunis Miko Wahyono, Putri Novia Choiri Insani, Welstin Wemi Loa, Leopardo Alvalius Ngetwa

Submitted to: Asian/Pacific Island Nursing Journal
on: August 05, 2025

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Abstract

Background: In 2022, an estimated 10.6 million people developed tuberculosis (TB) globally, with 6.3% co-infected with HIV. The Southeast Asia region accounted for 46% of global TB cases, while Africa contributed 23%. TB-HIV co-infection remains a major cause of death, with 167,000 deaths recorded among co-infected individuals in 2022. Nutritional status, particularly Body Mass Index (BMI), may influence mortality in this population. However, no comprehensive synthesis of the evidence currently exists.

Objective: To assess the association between BMI and mortality among TB-HIV co-infected patients in Asia and Africa.

Methods: A systematic review and meta-analysis of cohort studies published between 2000 and 2024 were conducted using PubMed, Scopus, and ProQuest. A random-effects model was applied to calculate pooled Risk Ratio (RR) and 95% confidence intervals.

Results: Eleven cohort studies met the inclusion criteria. Patients with low BMI (<18.5 kg/m²) had a 10% higher risk of mortality compared to those with normal or higher BMI (RR = 0.90; 95% CI: 0.86–0.94; $p < 0.05$). Heterogeneity was substantial ($I^2 = 78\%$), but the association remained statistically significant and robust.

Conclusions: Low BMI is significantly associated with increased mortality among TB-HIV co-infected patients in Asia and Africa. Routine nutritional screening and targeted support should be prioritized in TB-HIV clinical management strategies. Clinical Trial: This systematic review and meta-analysis has been registered with the Open Science Framework (doi: 10.17605/OSF.IO/74QWH).

(JMIR Preprints 05/08/2025:81905)
DOI: https://doi.org/10.2196/preprints.81905

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ABSTRACT

Background: In 2022, an estimated 10.6 million people developed tuberculosis (TB) globally, with 6.3% co-infected with HIV. The Southeast Asia region accounted for 46% of global TB cases, while Africa contributed 23%. TB-HIV co-infection remains a major cause of death, with 167,000 deaths recorded among co-infected individuals in 2022. Nutritional status, particularly Body Mass Index (BMI), may influence mortality in this population. However, no comprehensive synthesis of the evidence currently exists.

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Conclusions: Low BMI is significantly associated with increased mortality among TB-HIV co-infected patients in Asia and Africa. Routine nutritional screening and targeted support should be prioritized in TB-HIV clinical management strategies.

Systematic review registration: This systematic review and meta-analysis has been registered with the Open Science Framework (doi: 10.17605/OSF.IO/74QWH).

Keywords: body mass index, mortality, tuberculosis, HIV

Introduction

Tuberculosis (TB) and Human Immunodeficiency Virus (HIV) continue to pose major global public

health threats, particularly in low- and middle-income countries [1]. The interaction between TB and HIV is synergistically detrimental, as HIV significantly increases the risk of progression from latent TB infection to active disease, while TB accelerates the progression of HIV-related immunosuppression [2], [3]. In 2022, an estimated 10.6 million people developed TB globally, with the Southeast Asia region accounting for 46% and Africa for 23% of these cases. Among those affected by TB, 6.3% were co-infected with HIV, and the proportion of TB-HIV co-infection exceeded 50% in several parts of Southern Africa. TB remains a leading cause of death among people living with HIV (PLHIV), with approximately 167,000 deaths among co-infected individuals in 2022 alone [4].

Earlier estimates also emphasize the magnitude of the problem. In 2013, there were 1.1 million new TB/HIV co-infected cases globally, accounting for 12% of incident TB cases and 360,000 deaths [5]. The African region remains disproportionately affected, with an estimated TB-HIV co-infection rate of 72% [6]. South Africa alone reports 450,000 new TB cases annually, of which 270,000 occur among PLHIV [7]. While the Asia-Pacific region traditionally has lower TB-HIV co-infection prevalence, routine HIV testing among TB patients is not universally implemented, and the estimated HIV prevalence among new TB cases increased to 6.3% in 2013 [5].

Several factors exacerbate TB-HIV transmission and mortality. These include socio-environmental determinants such as poverty, overcrowding, malnutrition, smoking, and exposure to environmental pollutants like biomass fuel and mining dust [8], [9], [10]. HIV infection independently contributes to poor nutritional status, which in turn influences TB disease progression and treatment outcomes [11], [12], [13]. Compounding this, the COVID-19 pandemic has disrupted TB diagnosis and care services in both Africa and Asia-Pacific, contributing to delays in treatment initiation and poor follow-up [14].

The role of nutritional status—particularly Body Mass Index (BMI)—in predicting mortality among TB-HIV co-infected patients has gained increasing attention. Low BMI (<18.5 kg/m²) has been consistently associated with increased risk of early and all-cause mortality during TB treatment [15]. A prospective cohort study in Ethiopia demonstrated that BMI improvement following initiation of antiretroviral therapy (ART) was significantly associated with reduced mortality, regardless of initial BMI classification [16]. In contrast, BMI decline within the first month of TB treatment was linked to higher mortality among HIV-positive individuals in Myanmar and Zimbabwe [17]. Additional evidence from Taiwan suggests that underweight male patients have significantly higher TB-specific and non-TB-specific mortality risks during treatment [18].

HIV-associated wasting also presents with decreased mid-upper arm and muscle circumference—indicators of low lean body mass—which further underscores the critical intersection of nutrition and immunologic competence in TB-HIV care [11], [19]. While early ART initiation alongside TB therapy—especially for individuals with CD4+ counts <50 cells/μl—has been shown to improve survival [20], integration of nutritional assessment and interventions into co-infection management remains under-prioritized.

Despite a growing body of literature exploring BMI and mortality in TB-HIV co-infected populations, no systematic review or meta-analysis has been conducted to quantify the effect of BMI on mortality in this population, particularly in the high-burden regions of Asia and Africa. Furthermore, most existing studies utilize cross-sectional or retrospective designs, limiting causal inference. Prospective cohort studies, which provide stronger evidence of temporal relationships, are more appropriate for investigating the impact of BMI on mortality risk.

This study aims to address this critical evidence gap by conducting a systematic review and meta-analysis of cohort studies that evaluate the impact of BMI on mortality among patients with TB-HIV co-infection in Asia and Africa. The findings are expected to inform integrated interventions involving both clinical and nutritional care, with the potential to improve survival outcomes in this vulnerable population.

Methods

This systematic review and meta-analysis is being reported in accordance with the reporting guidance provided in the Preferred Reporting Items for Systematic Reviews and Meta-Analyses Protocols (PRISMA-P) statement [21], [22].

Eligibility Criteria

Eligibility criteria for this review included cohort studies (retrospective or prospective) published in the period 2000-2024 in PubMed, Scopus, and ProQuest databases, with a focus on adult patients (>15 years) with tuberculosis (TB) and HIV co-infection in Asia and Africa. Only academic journal articles with full-text access were included, while literature reviews, case reports, short reports, proceedings, and studies without mortality data were excluded. The primary outcome evaluated was mortality in populations with TB/HIV co-infection, so studies that did not report mortality rates or examine pediatric populations were excluded from the analysis.

Data Sources and Search Strategy

A comprehensive literature search was conducted in PubMed, Scopus, and ProQuest to identify relevant studies from 2000 – 2024. The search strategy combined MeSH terms and free-text keywords related to TB-HIV coinfection, body mass index, and mortality. Only studies published in English and involving adult populations (≥18 years) were included. Mendeley reference management software was used to import and maintain the retrieved studies. On October 30–31, 2024, a search was done to find studies that would be suitable for meta-analysis and systematic review. The full boolean search string used was ("Coinfection"[Mesh] OR “Co-infection” OR “Multiple infection”) AND ("Tuberculosis"[Mesh] OR “TB” OR “Tuberculosis”) AND ("HIV Infections"[Mesh] OR “HIV” OR “Human Immunodeficiency Virus” OR “TB?HIV”) AND ("Adult"[Mesh] OR “Mature” OR “Person over 18”) AND ("Body Mass Index"[Mesh] OR “BMI”) AND ("Mortality"[Mesh] OR “Fatal* OR “Death” OR “Case fatality rate” OR “Mortality rate”) AND ("Cohort Studies"[Mesh] OR “Cohort study” OR “Cohort”).

Screening and selection process

Three independent reviewers participated in the methodical and comprehensive screening and research selection procedure. To make it easier to filter titles and abstracts based on preset inclusion and exclusion criteria, all database search results were uploaded to the Rayyan AI application. Before moving on to the full-text screening phase, which was also carried out individually by the three reviewers, articles that were found to be duplicates were eliminated. Discussion and agreement were used to settle any disagreements. Data such as author name, year of publication, area, sample size, and number of events in the intervention group (BMI < 18.5) and control group (BMI ≥ 18.5) were retrieved from publications that satisfied the selection criteria. The data were then recorded in Microsoft Excel spreadsheets to facilitate further management and analysis.

Risk of bias assessment

The risk of bias assessment in this review was conducted using the Hoy Risk of Bias (Hoy RoB) instrument, which is specifically designed to assess bias in observational studies. The Hoy RoB instrument includes 10 questions representing the four main domains of bias, as well as one overall

risk of bias assessment question. Based on Hoy et al. 's findings, the instrument is easy to use and has a high level of inter-rater agreement, with an overall percentage agreement of 91% and a Kappa value of 0.82 (95% CI: 0.76-0.86). The final score is classified into three categories, namely high risk (score < 6), moderate risk (score 7-8), and low risk (score 9-10). In this study, studies assessed as having a high risk of bias were excluded from the analysis, so only studies with a moderate or low risk of bias were included [23].

Data extraction

Three researchers worked separately to extract the data using a consistent Microsoft Excel spreadsheet that was created following a predetermined checklist. The name of the author, the year of publication, the study region, the sample size, and the number of fatalities and surviving samples in each group—the intervention group (BMI < 18.5) and the control group (BMI ≥ 18.5)—were among the data taken from each main research. Any discrepancies in the data extraction were settled by consensus-building conversations, guaranteeing the precision and coherence of the data for further analysis.

Outcome variable and measures

The primary outcome of this study was mortality in patients with TB/HIV co-infection, which was measured by comparing the number of deaths between the intervention group (BMI < 18.5) and the control group (BMI ≥ 18.5). The measure of association used was the Log Risk Ratio (LogRR), which was then transformed into a Risk Ratio (RR) to facilitate interpretation of the results. Data extracted from each primary study included the number of deaths and the number of participants alive in both groups, allowing the calculation of RR estimates along with 95% confidence intervals (95% CI). This approach was applied in a random effects model to accommodate potential heterogeneity between studies, thus providing a comprehensive picture of the effect of nutritional status on mortality in TB/HIV co-infected populations.

Data synthesis and analysis

Data synthesis began with a narrative presentation summarizing the study characteristics, population, intervention, and primary outcome, namely mortality in TB/HIV patients, with a comparison of the intervention group (BMI < 18.5) and the control group (BMI ≥ 18.5). Furthermore, the meta-analysis was conducted using STATA version 15.1 to estimate the risk ratio (RR) obtained from the log risk ratio (logRR) transformation along with the 95% confidence interval. Heterogeneity between studies was analyzed using the I^2 statistic, where I^2 values were categorized as low (I^2: 0-25%), medium (I^2: 25-50%), or high (I^2: ≥50%) [24]. As the number of articles included was less than 10, subgroup analysis was not performed. Evaluation of publication bias was conducted through Egger's Regression-Based Test and Trim-and-Fill Analysis to detect potential asymmetry in the funnel plot. The results of the synthesis and analysis were presented comprehensively through text, tables, and graphs.

Results

Selection of studies

A comprehensive literature search yielded 814 articles from three major databases, namely PubMed (n=220), Scopus (n=292), and ProQuest (n=302). After 43 duplicate articles were removed, a total of 771 articles were screened at the title and abstract screening stage, of which 748 were excluded as they did not meet the inclusion criteria. A total of 23 articles were then retrieved for full review, but 1 article could not be retrieved, so 22 articles were assessed for eligibility. At this stage, 9 articles were eliminated (2 article had a high risk of bias, and 9 articles did not fit the topic or data required), leaving 11 articles that were finally included in the systematic review and 7 included in meta-

analysis. The study selection process is detailed in the PRISMA flow chart (Figure 1).

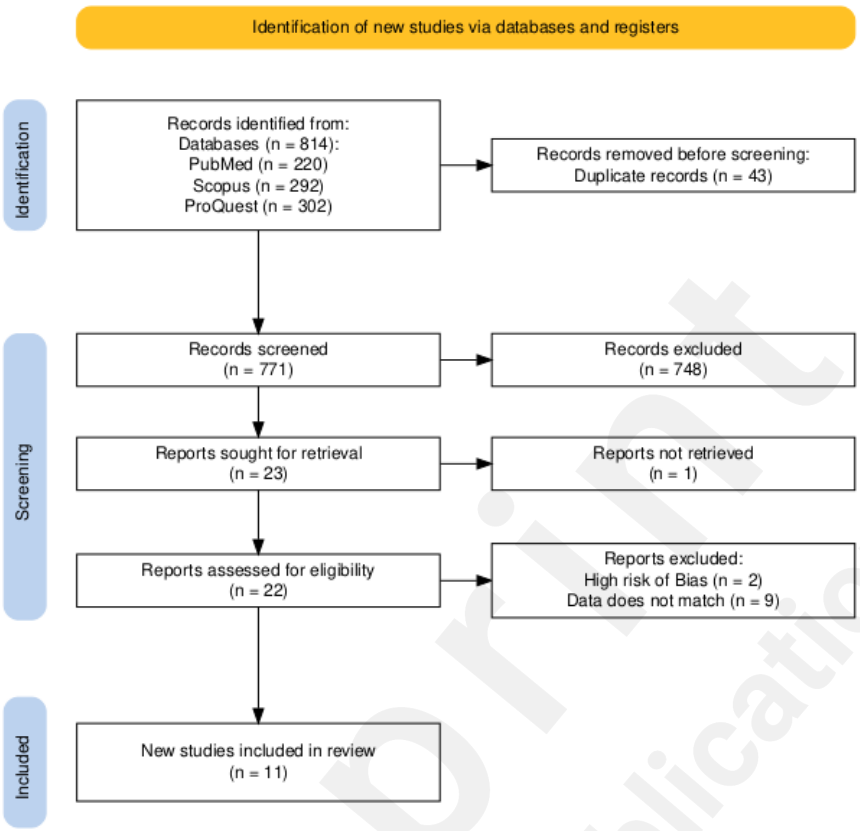

Figure 1. PRISMA Flowchart of the bibliographic research

Findings

Table 1. Data Extraction from Included Studies

No.	Author (Year)	Title	Country	Method	Population/ Sample	Result
1.	Teshager Worku Kegne et al. (2024).	Survival Rate and Predictors of Mortality Among TB-HIV Co-Infected Patients During Tuberculosis Treatment at Public Health Facilities in Bahir Dar City, Northwest Ethiopia.	Ethiopia.	A retrospective cohort study was conducted among TB-HIV co-infected patients who were treated for tuberculosis at public health facilities in Bahir Dar city.	The study included 401 TB-HIV co-infected patients treated between July 2018 and June 2022.	Among the 401 patients monitored, 59 (14.7%) passed away during the follow-up period. The research identified several significant predictors of mortality related to Body Mass Index (BMI). Specifically, patients with a BMI of less than 18.5 kg/m² experienced a mortality risk that was 3.00 times higher than those with a normal BMI. This finding was substantiated by an Adjusted Hazard Ratio (AHR) of 3.00, with a 95% Confidence Interval (CI) ranging from 1.44 to 6.28, indicating a statistically significant relationship between lower BMI and increased mortality risk ($p < 0.05$) [25].
2.	Joan Rokani Bayowa et al. (2023).	Mortality rate and associated factors among patients co-infected with	Uganda.	The study employed a retrospective cohort design that involved reviewing medical records of	The study included 390 participants who met the eligibility	The results indicated a mortality rate of 33.2% (95% CI: 28.7–38.1) among the study population. Specifically, regarding the relationship between body mass

		drug resistant tuberculosis/HIV at Mulago National Referral Hospital, Uganda, a retrospective cohort study.		patients co-infected with drug-resistant tuberculosis (DR-TB) and HIV who were registered at the Mulago Tuberculosis Unit from January 1, 2014, to December 31, 2019.	criteria of having confirmed DR-TB and documented HIV positive status, resulting from an initial review of 412 records. Participants were aged between 1 to 80 years, with a mean age of 34.6 years, and the majority were male (53.9%).	index (BMI) and mortality, a body mass index of less than 18.5 kg/m² was associated with an increased likelihood of death. The adjusted incidence rate ratio (aIRR) for those with BMI less than 18.5 kg/m² was 0.91 (95% CI: 0.85-0.97), with a p-value of 0.007, which suggests a statistically significant protective effect against mortality for individuals with a higher BMI. This highlights the critical importance of maintaining an adequate nutritional status as a determinant of mortality outcomes in this vulnerable population [26].
3.	Eleni Seyoum et al. (2022).	Increased Mortality in HIV Infected Individuals with Tuberculosis: A Retrospective Cohort Study, Addis Ababa, Ethiopia.	Ethiopia	Retrospective cohort using ART medical records from 2011–2018 in 28 facilities.	7,038 HIV-positive adults; 1,123 with TB coinfection.	TB-HIV coinfected individuals had over two times higher risk of mortality compared to HIV-only (AHR: 2.53; 95% CI: 1.63–3.91). BMI <18.5 kg/m² significantly increased mortality risk, indicating that malnutrition plays a critical role in survival outcomes for TB-HIV patients [27].
4.	Lilit Gevorgyan et al. (2021).	Factors associated with unfavourable treatment outcomes in people with HIV-associated tuberculosis in Armenia, 2015 to 2019.	Armenia.	The study was conducted in Armenia and employed a cohort study design using routine programmatic data of HIV-associated tuberculosis (TB) patients receiving treatment from 2015 to 2019.	The population for this research included both pulmonary and extrapulmonary HIV-associated TB patients, and the study comprised a total of 351 treatment episodes involving 320 individual patients. The authors detailed the socio-demographic and clinical characteristics of these patients through data collected from the National TB database, National HIV database, and patients' medical records.	The results indicated a significant association between body mass index (BMI) and mortality rates among the HIV-associated TB patients. Specifically, underweight patients had an increased risk of death, reflected in an adjusted hazard ratio (aHR) of 2.5 (95% confidence interval [CI]: 1.3-4.5), with a p-value of less than 0.01. This finding underscores the critical role of nutritional status in influencing health outcomes within this vulnerable population, highlighting the necessity for addressing malnutrition as a part of TB management and care protocols in clinical settings [28].
5.	Rose J. Kosgei et al.	Gender difference in mortality among	Kenya.	This study utilized a retrospective cohort design, analyzing	The study analyzed a total sample of	The findings revealed that men exhibited a higher mortality rate (11%) compared to women (9%),

	(2020).	pulmonary tuberculosis HIV co-infected adults aged 15-49 years in Kenya.		healthcare records from individuals treated for tuberculosis between 2012 and 2015. The primary outcome of interest was all-cause mortality during tuberculosis treatment.	9,026 smear-positive pulmonary tuberculosis patients, aged 15–49 years, who were co-infected with HIV.	with a statistically significant difference (p = 0.004). The risk ratio indicated that women had a 17% reduced risk of mortality compared to their male counterparts (adjusted hazard ratio [HR] 0.83; 95% confidence interval [CI] 0.72–0.96; p = 0.013). Regarding body mass index (BMI), a higher BMI was associated with a reduced risk of death during treatment; specifically, those with a BMI higher than 18.5 had a lower mortality risk compared to those with a BMI less than 15, underscoring the importance of maintaining a healthy body weight in this population for better treatment outcomes. These results suggest that both gender and BMI significantly influence survival among pulmonary tuberculosis HIV co-infected patients, highlighting areas for targeted interventions in healthcare delivery [29].
6.	Naidoo et al. (2018).	A retrospective cohort study of body mass index and survival in HIV infected patients with and without TB co-infection.	South Africa.	This study employed a retrospective cohort design. Clinical data from HIV-infected patients was evaluated, utilizing statistical methods to assess the correlation between body mass index (BMI) and mortality outcomes. Key analysis tools included multivariate proportional hazards regression to adjust for confounding variables, and the log-rank test for comparing survival distributions across BMI categories.	The study comprised a total of 1000 HIV-infected patients. However, due to missing height or weight measurements for 52 patients, the final analysis included 948 patients, split into different BMI categories for assessment. Among these, 389 patients were also co-infected with tuberculosis (TB).	The findings indicated that underweight patients (BMI < 18.5 kg/m²) faced a significantly increased risk of mortality compared to those with a normal BMI (18.5–24.9 kg/m²). Specifically, the adjusted hazard ratio (aHR) for mortality in underweight patients was 2.9 (95% Confidence Interval [CI]: 1.5–5.7; p = 0.002). This result underscores a notable correlation between low BMI and elevated mortality rates among HIV-infected individuals, highlighting that underweight patients possessed a nearly threefold elevated risk of death relative to their normally weighted counterparts. The study confirms the essential role of baseline BMI as a prognostic indicator, irrespective of TB co-infection status. Notably, mortality rates for those categorized as overweight (BMI 25.0–29.9) and obese (BMI ≥ 30.0) were not significantly different from those with normal BMI, further establishing the critical impact of being underweight on survival outcomes in this population [30].
7.	C. Wejse et al. (2015).	Impact of HIV-1, HIV-2, and HIV-1+2 dual infection on the outcome of Tuberculosis.	Guinea - Bissau.	The study employed a longitudinal, prospective cohort design. Patients were identified through daily visits by field assistants to local	The study included a total of 1,312 patients with tuberculosis who had completed	The findings of the study indicated a significant relationship between body mass index (BMI) and mortality among TB patients. Specifically, the results demonstrated that patients with a BMI less than 17 kg/m² had a

				health centers and a national referral TB hospital. The diagnosis of tuberculosis (TB) was made according to WHO criteria, and both smear-positive and smear-negative cases were included based on defined medical and clinical parameters.	their anti-TB treatment by September 1, 2013. Among these patients, 379 were HIV-infected, comprised of those with HIV-1, HIV-2, and dual infections.	crude hazard ratio (HR) of 1.42 (95% CI: 0.81–2.49), and this association reached statistical significance with a p-value of 0.021. This emphasizes that lower BMI is correlated with increased mortality rates in the context of tuberculosis management. The study underscores the necessity of monitoring and addressing nutritional status as a critical component of TB treatment protocols [31].
8.	Dam Anh Tran et al. (2013)	Survival and HIV Infection Among Patients with Tuberculosis in Ho Chi Minh City, Vietnam (1996–2004).	Vietnam	Retrospective cohort based on TB surveillance data from 1996 to 2004.	41,203 TB patients; 3,126 HIV-positive.	HIV-positive TB patients had a case fatality rate (CFR) of 26.3%, much higher than HIV-negative (2.8%). Although BMI data wasn't directly analyzed, the study emphasized poor survival among HIV-infected TB patients, and undernutrition was suggested as a major contributor [32].
9.	Hind Satti et al. (2012).	Outcomes of Multidrug-Resistant Tuberculosis Patients Co-Infected with HIV Treated with Integrated Therapy in Lesotho.	Lesotho	Prospective cohort study evaluating integrated MDR-TB and HIV care.	134 MDR-TB and HIV co-infected patients.	After 24 months of treatment, mortality was significantly higher among patients with BMI <18 kg/m². The study concluded that low BMI at baseline independently predicted poor treatment outcomes and higher death rates, even under integrated therapy protocols [33].
10.	Lenka Benova et al. (2012).	Association of BMI Category Change with TB Treatment Mortality in HIV-Positive Smear-Negative and Extrapulmonary TB Patients in Myanmar and Zimbabwe.	Myanmar and Zimbabwe.	This retrospective cohort study involved analyzing data collected over seven years from TB patients in clinical programs. The study employed Cox proportional hazards regression to evaluate the association between changes in BMI category during the first month of TB treatment and subsequent mortality. Adjustments were made for potential confounders, including sex, age group, project site, and ART status as a time-dependent covariate.	The study included a total of 1,090 new adult TB patients who were HIV-positive, specifically focusing on those diagnosed with smear-negative and extrapulmonary TB. Data were drawn from three clinical programs across the mentioned countries.	The analysis revealed a robust association between changes in BMI category during the initial month of TB treatment and mortality outcomes. Patients who remained severely underweight or moved to a lower BMI category had a hazard ratio (HR) of 4.05 (95% CI: 2.77–5.91, $p < 0.001$) for mortality compared to those who either maintained or moved to a higher BMI category. This indicates a significantly elevated risk of death associated with BMI category deterioration. Similarly, those who remained severely underweight or lost a BMI category showed over twice the rate of unfavorable TB treatment outcomes, with an adjusted hazard ratio of 2.53 (95% CI: 1.87–3.42). These findings underscore the importance of monitoring BMI changes in identifying individuals at heightened risk of mortality during TB treatment in HIV-positive populations [17].
11.	Sabina F Mugusi et al. (2011)	Survival of HIV-Infected Patients with Pulmonary Tuberculosis in the Era of Co-Trimoxazole	Tanzania	Prospective cohort (2003–2005) evaluating survival among HIV-positive pulmonary TB patients.	655 HIV-positive pulmonary TB patients.	Patients with BMI <18.5 kg/m² had significantly reduced survival. Low BMI was independently associated with mortality, even after adjusting for CD4 and clinical stage, supporting that undernutrition is a strong

Prophylaxis.	predictor of death in TB-HIV coinfected populations [34].

Meta-Analysis

In this study, the meta-analysis approach used a random-effects model to combine effect sizes from multiple studies, thus reflecting the diversity of the population studied [35]. Calculations were performed using the DerSimonian-Laird (DL) method to estimate the variance between studies [36]. Analyses were performed in STATA version 15.1, and results are presented as LogRR and 95% CI. Heterogeneity was measured using I^2, which indicates the absolute variance between studies [37]. The results of the meta-analysis can be seen in the following forest plot (Figure 2).

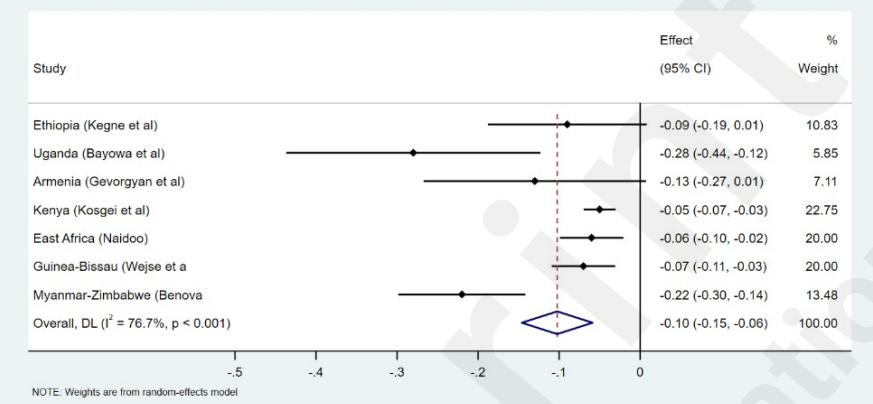

Figure 2. Forest Plot of the Relationship between BMI and Mortality of TB-HIV Co-infected Patients

This meta-analysis showed a statistically significant association between body mass index (BMI) and mortality in patients with TB-HIV co-infection, with an overall LogRR value of -0.10 (95% CI: -0.15 to -0.06). Transformation of the LogRR value into a Risk Ratio (RR) yielded a value of 0.90 (95% CI: 0.86-0.94), indicating that patients with BMI <18.5 had approximately 10% higher mortality risk compared to those with BMI ≥18.5. A p-value of <0.05 indicated that the strength of the association was statistically significant, while the high degree of heterogeneity (I^2=78%) justified the use of a random-effects model to accommodate the variation between studies. Epidemiologically, these findings confirm that higher BMI has a protective effect on mortality, making nutritional interventions an important component of efforts to improve survival in the TB-HIV population.

Assessment of publication bias

The assessment of publication bias in this meta-analysis was conducted using Egger's Regression-Based Test and Trim-and-Fill Analysis. Egger's regression-based test serves to detect potential asymmetry in the funnel plot that indicates publication bias. Meanwhile, trim-and-fill analysis was used to estimate and “add” the predicted missing studies, thus improving the distribution of the combined effect and providing a more comprehensive picture of the true effect size. Below is the funnel plot of the results of the publication bias assessment (Figure 3).

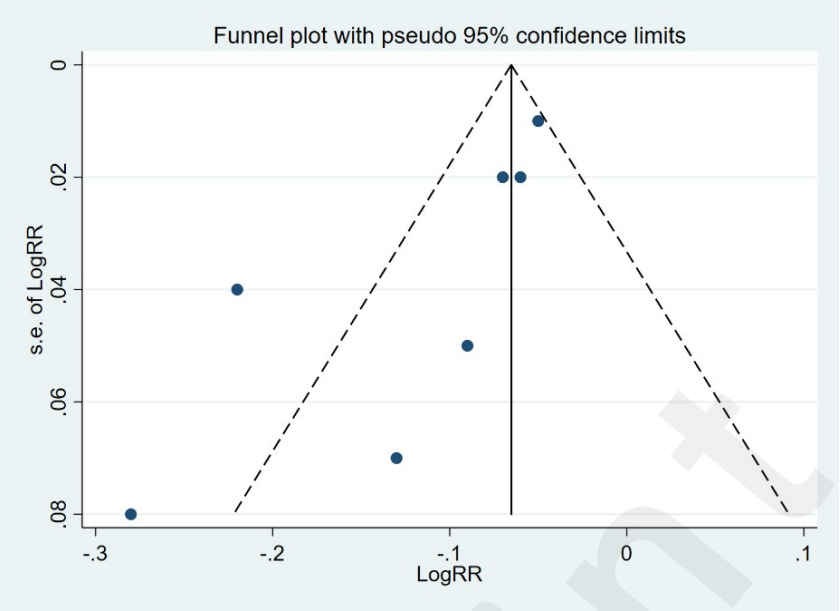

Figure 3. Funnel Plot Publication Bias Assessment

This funnel plot shows the possibility of publication bias and small-study effects in the meta-analysis of BMI and mortality in Asian and African TB-HIV patients. The X-axis represents the log risk ratio (logRR), which reflects the magnitude of the effect, while the Y-axis is the standard error, which indicates the precision of the study results (the higher the standard error value, the lower the precision). The funnel plot appears slightly asymmetrical, with a greater concentration of smaller studies showing negative logRR (protective effect of higher BMI), suggesting a potential small-study effect. This may lead to overestimation of the protective effect of IMT on mortality. To validate this alleged publication bias, we conducted Egger's Regression-Based Test and Trim-and-Fill Analysis. The following results were obtained (Table 2).

Table 2. Egger Regression-Based Test Results

Parameters	Coefficient	Std. Error	t	Sig (2–tailed)	95% Confidence Interval	
					Lower	Upper
(Intercept)	-0,033	0,0290	-1,129	0,310	-0,107	0,042
SE	-2,385	0,8893	-2,682	0,044	-4,671	-0,099

Egger's test showed that the intercept was negative with a value of 0.033 and a p-value of 0.310, indicating that the asymmetry was not statistically significant. However, the slope was significantly negative with a value of 2.385 and a p-value of 0.044, suggesting the presence of a small-study effect. This finding implies a potential publication bias, in which smaller studies are more likely to report stronger protective associations between higher BMI and reduced mortality. As a result, while the overall pooled estimate remains statistically robust, the magnitude of the protective effect should be interpreted with caution. Therefore, an additional sensitivity analysis, the trim-and-fill analysis, was conducted (Table 3).

Table 3. Trim-and-Fill Analysis Results

		Effect Size	Std. Error	Z	Sig (2–tailed)	95% Confidence Interval	
						Lower	Upper
Observed		-0,105	0,0223	-4,696	<0,001	-0,148	-0,061
Observed Imputed	+	-0,105	0,0223	-4,696	<0,001	-0,148	-0,061

Trim-and-fill analysis did not identify any potentially missing studies, indicating that the pooled effect size was not substantially influenced by asymmetry in the funnel plot. The observed effect size (LogRR = 0.105; 95% CI: 0.148 to 0.061; $p < 0.001$) remained consistent before and after adjustment, suggesting that the results were robust. However, considering the significant small-study effect detected in Egger's test, the possibility of publication bias cannot be entirely ruled out. From an epidemiological perspective, the negative LogRR value indicates that patients with low BMI (< 18.5 kg/m²) had a higher risk of mortality compared to those with normal or higher BMI. This finding reinforces the importance of nutritional status as a key risk factor for mortality among individuals with TB-HIV co-infection in Asia and Africa.

Discussion

The findings of this meta-analysis reveal a statistically significant association between body mass index and mortality among patients co-infected with tuberculosis and human immunodeficiency virus in Asia and Africa. The overall log risk ratio (LogRR) of -0.10 (95% CI: -0.15 to -0.06), corresponding to a risk ratio (RR) of 0.90 (95% CI: 0.86–0.94), suggests that patients with BMI <18.5 had approximately 10% higher mortality risk compared to those with BMI ≥18.5. These results support the hypothesis that higher BMI confers a protective effect against mortality in TB-HIV co-infected individuals.

This finding aligns with a body of existing literature demonstrating that improved nutritional status is associated with enhanced survival outcomes among TB-HIV patients, including both underweight and overweight populations. For instance, a study in South Africa reported that HIV-infected individuals with a BMI ≤18.5 experienced significantly higher mortality rates compared to those with a BMI >30, with corresponding rates of 10.4 and 1.6 per 100 person-years, respectively [38]. Similarly, Yen et al. (2016) found that TB patients with a BMI <18.5 exhibited significantly increased risks of all-cause mortality (adjusted odds ratio [AOR] 1.66), TB-specific mortality (AOR 2.14), and non-TB mortality (AOR 1.58)

Further supporting evidence is provided by studies conducted in Myanmar and Zimbabwe, which demonstrated that remaining severely underweight or experiencing a decline in BMI during the first month of TB treatment significantly increased mortality among HIV-positive patients with smear-negative and extrapulmonary TB [17]. Conversely, in the same South African cohort, overweight and obese HIV-infected individuals had notably lower mortality risks, with adjusted hazard ratios (AHR) of 0.59 and 0.48, respectively, compared to those with normal BMI [38]. These findings underscore the prognostic value of BMI as an indicator of clinical outcomes in this population.

Malnutrition appears to be a major risk factor contributing to elevated mortality in TB-HIV co-infected patients. In Taiwan, Lai et al. (2017) reported that TB patients with poor nutritional status

had a 2.22-fold higher risk of early death within the first eight weeks of treatment [15]. Likewise, in sub-Saharan Africa, Koethe et al. (2011) found that low baseline BMI at antiretroviral therapy (ART) initiation was a robust predictor of early mortality among HIV-infected adults.

Several biological and clinical mechanisms may underlie the observed association between BMI and mortality. Low BMI often reflects underlying malnutrition, compromising immune function, including reduced CD4 lymphocyte counts. A CD4 count <200 cells/mm³ is widely recognized as a critical threshold of severe immunosuppression, associated with heightened vulnerability to opportunistic infections and increased mortality [39], [40]. Additionally, a high HIV viral load (>100,000 copies/mL) reflects impaired immune control and has been linked to increased incidence of TB and mortality risk.

Beyond immunosuppression, malnutrition may exacerbate systemic inflammation. Individuals with low BMI often display a pro-inflammatory state, characterized by hypercoagulability, endothelial activation, and the development of disseminated intravascular coagulation (DIC)—a complication associated with poor clinical outcomes [40]. Elevated levels of pro-inflammatory cytokines and related biomarkers have also been observed in TB-HIV co-infected patients. They may contribute to tissue damage and multi-organ failure, further elevating the risk of death [41].

In contrast, a higher BMI may provide metabolic and energy reserves that help mitigate the physiological stress of chronic infection. Nutritional status has also been shown to influence treatment efficacy; malnutrition may delay therapeutic response, prolong hospitalization, and worsen overall prognosis [42]. Therefore, comprehensive and individualized nutritional assessments are essential for optimizing treatment outcomes [43]. Furthermore, interactions between food and medications may modulate treatment effectiveness or side effect profiles, reinforcing the bidirectional relationship between nutritional status and treatment success [44].

The implications of these findings are substantial for public health strategies. Given the consistent association between low BMI and increased mortality, nutritional interventions should be considered a fundamental component of TB-HIV management protocols. Timely nutritional support—such as the provision of food supplements and access to nutrient-rich diets—alongside early diagnosis may significantly improve clinical outcomes [6], [45].Community-based strategies that incorporate routine nutritional monitoring and adherence support also hold promise in enhancing survival in this population.

Finally, the integration of nutritional support into ART and directly observed therapy short-course (DOTS) programs should not be seen as ancillary but rather as essential. With strong policy backing, effective use of local resources, and international collaboration, such integrated approaches can improve therapeutic efficacy, reduce complication rates, and alleviate healthcare system burdens. If logistical barriers such as funding and supply chain issues are effectively addressed, this model offers a viable and sustainable long-term solution for managing TB-HIV co-infection in high-burden regions across Asia and Africa.

Conclusion and recommendations

This systematic review and meta-analysis demonstrate that a low Body Mass Index (BMI) significantly increases the risk of mortality among patients with tuberculosis (TB) and HIV co-infection in Asia and Africa. The pooled log relative risk (LogRR) was –0.10 (95% CI: –0.15, –0.06), indicating that patients with BMI <18.5 had approximately 10% higher mortality risk compared to those with BMI ≥18.5. These findings affirm that nutritional status is not only a modifiable factor but also a critical prognostic indicator in the clinical management of TB-HIV co-infected patients.

Despite observed heterogeneity across studies and the presence of small-study effects, the protective association between higher BMI and lower mortality remained consistent and statistically robust. These results highlight the urgent need to incorporate nutritional assessment and interventions as integral components of TB-HIV care, particularly in resource-constrained settings.

In light of these findings, we recommend that national TB and HIV programs in Asia and Africa systematically integrate routine nutritional screening, particularly BMI monitoring, into standard clinical protocols. Interventions should prioritize early nutritional support, especially for underweight patients and those initiating antiretroviral therapy (ART). Further research is needed to assess the effectiveness of targeted nutritional interventions in reducing mortality. Moreover, strengthening the integration of TB, HIV, and nutrition services is essential to optimize treatment outcomes and reduce preventable deaths among this highly vulnerable population.

Limitation

This study has several limitations that should be considered when interpreting the findings. First, the number of included studies was limited to seven, which may restrict the generalizability of the results and precluded further subgroup analyses, such as stratification by age, sex, or ART status. The limited number of eligible studies reflects the narrow availability of cohort data with mortality outcomes in TB-HIV co-infected populations within Asia and Africa, rather than a lack of relevance. This highlights the need for more prospective research in these high-burden region. Second, substantial heterogeneity was observed across studies (I^2 = 78%), potentially due to differences in study populations, settings, or methods of BMI measurement and mortality assessment. Third, Although the Egger's intercept was not statistically significant, the presence of a significant small-study effect raises concern for potential publication bias. Smaller studies may have been more likely to report protective associations between higher BMI and reduced mortality.

Fourth, variation in BMI categorization and measurement timing across studies could introduce misclassification bias. Fifth, while cohort designs allow for temporal inference, causal relationships between BMI and mortality cannot be definitively established due to potential residual confounding. Important covariates such as CD4 cell count, viral load, ART adherence, socioeconomic status, and comorbidities were not uniformly reported and therefore not adjusted for in this meta-analysis. Lastly, the inclusion of only English-language publications may introduce language bias, potentially excluding relevant studies published in other languages from Asia or Africa.

Despite these limitations, the study provides robust and consistent evidence of the prognostic value of BMI in TB-HIV co-infected populations and underscores the need for integrated nutritional interventions in clinical practice.

Acknowledgments

The author would like to sincerely thank the Indonesia Endowment Fund for Education Agency (LPDP) under the Ministry of Finance of the Republic of Indonesia for the grant that supported this research.

Funding

Indonesia Endowment Fund for Education Agency (LPDP).

Conflicts of interests

The authors declare no conflicts of interests.

Data availability

All data analyzed during this study are included in this published article.

Author contributions

MAS and TYM were responsible for developing the protocol. They were involved in various aspects of the study, including designing the study, selecting the eligible studies, extracting data, performing statistical analyses, drafting the initial versions, and revising the manuscript. PNC, WWL, and LAN edited the final draft of the manuscript, which was subsequently read and approved by the first and second authors.

Declaration of Use of AI in Academic Writing

Artificial intelligence tools (ChatGPT) were used during the writing process to improve the readability and language quality of this manuscript. The author affirms full responsibility for the content and interpretation presented.

Ethics approval and consent to participate

Not applicable to this section because it was conducted using secondary data.

Abbreviations

AIDS	Acquired Immunodeficiency Syndrome
ART	Antiretroviral Therapy
BMI	Body Mass Index
ETB	Extra Pulmonary Tuberculosis
TB	Tuberculosis
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analysis
RR	Risk Ratio
MeSH	Medical Subject Headings
HIV	Human Immunodeficiency Virus

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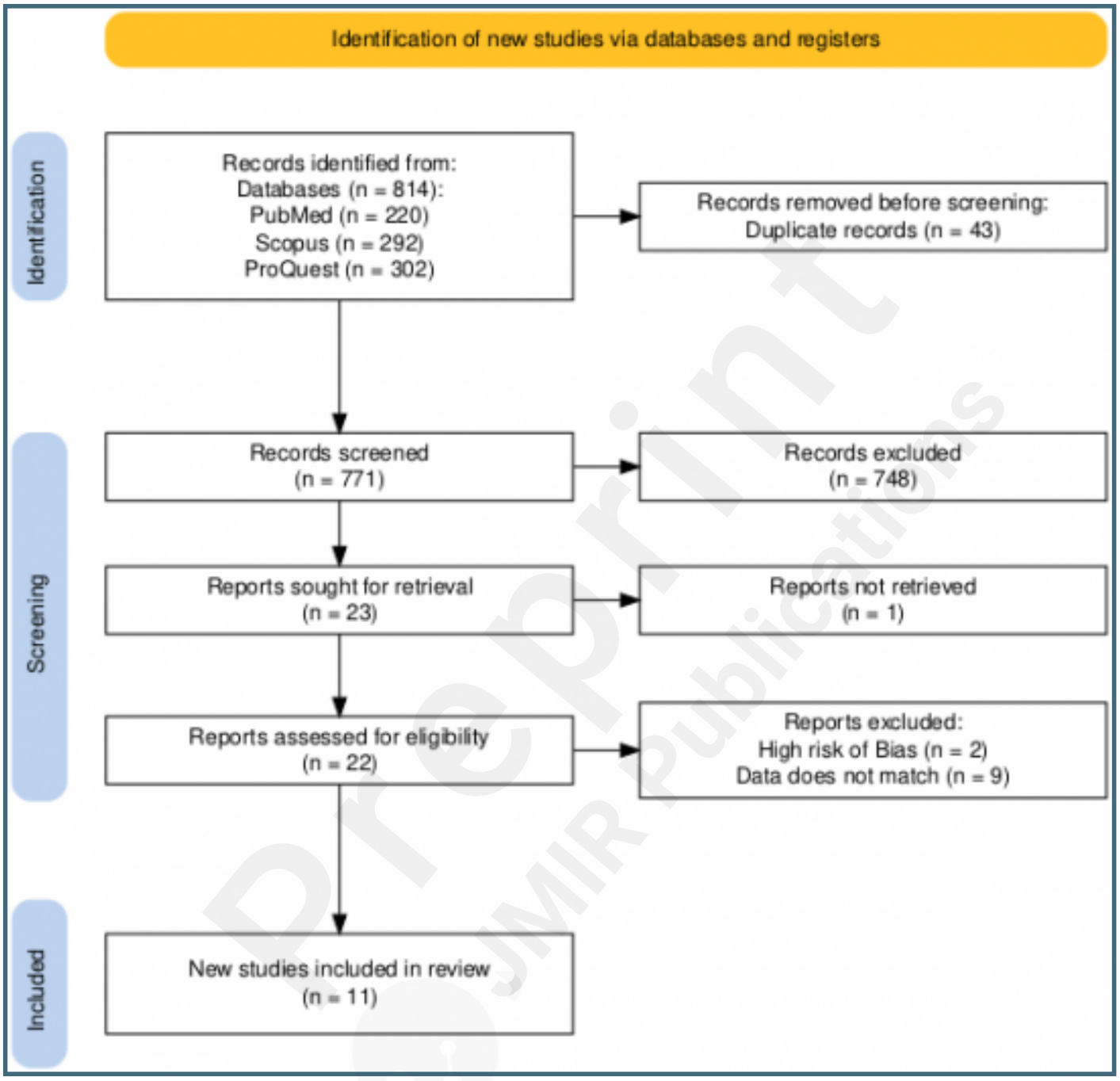
Supplementary Files

PRISMA Checklist.
URL: http://asset.jmir.pub/assets/19ccb82c833a00f4e4746e56c84ef21f.docx

Figures

PRISMA Flowchart.



TOC/Feature image for homepages

Feature Image.