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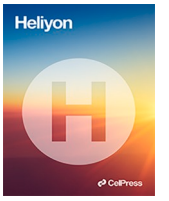

A systematic review and meta-analysis on the correlation between HIV infection and multidrug-resistance tuberculosis

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ABSTRACT

Background: The emergence of multidrug-resistant tuberculosis (MDR-TB) in HIV-positive people poses a significant challenge to international efforts to eradicate tuberculosis (TB). Many studies found conflicting results when examining the correlation between HIV and MDR-TB. The purpose of the present investigation was to comprehensively review the literature on the association between HIV infection and MDR-TB in order to evaluate the impact of HIV on MDR-TB worldwide.

Methods: Utilizing the databases PubMed, Scopus, Google Scholar, and ScienceDirect, studies published between January 2000 and March 2023 that are eligible for meta-analysis were selected. Using the random-effects model, the aggregated odds ratio of the empirical relationship between HIV and MDR-TB was calculated, along with a confidence interval ranging from 0 to 95 %. Examining the asymmetry of the funnel plot and utilizing Egger's and Begg's test, the possibility of publication bias was investigated. The extent of heterogeneity was determined using the I2 statistics.

Results: Through a database search, we identified 1214 studies, from which we ultimately selected 15 studies involving 9667 patients. The odds ratio of 2.78 (95 % confidence interval: 1.07–7.20) between HIV/AIDS and MDR-TB indicates a significant positive correlation. Tau 2 = 3.46, chi 2 = 1440.46, df = 14, I2 = 99.0 %, z = 2.10, and p 0.05 indicate that there is substantial heterogeneity among pooled studies. Since I^2 is 99 % (>50 %), a random effect model was employed. The percentage of multidrug-resistant HIV-positive patients across all included studies follows a normal distribution, as shown by a Box and whisker plot with a symmetric skewness and a mesokurtic tail and a scatter plot with a significant R2 value below 1 [R2 = 0.2476] showed the positive correlation between multidrug resistance and HIV infection.

Conclusion: HIV infection increases MDR-TB risk, and the preceding pooled analysis showed an increased risk trend. Thus, MDR-TB, especially in HIV-positive patients, requires early case detection, quality-assured bacteriology diagnosis, and an effective infection control program.

1. Introduction

Tuberculosis, a chronic infectious disease caused by Mycobacterium tuberculosis, is the second top infectious killer after COVID-19 and 13th major cause mortality around the world [1]. HIV and the immunosuppression it causes have contributed to an increase in the

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incidence and prevalence of tuberculosis [2]. According to projections for the year 2021, approximately 6.5 million people worldwide will die due to HIV-related causes [3]. HIV-positive individuals are 26–31 times more likely to develop tuberculosis than HIV-negative individuals [4]. The convergence of these two epidemics wreaks havoc in high-incidence environments. The complex relationship between HIV and tuberculosis involves reciprocal deterioration of disease severity [5]; therefore, it is essential to diagnose infection and prevent reactivation of latent TB in HIV-infected individuals in order to reduce morbidity and mortality associated with these diseases [6]. The Guideline Development Group of the World Health Organization (WHO) recommends both isoniazid and rifampin for the routine anti-tuberculosis treatment of HIV-positive patients [7]. MDR tuberculosis, also known as multidrug-resistant tuberculosis, is a new form of tuberculosis caused by tuberculosis pathogens that are resistant to the two most effective TB medications, isoniazid and rifampin, which are administered to all tuberculosis patients [8]. The prevalence of TB-HIV co-infection is highly variable, ranging from 3.8 % to 72.3 % among TB patients. MDR-TB is becoming a significant concern for tuberculosis control efforts, and its prevalence is increasing globally. It is a problem not only from the standpoint of public health but also in the context of the global economy, particularly in underdeveloped nations where there is no national program-level treatment for MDR-TB [9,10]. Since 1994, the WHO has compiled and analysed data on the prevalence of drug-resistant tuberculosis in member states and territories and projected the annual growth rate and proportion of tuberculosis cases with varying levels of resistance to first- and second-line drugs for the previous calendar year [11]. In the year 2021, approximately 450 000 cases of MDR- TB or Rifampicin Resistant (RR)TB were reported globally (95 % confidence interval: 399, 000–501,000). The COVID-19 pandemic had a negative impact on tuberculosis (TB) detection in 2020 and 2021, resulting in an increase in TB incidence. In 2021, MDR/RR- TB was responsible for 191 000 deaths (range: 119 000–264 000) [12]. Compared to standard tuberculosis, MDR tuberculosis is associated with a higher mortality rate and a substantially shorter survival duration [13]. HIV-positive individuals are more likely to contract an MDR infection because Human Immunodeficiency Virus compromises the functionality of the immune system, resulting in immunosuppression. Consequently, the body's ability to combat tuberculosis pathogens is significantly hindered. HIV and MDR-TB are equally lethal when paired together Although the impact of HIV infection on MDR-TB is vital to public health, the relationship between HIV and MDR-TB is inadequately understood. Regarding the relationship between HIV co-infection and treatment resistance in tuberculosis patients, a number of studies have produced contradictory conclusions. Some found higher infection risk of MDRTB in HIV-positive individuals while other studies didn't [14–16]. As a result, HIV-co-infected patients should be closely monitored for MDR- TB, since it is largely unknown whether HIV co-infection increases the risk of developing multidrug resistance TB. Therefore, this study evaluated the correlation between HIV infection and multidrug-resistant tuberculosis by conducting a literature review and meta-analysis of the selected articles [17–31].

2. Materials & methods

The present meta-analysis was undertaken following the Preferred Reporting Items of Systematic Reviews and Meta-Analyses (PRISMA) guidelines [32].

2.1. Data sources and searches

An inclusive literature search was conducted without any restrictions on the year and language of publication utilizing the electronic databases Cochrane Library, EMBASE, Scopus, and PubMed up to March 2023. In addition, relevant meta-analyses and studies' bibliographies were also searched. An inclusive literature search was conducted with the following inclusion criteria: (i) cross-sectional or retrospective studies related to the association of MDRTB in HIV-positive individuals; (ii) HIV-positive person with multidrug resistance or resistance to different first or second line anti-TB medications; and (iii) Studies providing the primary outcome data: percentage of multidrug resistance and resistance to isoniazid, rifampin or other anti-TB drugs (iv) articles published in English language using the following keywords: "HIV-positive patients"; "Tuberculosis" OR "TB"; "Multidrug resistance tuberculosis" OR "MDRTB" "Isoniazid resistance"; "Rifampin resistance"; "Multi-drug resistance" OR "MDR"; "Meta-analysis"; "cross-sectional studies, "systematic review". We used the Boolean operator "AND" to join the Medical Subject Headings (MeSH) with the text keywords within the search strategy. Firstly, duplicate articles were deleted from the search results, followed by a title and abstract screening of the remaining articles. Finally, the full texts of all eligible studies were retrieved and reviewed for inclusion and exclusion based on the inclusion and exclusion criteria as per the PRISMA guidelines.

2.2. Study selection

The literature search was conducted separately by two authors. Through discussion, a consensus was obtained in the event of dispute. The following conditions must be met for a study to qualify: (a) Cross-sectional studies evaluating the association of MDRTB with HIV/AIDS; (b) studies evaluating the primary outcomes: multidrug resistance and resistance against first or second line of Anti-TB medications. Exclusion criteria included clinical trials with a follow-up time of less than one month. Studies that were conducted on healthy volunteers or on HIV patients suffering from conditions other than TB were also not included in this meta-analysis.

2.3. Data extraction

A computerised data extraction form was developed in Microsoft Excel and utilised for the purpose of documenting the fundamental information of the studies selected for this meta-analysis. This included the first author's name, the year of publication, Journal of publication, type of Study, country where the study was conducted, duration of Study, total number of patients studied, gender of

patients, prevalence of MDRTB, HIV coinfection and resistance to drugs in patients. Two different authors independently extracted the data, and then the results of both authors' extractions were compared. In the case of divergent opinions, an agreement was obtained via discussion. Depending on the circumstances, a third author was also included.

2.4. Quality assessment

The Cochrane Risk of Bias tool was applied in order to evaluate the methodological validity of each and every study that was incorporated into the meta-analysis. During the process of data extraction, selected articles were given a score of "low," "high," or "some concern." on the basis of their pattern of generation of random sequences, concealment of allocation, blinding of participants and staff members, blinding of outcome assessment, insufficiency of outcome data, selective reporting, and other possible sources of bias. Later, using RevMan software version 5.4 [33] was used to construct a quality evaluation risk of bias summary and graph. Egger's test [34], Begg's test [35] and Deek's funnel plot [36] were also used to analyze the publication bias using the MedCalc software [37].

2.5. Data analysis

RevMan version 5.4.0 and MedCalc software were used throughout the data processing procedure. The Mantel-Haenszel approach with the random effect model [38] was used in order to calculate the pooled odds ratio and the 95 % confidence interval (CI) for the study outcome. Result was considered statistically significant if its p-value was less than 0.05 [39]. Randomized controlled trials (RCTs) that did not have any outcomes' events recorded in the research groups were excluded from the analysis. Forest plot [40] was

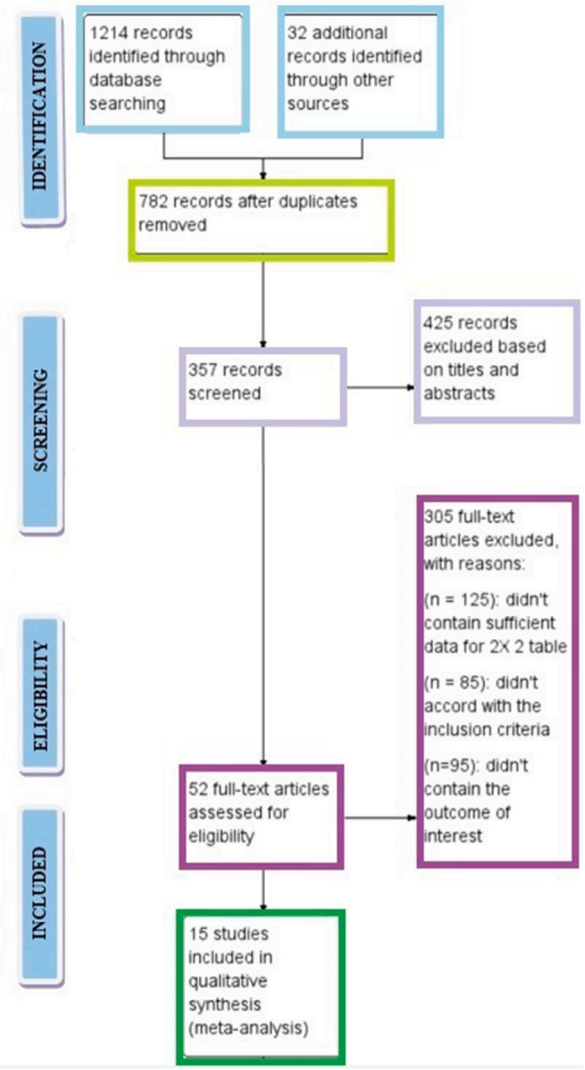

Fig. 1. PRISMA flowchart of selection of studies.

used to visually represent the risk ratio and the 95 % confidence range. I^2 statistics [41] was used to assess the level of heterogeneity present in the study's results. In instances where the level of heterogeneity was greater than or equal to 50%, a random-effects model was used to analyze the data. In contrast, a fixed-effects model was used when the level of heterogeneity was less than or equal to 50%. Scatter plot [42], Box and whisker plot [43] and Bar plot [44] were designed to evaluate the correlation between HIV infection and Multidrug-Resistance Tuberculosis.

Table 1
Characteristics of the included studies.

Study et al.	Journal of publication	Type of Study	Country	Duration of Study	Total number of patients	Gender of patients	Prevalence of MDRTB (%)	HIV coinfection present in patients (%)	Resistance to Drugs (%)
Arthur et al., 2022 [17]	The International journal of Tuberculosis and lungs disease	Cross-sectional study	Mozambique	9 months	709	57.2 % M; 42.8 % F	22.5 %	25.5 %	INSR 5.2 %; MDR 3.4 %
Campos et al., 2003 [18]	Emerging Infectious diseases	Cross-sectional study	Peru	12 months	415	33 % M; 67 % F	43 %	25 %	INR 52 %; RR 48 %; SR 24 %; ER 48 %; MDR 35 %
Dubrovina et al., 2008 [19]	The International journal of Tuberculosis and lungs disease	Cross-sectional study	Ukraine	12 months	1496	82 % M; 18 % F	16 %	27 %	INR 39.2 %; RR 30.5 %; MDR15 %
Haar et al., 2007 [20]	Emerging Infectious diseases	Cross-sectional study	Netherlands	12 months	1702	71 % M; 29 % F	17 %	32 %	INR 23.1 %; RR19.8 %; MDR 5 %
Isaakidis et al., 2014 [21]	PLOS ONE	Cross-sectional study	India	10 months	1724	60.4 % M; 39.6 % F	34 %	100 %	INR 16.2 %; RER 8.8 %; MDR 4.1 %
Joseph et al., 2006 [22]	AIDS	Cross-sectional study	Haiti	2 years	330	54 % M; 46 % F	36 %	40 %	INR 15 %; RR 9 %; SR 2 %; ER 8 %; MDR 6 %
Joh et al., 2012 [23]	Infectious diseases, Microbiology and parasitology	Cross-sectional study	Korea	6 years	55	98.2 % M; 0.2 % F	27.8 %	32.7 %	INRR 61.8 %; MDR 32.7 %
Lee et al., 2016 [24]	Yonsei Medical Journal	Cross-sectional study	Korea	8 years	1606	59.4 % M; 40. 6 % F	11.1 %	32.7 %	INR 13.3 %; RR11.1 %; PR 4.4 %; MDR11.1 %
Lee et al., 2021 [25]	Infection and chemotherapy	Cross-sectional study	Korea	22 years	87	71.4 % M; 28 6 % F	32.7 %	100 %	INR 20.5 %; RR 15.9 %; MDR 15.9 %
Mai et al., 2017 [26]	Journal of Global Antimicrobial resistance	Cross-sectional study	Vietnam	5 years	200	84.5 % M; 15.5 % F	63.8 %	63.8 %	INR 10 %; SR 14 %; MDR 42 %
Post et al., 2014 [27]	The Journal of infection	Cross-sectional study	Europe	2 years	587	18 % M; 82 % F	62.5 %	61.8 %	INR 51 %; RR 33 %; MDR 28 %
Robert et al., 2003 [28]	The European Respiratory Journal	Cross-sectional study	France	8 years	264	69.7 % M; 30.3 % F	16 %	20.8 %	INRR 37.9 %; SER 25.8 %; MDR 45 %
Saldanha et al., 2019 [29]	BMC Infectious diseases	Cross-sectional study	Western India	3 years	200	67 % M; 33 % F	12.5 %	60 %	INR 9 %; RR 2.5 %; MDR 12.5 %
Sintchenko et al., 2018 [30]	The American journal of tropical medicine and hygiene	Cross-sectional study	Vietnam		200	86.5 % M; 13.5 % F	42 %	87 %	INRR7.4 %; MDR 8.5 %
Wang et al., 2021 [31]	Journal of Global Antimicrobial resistance	Cross-sectional study	Southwest China	3 years	201	84.6 % M; 15.4 % F	7 %	7 %	INRR 5 %; MDR 7 %

Table 2
Risk assessment of included studies.

Study ID and Year	Arthur et al., 2022 [17]	Campos et al., 2003 [18]	Dubrovina et al., 2008 [19]	Haar et al., 2007 [20]	Isaakidis et al., 2014 [21]	Joseph et al., 2006 [22]	Joh et al., 2012 [23]	Lee et al., 2016 [24]	Lee et al., 2021 [25]	Mai et al., 2017 [26]	Post et al., 2014 [27]	Robert et al., 2003 [28]	Saldanha et al., 2019 [29]	Sintchenko et al., 2018 [30]	Wang et al., 2021 [31]
Did the study avoid inappropriate exclusions	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Did all patients receive the same reference standard	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Were all patients included in the analysis	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Was the sample frame appropriate to address the target population?	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Were study participants sampled in an appropriate way?	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Were the study subjects and the setting described in detail?	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Were valid methods used for the identification of the condition?	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Was the condition measured in a standard, reliable way for all participants?	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y

3. Results

3.1. Literature search results

Fig. 1 depicts the PRISMA chart for the selection of research. Through a comprehensive search of online databases, 1214 studies were identified in total. After eliminating duplicates, the abstracts and titles of 782 studies were screened. Then, 357 studies were screened, and 305 of them were excluded because they didn't have enough information for a 2 x 2 table, didn't report the result of interest, or didn't meet the criteria for inclusion. Later 52 articles were qualified for full-text evaluation and among them only fifteen relevant publications were finally included in the present meta-analysis. The characteristics of all included trials including 9776 patients are shown in Table 1. Included studies evaluated the association between HIV infection and MDRTB and reported the primary outcomes: multidrug resistance and drug resistance to first- or second-line Anti-TB medications.

3.2. Risk of bias assessment and publication bias

The quality assessment of the included studies is assessed as shown in Table 2. Fig. 2 depicts a summary of the risk of bias, whereas Fig. 3 depicts a graph showing the risk of bias. Six of the fifteen included studies had a low risk of bias whereas, six studies had a moderate risk attributable to bias due to confounding and missing data. Three of the included studies arising from the measurement of the exposure. Fig. 4 depicts the funnel plot, which indicated a low probability of publication bias with a non-significant p value of

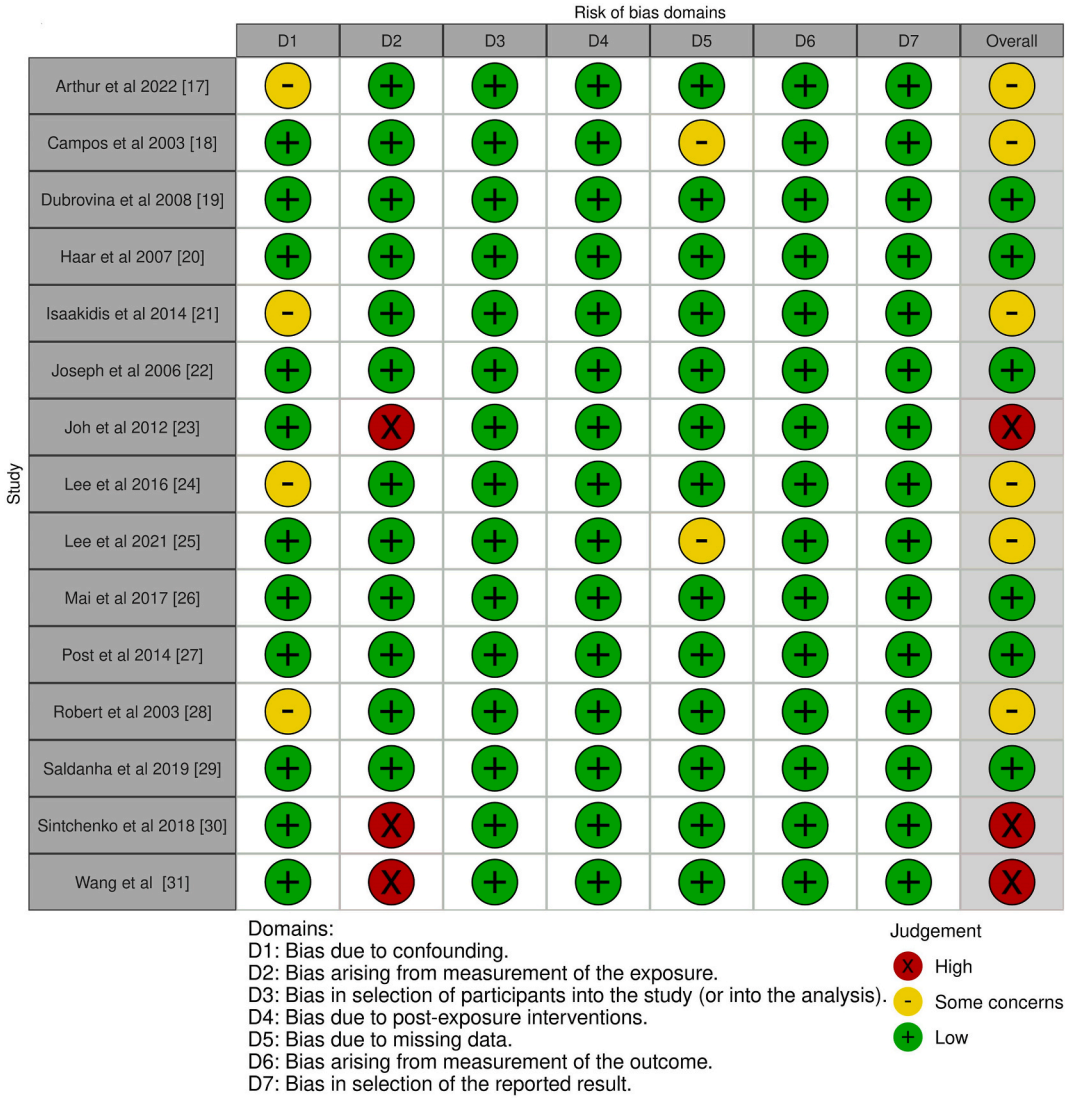

Fig. 2. Risk of Bias summary.

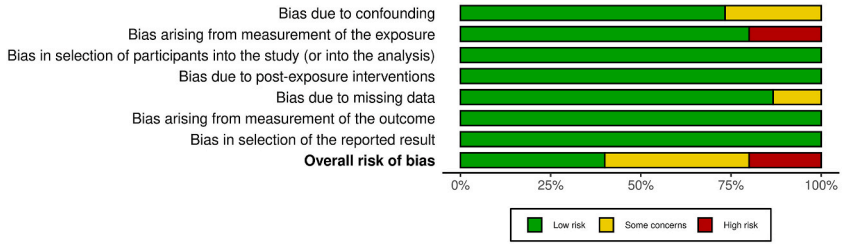

Fig. 3. Risk of bias graph.

0.256 for Begg's test and 0.412 for Egger's test.

3.3. Statistical outcomes

Fig. 5 summarizes the measure of association between HIV/AIDS and MDR-TB based on the data extracted from the 15 selected studies. The forest plot revealed a significant positive association between HIV/AIDS and MDR-TB with a pooled OR of 2.78 (95 % confidence interval: 1.07–7.20). There is considerable heterogeneity amongst pooled studies with Tau^2 value of 3.46, chi ^{2} value 1440.46, df value 14, I^2 value 99 %, z-value 2.11 and $p < 0.05$. Since the I^2 value is greater than 50 %, a random effect model was used.

All the 15 included studies showed the existence of MDRTB in HIV-positive patients with substantial percentage of multi-drug resistance and resistance to Isoniazid, rifampin and other anti-TB medications as shown in Table 3 and Bar plot shown in Fig. 6. Among these 15 studies, all MDRTB and HIV-positive individuals have multidrug-resistant. 10 studies [18-22,24-27and29] showed resistance to first line anti-TB drug Isoniazid and 8 studies [18–20,22,24,25,27,29] showed resistance to another first line anti-TB drug Rifampin. Along with this, 3 studies [18,22,26] showed streptomycin resistance; one study [17] showed isoniazid streptomycin resistance, two studies [18,22] ethambutol resistance; one study [21] showed rifampin and ethambutol resistance, four studies [23,28, 30,31] showed isoniazid and Rifampin resistance, one study [24] showed Pyrazinamide resistance and one study [28] showed Streptomycin and ethambutol Resistance. The variation among the different data sets was assessed by the Box and whisker plots shown in Figs. 7 and 8. Fig. 7 shows the variation among data sets of percentage resistance of all drug types in MDRTB and HIV-positive patients of all included studies with the median value ranges from 5.2 to 28, Q1 ranges from 5.2 to 13.3 and Q3 ranges from 5.2 to 49.84. Fig. 8 shows the variation particularly among the main data sets of percentage multidrug resistance and percentage of Isoniazid and rifampin resistance in MDRTB and HIV-positive patients of all included studies with the median value ranges from 12.5 to 145, Q1 ranges from 6.5 to 112 and Q3 ranges from 30.5 to 172. Both the box and whisker plots have symmetrical skewness shape and mesokurtic tail shape which indicates normal distribution of data points and positive correlation between MDRTB and HIV infection among patients. Similar result is indicated by the scatter plot shown in Fig. 9 with R^2 value of less than 1 [$R^2 = 0.2476$] confirms positive correlation between multidrug resistance and HIV infection.

4. Discussion

HIV-positive individuals have a compromised immune system, which makes them more likely to acquire multidrug-resistant tuberculosis (MDR-TB) disease if they become infected. These individuals also have an increased rate of mortality. As a result, this meta-analysis was carried out in order to investigate the correlation between HIV infection and MDRTB. In this investigation, 15 relevant articles relating to the connection between MDRTB and HIV-positive individuals were considered. The pooled OR was 2.78, with a 95 % confidence interval of 1.07–7.20. HIV-positive people in the population were three times more likely to get disease,

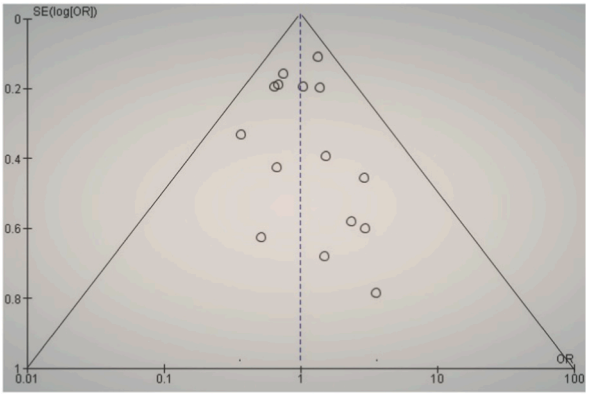

Fig. 4. Funnel plot.

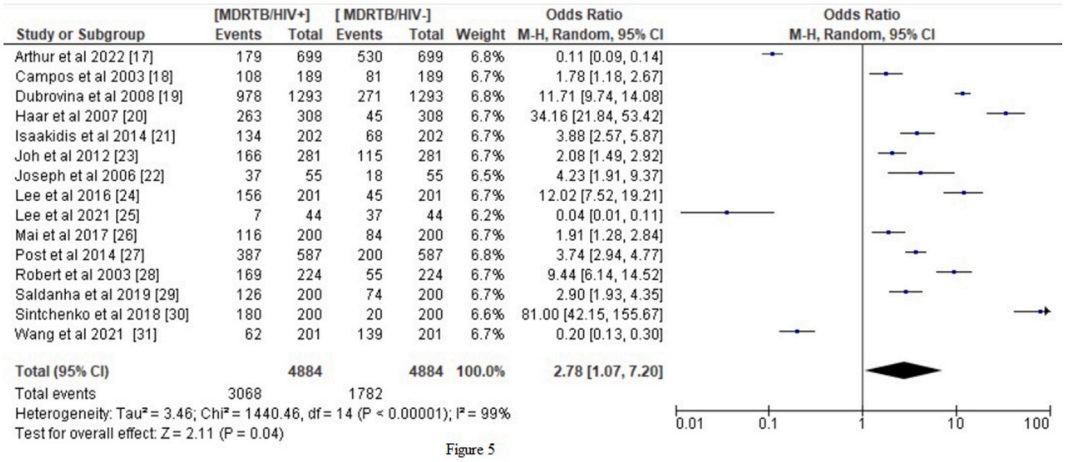

Fig. 5. Forest plot Odds ratio of the included studies.

Table 3
Primary outcome of the Included studies.

Study	MDR+	MDR-	MDRTBHIV	INR (%)	RR (%)	SR (%)	INSR (%)	ER (%)	RER (%)	INRR (%)	PR (%)	SER (%)
Arthur et al. [17]	3.4	96.6	179	–	–	–	5.2		–	–	–	–
Campos et al. [18]	35	65	108	52	48	24	–	48	–	–	–	–
Dubrovina et al. [19]	15	85	978	39.2	30.5	–	–	–	–	–	–	–
Haar et al. [20]	5	95	263	23.1	19.8	–	–	–	–	–	–	–
Isaakidis et al. [21]	4.1	95.9	134	16.2	–	–	–	–	8.8	–	–	–
Joseph et al. [22]	6	94	166	15	9	2	–	8	–	–	–	–
Joh et al. [23]	32.7	67.3	37	–	–	–	–	–	–	61.8	–	–
Lee et al. [24]	11.1	88.9	156	13.3	11.1	–	–	–	–		4.4	–
Lee et al. [25]	15.9	84.1	7	20.5	15.9	–	–	–	–	–	–	–
Mai et al. [26]	42	58	116	10	–	14	–	–	–	–	–	–
Post et al. [27]	28	72	387	51	33	–	–	–	–	–	–	–
Robert et al. [28]	45	55	169	–	–	–	–	–	–	37.9	–	25.8
Saldanha et al. [29]	12.5	87.5	126	9	2.5	–	–	–	–	–	–	–
Sintchenko et al. [30]	8.5	91.5	180	–	–	–	–	–	–	7.4	–	–
Wang et al. [31]	7	93	62	–	–	–	–	–	–	5	–	–

MDRTB: Multidrug-Resistant Tuberculosis; HIV: Human immunodeficiency virus; INR: isoniazid resistance; RR: rifampin resistance; INRR: isoniazid rifampin resistance; SR: streptomycin resistance; INSR: isoniazid streptomycin resistance ER: Ethambutol resistance; PR: Pyrazinamide resistance; SER: Streptomycin and ethambutol Resistance; RER: rifampin and ethambutol resistance; MDR: Multidrug-Resistance.

corresponding to an odds ratio of 2.78. The aggregated studies exhibited considerable heterogeneity ($I2 = 99$ %, Z-effect $= 2.11$, $p < 0.05$). A high heterogeneity shows that the proportion of the variance in observed effects is due to variance in genuine effects rather than sampling error [45], and a p value of less than 0.05 indicates the statistical significance of the meta-analysis results [46].

Since MDRTB is defined as the presence of single or multiple drug resistance in M. tuberculosis against first- and second-line anti-TB drugs like rifampin, isoniazid, streptomycin, ethambutol, and others, we found that HIV-positive patients in the included population also showed significant levels of multidrug resistance or resistance to certain anti-TB drugs from our thorough analysis of the 15 selected studies. when the extracted drug resistance percentage in HIV-positive individuals was plotted as bar plots, where percentage of multidrug resistance or individual drug resistance of each included study was represented as a bar, then the size of the bar represents the significant numeric value and existence of MDRTB in HIV-positive patients. Similar results are supported by the box and whisker plot, which shows a normally distributed set of numbers with significant minimum, first quartile, median, third quartile, and maximum values [47], and by the scatter plot, which shows a positive correlation between MDRTB and HIV infection based on the significant R2 value of less than 1 [48]. These findings conclude that HIV-positive people, due to their weakened immune systems, are very susceptible to MDRTB and require additional precautions.

In conjunction with the findings of a prior meta-analysis and systematic review, our findings have been analysed to determine whether or not there is a correlation between HIV/AIDS and MDRTB. For example, a systematic review and meta-analysis conducted by Mesfin et al., in 2013 [49] found a pooled OR of 2.28 with a 95 % CI of 1.52–3.04 for primary multi-drug-resistant tuberculosis. This study concludes that there is a moderate association between HIV/AIDS and MDR-TB among population-based studies, and it suggests increasing the amount of antiretroviral treatment as well as collaborating between HIV and TB control programs. Additionally, Sultana

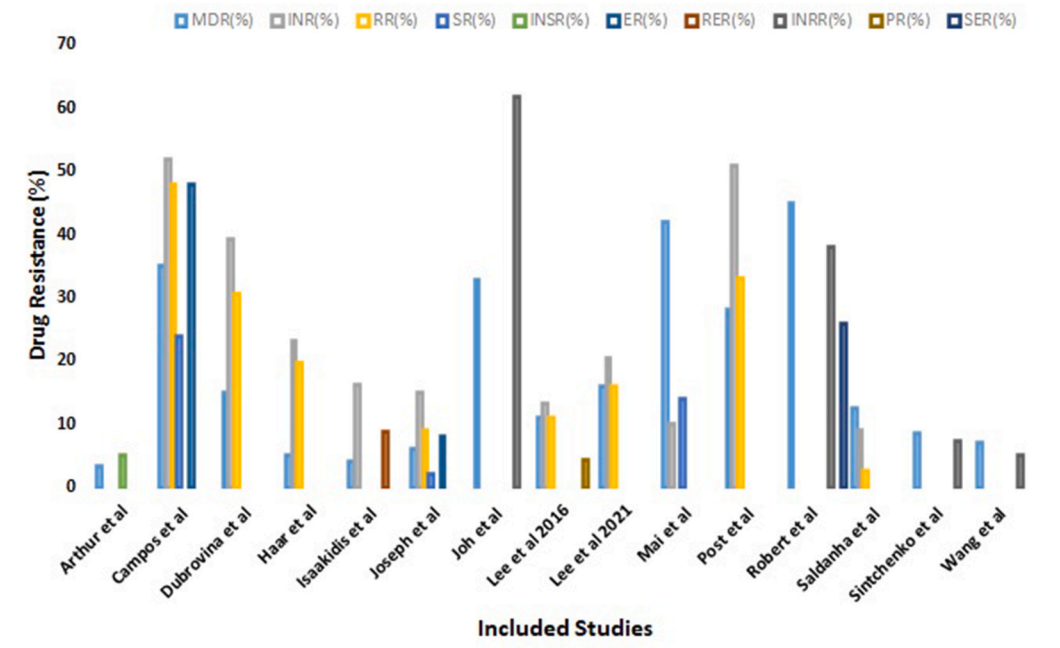

Fig. 6. Bar plots showing multidrug and individual drug resistance.

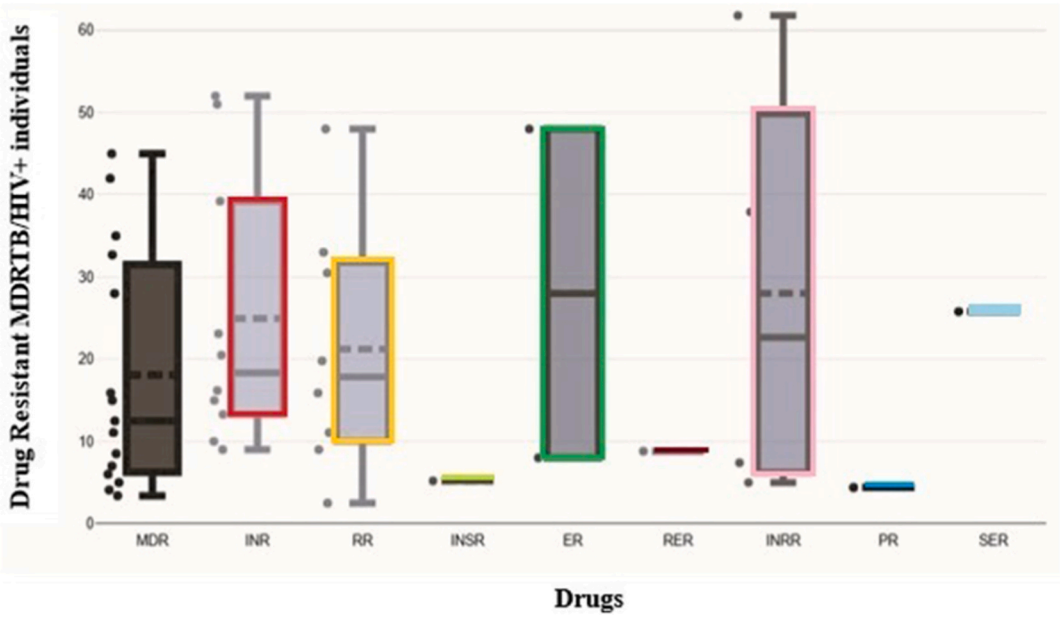

Fig. 7. Box and Whisker plot comparing multidrug and individual drug resistance.

et al., in 2021 [50] achieved an OR of 2.76 with a 95 % confidence interval ranging from 1.70 to 4.46, which indicates that HIV infection increases the risk of MDR-TB. The occurrence of co-infection of HIV and TB is more prevalent among males compared to females, which can be attributed to both biological traits and socioeconomic factors. The rising prevalence of multidrug-resistant tuberculosis (MDR-TB) in HIV patients is indicative of a high risk and an upward trend of MDR-TB among HIV-positive individuals, both of which call for extremely effective strategies for prevention and control.

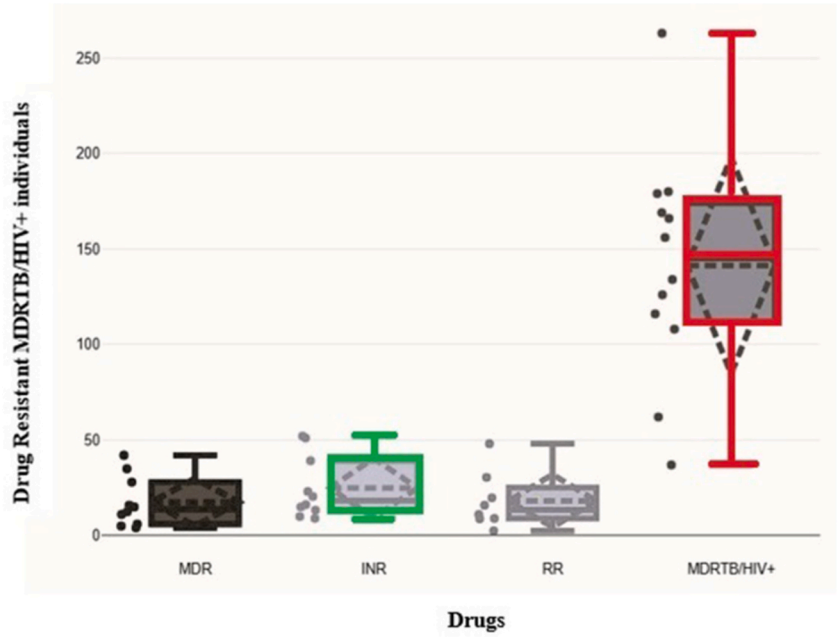

Fig. 8. Box and Whisker plot comparing multidrug and Isoniazid and Rifampin drug resistance.

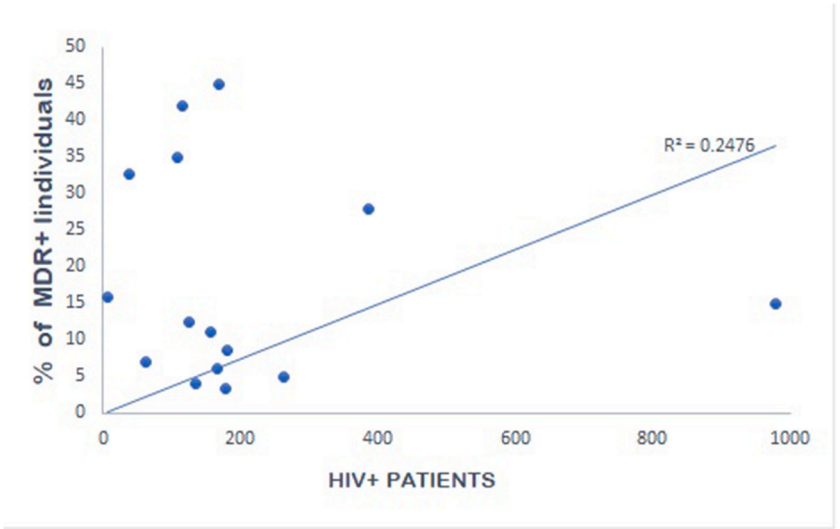

Fig. 9. Scatter Plot of MDRTB in HIV-positive individuals.

5. Limitation

There are certain limitations to this meta-analysis. Firstly, while this analysis was conducted with the suggested methodological rigor, the results are constrained by the availability of just 15 studies with moderate to high heterogeneity. Secondly, all of these studies were undertaken in countries with a high incidence of tuberculosis, limiting the worldwide applicability of this research. Thirdly, the estimations included in the analysis were from observational studies that are at high risk of being influenced by variables unrelated to either HIV or MDR-TB. And lastly, odds ratio values were mostly employed to determine the association between MDRTB and HIV infection, which may introduce bias when comparing the outcomes of cross-sectional studies of varying durations.

6. Conclusions

This meta-analysis showed considerable but limited evidence of HIV-associated MDR-TB. Despite some variation between cross-

sectional, surveillance, and institution-based studies, this study concludes that HIV infection is significantly correlated with MDR-TB. The findings substantially impact public health and programmatic work. Multidrug-resistant tuberculosis (MDR-TB) detection, commencement, and scaling up of antiretroviral treatment, as well as HIV/TB interaction, must be investigated and strengthened. Early case detection, quality-assured bacteriology diagnosis, and an effective infection control program can reduce the spread of MDR-TB, especially in HIV-positive patients and healthcare facilities.7. Additional Information.

Ethics approval and consent to participate

Ethical approval was not required as this study was based on publicly available data'.

Consent to participate

N/A.

Consent for publication

N/A.

Availability of data and materials

All data generated or analysed during this study are included in this article. Further enquiries can be directed to the corresponding author.

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Additional information

No additional information is available for this paper.

MDRTB: Multidrug-Resistant Tuberculosis; HIV: Human immunodeficiency virus; M: Males; F: Females; INR: isoniazid resistance; RR: rifampin resistance; INRR: isoniazid rifampin resistance; SR: streptomycin resistance; INSR: isoniazid streptomycin resistance ER: Ethambutol resistance; PR: Pyrazinamide resistance; SER: Streptomycin and ethambutol Resistance; RER: rifampin and ethambutol resistance; MDR: Multidrug-Resistance.

CRediT authorship contribution statement

Yulong Song: Conceptualization. **Qian Jin:** Formal analysis. **Jiahi Qiu:** Investigation, Methodology, Validation. **Dan Ye:** Validation, Writing – original draft, Writing – review & editing.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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