Risk Factors for Mycobacterium Tuberculosis Infection Among HIV/AIDS Populations in China

Zhao Junpeng[1,2,3], Richard Avoi[1*], Azman Bin Atil Azmi[1], Zheng Baiqin[2], Wang Lei[2], Qiang Rundong[2], Cao Huihui[2], Gao Weilin[2], Zhang Xu[2], Du Ruihuan[2], Yao Yuhong[4], Qi Wenjie[4], Wang Lifang[5]

Abstract

Background: HIV/TB coinfection remains a significant concern, particularly in high-risk populations. In China, the HIV/AIDS population is at a heightened risk for TB, with those infected showing a 20-37 times higher likelihood of developing TB. This study aims to explore factors contributing to Mycobacterium tuberculosis (MTB) infection within the HIV/AIDS population in Hebei Province, China, a region with a notable TB burden despite its moderate HIV prevalence. Method: A retrospective cohort study was conducted using data from the Infectious Disease Monitoring System of the China Center for Disease Control and Prevention (IDMS CDC). Data were collected from HIV/AIDS patients in high-risk counties of Hebei Province, focusing on demographic, clinical, and transmission-related factors. A total of 608 HIV/AIDS patients were included, with 504 completing the cohort study. The analysis employed Cox proportional hazards regression to assess the relationship between transmission routes, CD4+ T lymphocyte counts, and MTB infection. Results: Among the 504 participants, 54 developed TB, with significant correlations found between transmission routes and initial CD4+ T lymphocyte counts. HIV patients with a same-sex transmission route were 4.77 times more likely to develop TB compared to those with blood-borne transmission. Furthermore, individuals with an initial CD4+ count of 0–350/μl had nearly three times the risk of TB infection compared to those with higher counts. These findings highlight the critical role of immune status and transmission routes in determining TB infection risk. Conclusion: This study underscores the importance of CD4+ T lymphocyte counts and transmission routes as key predictors of TB risk in HIV-positive individuals. Tailored interventions, including targeted TB screening for MSM populations and those with lower CD4+ counts, are crucial for improving TB prevention and control.

Keywords: HIV-TB coinfection, Hebei Province, CD4+ T lymphocytes, Transmission routes, Tuberculosis prevention.

Significance | This study identified key factors influencing MTB infection risk in HIV/AIDS patients in Hebei, guiding effective TB prevention strategies.

*Correspondence. Richard Avoi, Faculty of Medicine and Health Sciences, Universiti Malaysia Sabah, Jalan UMS, 88400 Kota Kinabalu, Sabah, Malaysia. E-mail: richard.avoi@ums.edu.my.

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Introduction

On November 7, 2023, the World Health Organization (WHO) published the "2023 Global Tuberculosis (TB) Report," highlighting the ongoing global burden of tuberculosis. The report estimated that in 2022, 10.6 million new TB infections occurred worldwide, with individuals co-infected with HIV accounting for approximately 6.3% of these cases. HIV-TB coinfection is a significant concern due to its higher incidence, complex pathogenesis, and challenges in diagnosis. Among the 30 countries with the highest TB burden, China had an estimated 748,000 new TB cases in 2022, placing it just below Indonesia and India (World

Author Affiliation.
[1] Faculty of Medicine and Health Sciences, Universiti Malaysia Sabah, Jalan UMS, 88400 Kota Kinabalu, Sabah, Malaysia.
[2] Tangshan Food and Drug Comprehensive Inspection and Testing Center, Tangshan, China.
[3] Tangshan Center for Disease Control and Prevention, Tangshan, China.
[4] Tangshan Maternal and Child Health Hospital, Tangshan, China.
[5]. Hebei Provincial Center for Disease Control and Prevention, Hebei, China.

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Health Organization, 2022).

The HIV/AIDS population remains a primary high-risk group for TB, exhibiting unique characteristics that complicate TB control efforts. Studies have shown that HIV-positive individuals face a TB infection risk 20 to 37 times higher than HIV-negative individuals, with a concerning global increase in TB cases among those with HIV/AIDS at an estimated 10% annually (Ho, 2021; Sinba, 2021; Li, 2021; White, 2022). The dual infection presents unique challenges in diagnosis, as standard diagnostic tools like sputum culture and immunological tests have reduced sensitivity in HIV-infected patients compared to non-HIV individuals (Nakiyingi, 2021; Dutschke, 2022; Chongxing, 2023). This diagnostic gap underscores the urgent need for targeted TB control measures within HIV-affected populations.

In China, the Hebei Province, though not designated as a high-risk area for HIV, holds strategic importance due to its proximity to Beijing and Tianjin. The "Compilation of Final Evaluation Data of Tuberculosis Prevention and Control Plan of Hebei Province during the 13th Five-Year Plan (2016-2020)" reported a persistent TB burden in the region, signaling the need for more effective TB prevention and control initiatives across China (SinLi, 2022). Given these factors, understanding the determinants of Mycobacterium tuberculosis (MTB) infection among HIV/AIDS patients in Hebei is critical to developing effective intervention strategies.

This study examined the factors contributing to MTB infection within the HIV/AIDS population in Hebei Province, aimed to provide actionable insights for local TB prevention and control policies. Given Hebei's unique geographical and demographic context, the study's findings are expected to support targeted measures that address the specific challenges of managing TB among high-risk groups. By focusing on the characteristics of MTB infection in the HIV-positive population, this research can inform policy adjustments to reduce the TB burden in Hebei and improve the health outcomes of those most vulnerable to coinfection.

Effective TB control requires a multifaceted approach, particularly in areas where HIV/AIDS prevalence increases the risk and complexity of TB cases. Policymakers and healthcare providers need to prioritize diagnostic advancements and prevention strategies tailored to populations with heightened susceptibility. For instance, enhanced screening protocols, combined with the development of more sensitive diagnostic tools, could improve detection rates among HIV-positive individuals. Additionally, integrating HIV and TB services may facilitate early identification and management of coinfected cases, reducing transmission risks and improving overall health outcomes.

This research contributed valuable data to the discourse on TB management within high-risk groups, serving as a foundation for more precise and responsive TB control strategies in Hebei and beyond. By addressing the intersection of TB and HIV within regional health policy, Hebei can make strides toward mitigating the TB epidemic and supporting WHO's broader global health objectives.

2. Methodology

2.1 Data Source

This project, initiated in 2005, utilized data from the Infectious Disease Monitoring System of the China Center for Disease Control and Prevention (IDMS CDC). Information on the HIV/AIDS population was collected from high-risk counties within Hebei Province, specifically in the cities of Baoding, Chengde, Handan, Langfang, Tangshan, Shijiazhuang, Xingtai, and Zhangjiakou. Ethical approval for data collection was granted by the relevant ethics committee.

2.2 Methodology

A retrospective cohort study design was employed to gather pertinent information on study participants. Data collected included demographic details (e.g., gender), the estimated time of suspected HIV infection, geographic location, transmission routes, the timing of Mycobacterium tuberculosis (MTB) infection, and the status of antiviral treatment. For the study, the final clinical diagnosis was used as the definitive criterion for confirming MTB infection.

2.3 Definitions of Key Indicators

In this study, several key indicators were defined to guide the analysis of MTB infection among individuals with HIV. The **starting event** was identified as the estimated time of initial HIV infection, determined through epidemiological investigation. The **termination event** occurred when an individual in the HIV/AIDS population was documented to have an MTB infection. To ensure consistency, the **follow-up deadline** was set as December 31, 2022. **Survival time** was measured as the duration from the estimated time of initial HIV infection to the point of confirmed MTB infection. Cases that were lost to follow-up before the study deadline or involved deaths unrelated to TB were considered **left-censored events**. Conversely, **right-censored events** included cases in which no MTB infection was documented by the end of the follow-up period. These indicators allowed for a structured and comprehensive assessment of the data.

2.4 Statistic Analysis

Data analysis was conducted using PASS 15.0 and SPSS 22.0 software. To evaluate the factors influencing the time to MTB infection in HIV/AIDS patients, the Log-rank test and Cox proportional hazards regression model were applied. For univariate survival analysis, statistical significance was set at $p < 0.10$, while in multivariate survival analysis, $p < 0.05$ was considered significant.

2.5 Quality Control Measures

Quality control was prioritized at every stage of the study. Questionnaires were carefully designed with clear inclusion and

Table 1. Basic information and variable assignment of HIV/AIDS entering the cohort study

	Basic information	*Case*	*Composition ratio (%)*	*Assignment*
Gender	male	320	52.63	0
	female	288	47.37	1
Age of entering the cohort	<26	214	35.20	0
	26~51	391	64.31	1
	>51	3	0.49	2
Territoriality	landlocked	329	54.11	0
	coastal	279	45.89	1
Route of transmission	Blood transmission	333	54.77	0
	Maternal-to-child transmission	44	7.24	1
	Heterosexual transmission	131	21.55	2
	Same-sex transmission	100	16.45	3
Antiviral therapy	Received antiviral treatment	496	81.58	0
	Not receiving antiviral treatment	112	18.42	1
First $CD4^+$T lymphocyte count(number/μl)	>350	244	40.13	0
	0~350	340	55.92	1
	Not detected	24	3.95	2

Table 2. Results of contingency correlation analysis of independent variables

		Gender	*Age of entering the cohort*	*Territoriality*	*Route of transmission*	*Antiviral therapy*	*First CD4+T lymphocyte count(number/μl)*
Gender	*r*	1	0.006	0.057	0.438	0.074	0.121
	P	-	0.992	0.196	0.000	0.094	0.024
Age of entering the cohort	*r*	0.057	1	0.263	0.365	0.169	0.114
	P	0.196	-	0.000	0.000	0.001	0.155
Territoriality	*r*	0.006	0.263	1	0.334	0.000	0.129
	P	0.992	0.000	-	0.000	0.996	0.014
Route of transmission	*r*	0.438	0.365	0.334	1	0.207	0.220
	P	0.000	0.000	0.000	-	0.000	0.000
Antiviral therapy	*r*	0.074	0.169	0.000	0.207	1	0.315
	P	0.094	0.001	0.996	0.000	-	0.000
First $CD4^+$T lymphocyte count (number/μl)	*r*	0.121	0.114	0.129	0.220	0.315	1
	P	0.024	0.155	0.014	0.000	0.000	-

Table 3. Single-factor survival analysis of log-rank test on the failure time of TB infection among HIV/AIDS population

Basic information	*Wald* χ^2	*v*	*P*
Gender	0.462	1	0.497
Age of entering the cohort	0.162	2	0.922
Territoriality	0.249	1	0.618
Route of transmission	7.177	4	0.066
Antiviral therapy	2.266	1	0.132
First $CD4^+$T lymphocyte count(number/μl)	9.074	2	0.011

Table 4. Multi-factor survival analysis of Cox-regression test on the failure time of TB infection among HIV/AIDS population

Basic information	*β*	$S_{\bar{x}}$	*Wald* χ^2	*v*	*P*	*HR (95%CI)*
Route of transmission	-	-	10.200	3	0.017	-
Blood transmission	-	-	-	-	-	1.000
Maternal-to-child transmission	0.449	0.446	1.011	1	0.315	1.566(0.653~3.755)
Heterosexual transmission	0.604	0.388	2.416	1	0.120	1.829(0.854~3.914)
Same-sex transmission	1.563	0.510	9.387	1	0.002	4.774(1.756~12.975)
First $CD4^+$T lymphocyte count(number/μl)	-	-	11.003	2	0.004	-
>350	-	-	-	-	-	1.000
0~350	1.092	0.347	9.922	1	0.002	2.981(1.511~5.882)
Not detected	1.969	1.054	3.492	1	0.062	7.167(0.908~56.543)

exclusion criteria. During data collection, all investigators underwent rigorous training, and a strict tracking process was implemented to maintain consistency. Additionally, data processing was conducted using a "blind method" to uphold the authenticity and reliability of the study results.

3. Results

3.1 The basic information of the research object

After calculation, the sample size is 502.

$$N = \frac{\left(z_{1-\alpha/2} + z_{1-\beta}\right)^2}{P\left(1 - R^2\right)\sigma^2 B^2}$$

In this study, key statistical parameters were defined to analyze the factors influencing TB infection in HIV/AIDS patients. The first type of error probability (α) was set at 0.05, while the second type of error probability (β) was defined as 0.8. The incidence rate of outcome events (P) was set to 0.2, and the coefficient of the independent variable (B) was set at values ranging from -3 to -3. Additionally, the proportion of independent variable variance explained by covariates (R^2) was defined within the range [0, 1), and the standard deviation (σ) of the independent variable was included in the PASS software for auxiliary calculations. A total of 608 HIV/AIDS patients were enrolled in the cohort, with a mean age of 28.67 ± 11.65 years. Details on basic information, log-rank test results, and variable assignments for the Cox proportional risk regression model are provided in Table 1.

Among the 608 patients, 104 cases were excluded from the analysis due to death or other reasons, leaving 504 individuals who completed the cohort study. For these participants, the mean survival time was calculated at 168.50 ± 4.79 months. Throughout the study, a total of 450 cases were truncated, while 54 individuals developed TB, with an average survival time of 118.74 ± 68.17 months for those who became infected.

3.2 Correlation Analysis of Independent Variables

A contingency correlation analysis of the independent variables was conducted, as shown in Table 2. This analysis helped identify associations between variables that may influence TB infection rates among the HIV/AIDS population.

3.3 Single-Factor Survival Analysis Using the Log-Rank Test

A single-factor survival analysis was performed using the log-rank test to assess the factors influencing TB infection among HIV/AIDS patients. The analysis revealed that the mode of transmission and the initial CD4+ T lymphocyte count were significantly associated with differences in survival times, with χ^2 values of 9.337 and 9.074, respectively, and a p-value of less than 0.10. These results suggest that these factors may play a substantial role in determining the time to TB infection in this population, as presented in Table 3.

3.4 Multifactor Survival Analysis Using the Cox Regression Model

To further explore the impact of transmission routes and initial CD4+ T lymphocyte count on TB infection, a multifactor survival analysis was conducted using the Cox proportional hazards regression model. Results indicated that HIV/AIDS patients with same-sex transmission routes had a 4.774 times higher risk of TB infection compared to those with blood-borne transmission routes. Moreover, individuals with an initial CD4+ T lymphocyte count of 0–350/μl had a 2.981 times higher risk of TB infection than those with a count exceeding 350/μl. These findings, detailed in Table 4, emphasize the need for targeted prevention efforts for high-risk groups, particularly those with low CD4+ T cell counts and specific transmission routes.

In conclusion, the study's findings underscore the importance of considering both transmission routes and immunological status in predicting TB infection risk among HIV/AIDS patients. Tailored interventions and continuous monitoring of high-risk groups could enhance TB prevention efforts in the HIV/AIDS population.

4. Discussion

During the 13th Five-Year Plan period, Hebei Province prioritized TB screening for the HIV/AIDS population, achieving a screening rate of over 90% (SinLi, 2022). This research, based on the 6th China Global Fund AIDS Project (GF6-HIV) and pilot projects on TB and HIV, examined the risk factors associated with MTB infection among HIV/AIDS populations, specifically focusing on CD4+ T lymphocyte counts and transmission routes. The findings provide important insights into the intersections of TB and HIV in Hebei's HIV-positive population.

This study provides a valuable epidemiological foundation for understanding MTB infection risk among HIV/AIDS populations in Hebei Province. Given its focus on a representative sample from the Hebei area, it partially bridges the gap in domestic research on dual susceptibility to HIV and TB, serving as a regional model for co-infection prevention strategies. Moreover, the study's findings can contribute to broader epidemiological frameworks for investigating mortality factors associated with HIV-TB co-infection, while also guiding molecular biology research on co-infection mechanisms. Moving forward, these insights may inform public health policies aimed at improving screening and treatment protocols for co-infected individuals in other high-risk regions.

One of the main risk factors identified was the initial CD4+ T lymphocyte count, which was significantly associated with survival time. This finding aligns with studies by experts such as Xiao (2023), Gopalakrishnan (2020), and Teng (2021), who have shown that lower CD4+ T cell counts contribute to weakened immune responses in HIV-positive individuals. Immunologically, HIV infection compromises CD4+ T lymphocytes through the DC-SIGN pathway, thereby reducing cellular immunity (Lugo-Villarino, 2018; Pouget, 2021; Correia-Neves, 2022). Additionally,

HIV negatively impacts the balance of Th1 and Th2 cytokines, impedes macrophage activity, and reduces B cell activation and proliferation (Doolan, 2022; Ikhtiyarova, 2021). These processes make it difficult for individuals with HIV to clear MTB from their bodies. Further supporting this, molecular and epigenetic studies have indicated changes in protein and nucleic acid expression related to CD4+ T lymphocytes (DiNardo, 2020; Sengupta, 2021), emphasizing the critical role of CD4+ T cells in HIV-related immune suppression.

The study also found a notable difference in MTB infection risk between different transmission routes, with homosexual HIV transmission posing a greater risk than bloodborne routes. Some studies have suggested that blood-transmitted HIV has a higher viral load and thus inflicts greater immune system damage, increasing the susceptibility to MTB (Carlander, 2021; Lei, 2021). However, emerging evidence indicates a rising incidence of HIV among men who have sex with men (MSM), which has led to an increase in the proportion of MTB infections in this group (Safren, 2021). Furthermore, stigma and discrimination may limit access to HIV treatment and standardized TB prevention for MSM individuals, which could indirectly raise their risk for MTB. The confined nature of activity areas within the MSM population may also facilitate MTB transmission. These findings underline the need for more inclusive and stigma-free healthcare policies that encourage proactive TB prevention measures in high-risk groups, including the MSM population.

While the contingency analysis of independent variables in this study did not reveal significant correlations, avoiding multicollinearity issues, the retrospective cohort design does present certain limitations. Independent variables, such as occupation, marital status, education level, HIV subtype, self-management abilities, and medication adherence, were not included but are known to influence TB infection rates in HIV-positive individuals (White, 2022; Jeremiah, 2021; Henry, 2021; Anccunk, 2023; Palamit, 2022; Ranganath, 2021; Alayu, 2021; Akopyan, 2021). For instance, adherence to antiretroviral therapy is crucial in preventing HIV-related immunosuppression, which lowers TB risk. Additionally, socioeconomic factors such as marital and employment status influence health-seeking behavior, which affects timely diagnosis and treatment of both HIV and TB. Including these factors in future research could yield a more comprehensive understanding of TB risk in HIV-positive populations.

The study also encountered left-censoring challenges due to participant loss during follow-up. Although welfare benefits—such as free two-way referral, screening strategies, and treatment for co-infections, alongside transportation and nutrition subsidies—were offered to participants, left-censoring issues impacted the study's reliability. Some participants could not complete the study due to socio-economic challenges or health deterioration, leading to potential biases in the dataset. Future research efforts could benefit from closer collaboration with the IDMS CDC to enhance data collection and retention strategies, potentially using mobile health (mHealth) tools to track participants more effectively.

5. Conclusion

In conclusion, this study highlights the critical factors influencing MTB infection risk among the HIV/AIDS population in Hebei Province, emphasizing the impact of CD4+ T lymphocyte counts and transmission routes. Individuals with lower CD4+ counts and those in the MSM group were found to be at higher risk, underscoring the need for targeted TB screening and prevention strategies within high-risk subgroups. Despite limitations due to retrospective data and left-censoring issues, this research provides essential insights into co-infection patterns, bridging gaps in understanding HIV-TB susceptibility in this population. Future studies should incorporate broader socio-economic and behavioral variables to enhance the predictive accuracy of TB risk models. Overall, this work contributes valuable epidemiological evidence for improving TB-HIV co-infection management and prevention, with implications for public health policies aimed at mitigating the dual burden of these infections in high-risk areas.

Author contributions

Z.J., R.A., and A.B.A. conceptualized and designed the study. Z.B., W.L., Q.R., C.H., G.W., Z.X., and D.R. contributed to data collection and analysis. Y.Y. and Q.W. assisted in data interpretation, while W.L. provided critical revisions to the manuscript. All authors reviewed and approved the final version for publication.

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Competing financial interests

The authors have no conflict of interest.

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