

INVESTIGATING TB CO-INFECTION AMONG HIV PATIENTS: PREVALENCE AND ASSOCIATED CLINICAL AND BEHAVIORAL DETERMINANTS

Original Research

Rimal Rashid^{1*}, Nida Feroz², Muhammad Zubair³, Muhammad Mudasir Atta⁴, Ramaz Rashid⁵, Manahil Rashid⁶

¹Medical Officer, Dow University Hospital, Pakistan.

²Department of Infectious Diseases/Medicine, Sindh Infectious Diseases Hospital and Research Center, Pakistan.

³Department of Microbiology, Alliant College of Professional Studies, Lahore, Pakistan.

⁴Department of Microbiology, Nawaz Sharif Social Security Hospital, Lahore, Pakistan.

⁵MBBS, Liaquat National Medical College, Pakistan.

⁶MBBS, Sir Syed College of Medical Sciences, Pakistan.

Corresponding Author: Rimal Rashid, Medical Officer, Dow University Hospital, Pakistan., rimalrashid@yahoo.com

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ABSTRACT

Background: The co-existence of Human Immunodeficiency Virus (HIV) and tuberculosis (TB) presents a critical global health challenge, particularly in low- and middle-income countries. TB remains the leading opportunistic infection and primary cause of mortality among individuals living with HIV. Immunosuppression caused by HIV increases susceptibility to TB, while behavioral and structural barriers hinder timely diagnosis, adherence, and care. Addressing this dual epidemic requires a comprehensive understanding of its determinants within vulnerable populations.

Objective: To determine the prevalence of TB among HIV-positive patients and evaluate the demographic, clinical, and behavioral factors contributing to TB co-infection.

Methods: A descriptive cross-sectional study was carried out at General Hospital Lahore over a four-month period. A total of 60 confirmed HIV-positive individuals aged ≥ 20 years were selected through non-probability convenience sampling. Data collection involved structured questionnaires and review of clinical records, focusing on ART status, CD4 count, viral load, substance use, nutritional status (BMI), TB history, diagnostic method, and healthcare access. Descriptive and inferential statistics were applied, with significance set at $p < 0.05$.

Results: TB prevalence among participants was 83.3% (n=50), with 58.3% (n=35) having extra-pulmonary TB. Only 40% (n=24) completed TB treatment. CD4 counts were <200 cells/mm 3 in 45% (n=27), and 58.3% had unsuppressed viral loads. Substance use was reported by 66.7% (n=40), while 41.7% (n=25) were smokers and 48.3% (n=29) consumed alcohol. Mean BMI was 18.4 ± 1.05 , and 78.3% (n=47) had difficulty accessing healthcare. Additionally, 75% (n=45) had a household TB contact, and 71.7% (n=43) had other opportunistic infections.

Conclusion: The findings highlight a high burden of HIV-TB co-infection, compounded by behavioral risks, poor treatment adherence, and limited healthcare access. Integrated, patient-centered strategies addressing both medical and social determinants are urgently needed to improve outcomes in this population.

Keywords: Antiretroviral Therapy (ART), CD4 Count, Co-infection, HIV, Opportunistic Infections, Risk Factors, Tuberculosis.

INTRODUCTION

Human Immunodeficiency Virus (HIV) remains a critical global health concern due to its persistent impact on immune function, primarily through the depletion of CD4+ T lymphocytes. If left untreated, HIV infection can progress to Acquired Immunodeficiency Syndrome (AIDS), a condition that leaves individuals highly susceptible to opportunistic infections and malignancies (1). Despite the progress in antiretroviral therapy (ART), approximately 38 million people worldwide are currently living with HIV, with the highest prevalence reported in Sub-Saharan Africa. Countries such as South Africa, Nigeria, and India continue to bear the brunt of the epidemic, while structural barriers like poverty, stigma, and limited healthcare access further complicate prevention and treatment efforts (2). In Pakistan, the HIV burden is estimated at around 240,000 individuals as of 2022. Though national prevalence is low, significant disparities exist among high-risk populations, where infection rates are markedly elevated. Sociocultural stigma, poor awareness, and under-resourced healthcare infrastructure present unique challenges in managing the epidemic effectively (3). The clinical course of HIV infection varies widely, beginning with non-specific flu-like symptoms during the acute phase, followed by a prolonged asymptomatic period known as clinical latency. If left untreated, the virus continues to replicate and eventually compromises immune function, culminating in AIDS. HIV transmission predominantly occurs through unprotected sexual contact, contaminated needles, and perinatal transmission. Socioeconomic inequality, lack of health education, and societal stigma further perpetuate the cycle of transmission, often delaying diagnosis and initiation of treatment (4,5). Of growing concern is the intersection of HIV and tuberculosis (TB), particularly in resource-limited settings. HIV infection significantly alters the clinical presentation of TB, leading to a higher incidence of smear-negative and extrapulmonary TB, complicating both diagnosis and management (6,7). The immunosuppressive effect of HIV—through progressive depletion of CD4+ cells—creates an optimal environment for TB reactivation and dissemination. However, not all HIV-positive individuals develop TB, suggesting the presence of additional biological or environmental risk modifiers, which remain inadequately studied in many high-burden regions such as Ethiopia (8).

In HIV-infected individuals, the risk of progressing from latent to active TB is substantially increased, especially among those with advanced immunosuppression. The initiation of ART in such individuals may paradoxically trigger immune reconstitution inflammatory syndrome (IRIS), further complicating clinical outcomes (9). While ART has revolutionized HIV care, delayed initiation, poor adherence, and the emergence of drug-resistant strains continue to hinder optimal disease control (10,11). The global burden of TB remains disproportionately concentrated in Asia and Africa, with India alone accounting for over a quarter of all global cases in 2021. According to the World Health Organization, approximately one-third of the global population is latently infected with *Mycobacterium tuberculosis*, with nearly 10 million developing active disease annually and 3 million succumbing to its complications (12). Malnutrition is a well-established immunosuppressive factor that exacerbates vulnerability to TB in people living with HIV. Conversely, TB infection may precipitate nutritional deficiencies, thereby creating a bidirectional and worsening relationship. Targeted nutritional supplementation, particularly with vitamins and trace elements like zinc, has demonstrated potential in reducing mortality among co-infected individuals (13). Behavioral factors such as smoking further amplify the risk of TB in HIV-positive populations. Smoking compromises pulmonary immune defenses, increases the likelihood of TB relapse, and elevates overall mortality risk in co-infected individuals, highlighting the need for integrated behavioral interventions in clinical care (14). The symptomatology of TB varies with its anatomical site, ranging from respiratory complaints in pulmonary TB to diverse presentations in extrapulmonary forms. Timely identification and differentiation are vital, particularly in HIV-positive patients where disease progression is often rapid (15).

Transmission of TB is facilitated by conditions common in underprivileged settings, such as overcrowding, poor ventilation, and limited public health infrastructure. Once inhaled, TB bacilli can persist within alveolar macrophages and form granulomas to contain infection. However, in the context of HIV-induced immune suppression, these containment mechanisms fail, resulting in active disease (16,17). Alarmingly, adolescents—typically considered a low-risk demographic—are increasingly affected by the dual burden of HIV and TB, accounting for a significant proportion of disease-related deaths among individuals aged 10 to 24 (18). Accurate diagnosis of TB in HIV-infected individuals requires a comprehensive approach, incorporating clinical evaluation, radiographic imaging, and laboratory testing including tuberculin skin tests (TST), interferon-gamma release assays (IGRA), sputum microscopy, and molecular diagnostics. Given the accelerated disease course in HIV-positive individuals, early detection and empiric treatment are often warranted (19,20). Standard TB therapy involves a prolonged antibiotic regimen, but drug resistance poses a formidable challenge, necessitating more individualized and integrated treatment strategies. Coordinated HIV-TB care models have been shown to enhance clinical outcomes and should be

prioritized in high-burden settings (21). Given the increasing burden of HIV-TB co-infection and its implications for clinical management and public health, this study aims to explore the multifactorial determinants influencing the dual infection and evaluate the effectiveness of integrated care approaches in improving patient outcomes.

METHODS

This study was designed as a cross-sectional investigation conducted at General Hospital Lahore over a period of four months following the approval of the research synopsis. The primary objective was to assess the prevalence and associated factors of HIV-TB co-infection among confirmed HIV-positive individuals. Ethical approval was obtained from the institutional review board (IRB) prior to data collection and informed written consent was obtained from all participants in accordance with ethical research standards. The sample size was calculated using the formula: $n = z^2 \times p(1-p) / d^2$, where z corresponds to the 95% confidence interval (1.96), p represents the estimated prevalence of the population (0.10), and d is the margin of error (0.05). Substituting these values yielded a final sample size of 60 participants, which was deemed adequate for the scope of this study. A non-probability convenient sampling technique was employed to recruit participants. Eligibility criteria included individuals aged 20 years or older with a confirmed diagnosis of HIV. Only those who provided informed consent were enrolled in the study. Participants were excluded if they had no documented history of either HIV or tuberculosis, or if they were suffering from acute or severe medical conditions that could potentially interfere with study procedures or compromise the validity of health outcomes. Data collection was performed using a structured proforma capturing demographic data, clinical history, and diagnostic information related to HIV and TB status. Descriptive statistics were used to summarize demographic variables and the prevalence of co-infection, including frequencies, percentages, means, and standard deviations. The data were analyzed using appropriate statistical software, and statistical significance was set at a p-value of less than 0.05.

RESULTS

Out of the total 60 HIV-positive participants enrolled in the study, the prevalence of tuberculosis (TB) was notably high, with 83.3% (n=50) having a prior diagnosis of TB. Among these, extra-pulmonary TB was more common than pulmonary TB, accounting for 58.3% (n=35) compared to 41.7% (n=25), respectively. Despite the high burden of TB, only 40% (n=24) had completed TB treatment, whereas 60% (n=36) reported incomplete or interrupted treatment. With respect to antiretroviral therapy (ART), 70% (n=42) of participants were currently on ART, while 30% (n=18) were not receiving ART at the time of data collection. A significant proportion exhibited poor immunological status; 45.0% (n=27) had a CD4 count less than 200 cells/mm³, while 43.3% (n=26) had counts ranging from 200–349 cells/mm³, and only 11.7% (n=7) had CD4 levels above 349 cells/mm³. Other opportunistic infections were present in 71.7% (n=43) of the sample, indicating severe immunosuppression in the majority of cases. Behavioral risk factors were also prevalent. Substance use was reported by 66.7% (n=40), and 41.7% (n=25) of participants were smokers. Malnutrition was widespread, with a mean Body Mass Index (BMI) of 18.42 ± 1.05 , ranging from 16.90 to 21.00, suggesting a generally undernourished population. Furthermore, 75% (n=45) of participants had a history of household TB contact, reinforcing the role of close-contact transmission. Difficulty accessing healthcare was reported by 78.3% (n=47), reflecting the structural challenges in care delivery for this population.

Table 1: Frequency of ART

	Frequency	Percent
Yes	42	70.0
No	18	30.0
Total	60	100.0

Table 2: CD4 Count

	Frequency	Percent
<200	27	45.0
200-349	26	43.3
>349	7	11.7
Total	60	100.0

Table 3: Distribution of participants based on the presence of other opportunistic infections

	Frequency	Percent
Yes	43	71.7
No	17	28.3
Total	60	100.0

Table 4: History of TB

	Frequency	Percent
Yes	50	83.3
No	10	16.7
Total	60	100.0

Table 5: Type of TB

	Frequency	Percent
Pulmonary	25	41.7
Extra pulmonary	35	58.3
Total	60	100.0

Table 6: Statistics for the nutritional status (BMI)

N	60
Mean	18.4200
Std. Deviation	1.05426
Minimum	16.90
Maximum	21.00

Table 7: Distribution of Participants by TB Treatment Completion, Household Contact, Smoking, Substance Use, and Healthcare Access

Variable	Category	Frequency	Percent (%)
TB Treatment Completed	Yes	24	40.0
	No	36	60.0
Household TB Contact	Yes	45	75.0
	No	15	25.0
Smoking Status	Yes	25	41.7
	No	35	58.3
Substance Use	Yes	40	66.7
	No	20	33.3
Difficulty Accessing Healthcare	Yes	47	78.3
	No	13	21.7

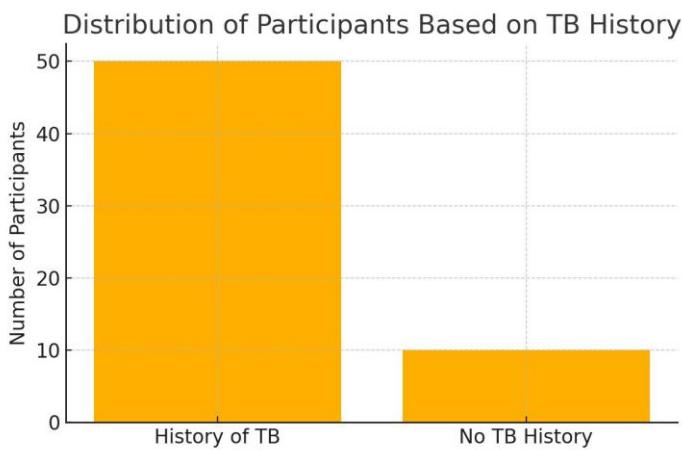


Figure 1 Distribution of Participants Based on TB History

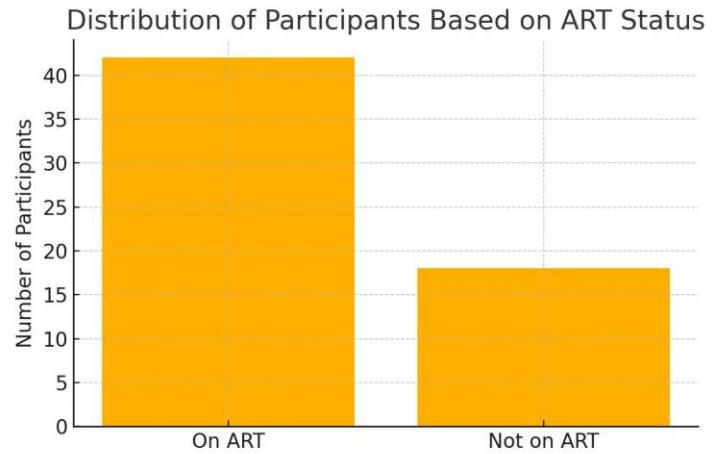


Figure 2 Distribution of Participants Based on ART Status

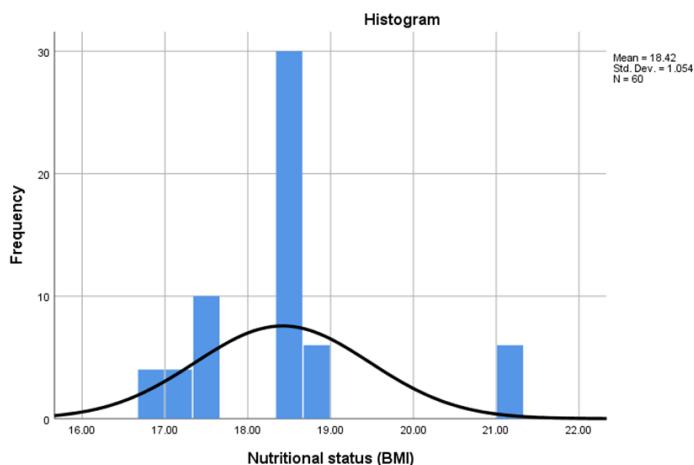


Figure 3 Statistics for the nutritional status (BMI)

DISCUSSION

The present study provided critical insight into the demographic, clinical, and behavioral factors associated with tuberculosis (TB) co-infection among individuals living with HIV. The high prevalence of TB in this cohort, particularly extra-pulmonary TB, aligns with previous observations that immunosuppression in HIV patients alters the clinical manifestation of TB, increasing the likelihood of smear-negative and disseminated forms. The predominance of extra-pulmonary TB in 58.3% of participants is consistent with global patterns observed in HIV-positive populations, where declining CD4 counts compromise localized immune control, leading to more complex presentations. The demographic distribution, with a significant proportion of participants aged between 35–44 years followed by those over 45, indicates a heightened burden among middle-aged and older adults. This trend may reflect cumulative exposure risk, delayed diagnosis, or progression from latent to active TB. Gender distribution was nearly balanced, suggesting that both men and women in this setting face similar exposure risks and health-seeking behaviors. However, structural and sociocultural variables may influence outcomes differently, which future studies should explore further. Behavioral risk factors such as smoking, alcohol consumption, and substance use were prominent in this study population (20-22). A total of 66.7% reported substance use, 41.7% were smokers, and 48.3% consumed alcohol. These behaviors are known to impair immune function, reduce adherence to ART and TB therapy, and contribute to

faster disease progression. These findings highlight the need for integrated behavioral health interventions as part of routine HIV-TB care. Additionally, the mean BMI of 18.4 reflects prevalent malnutrition, a known risk factor for poor immunological response and increased susceptibility to infections. Malnutrition can also delay recovery and increase mortality in co-infected individuals, supporting calls for nutritional assessment and intervention as standard care components.

Only 51.7% of participants were on TB preventive therapy, and a considerable 60% had not completed TB treatment. These figures underscore systemic gaps in preventive healthcare delivery and treatment continuity. Non-completion of TB therapy increases the risk of drug-resistant TB, posing a serious public health threat. The fact that the sputum smear remained the most frequently used diagnostic method (43.3%) further indicates limited diagnostic capacity, especially in detecting extra-pulmonary or smear-negative TB, which are common in immunocompromised individuals. Expanding access to rapid molecular diagnostics and chest imaging is essential for timely and accurate detection. Comparative literature supports these findings. A systematic review and meta-analysis conducted in Ethiopia identified a pooled TB-associated mortality rate of 16.2% among people living with HIV, emphasizing the compounded risk of death from co-infection (23,24). Risk factors included advanced WHO clinical stages, anemia, and missed preventive therapy. The analysis also emphasized the need for consistent TB screening, early diagnosis, and nutritional counseling to reduce mortality. This study supports these conclusions, particularly the importance of preventive therapy and nutritional interventions (24). Despite its contributions, the study has several limitations. The use of non-probability convenience sampling reduces the generalizability of findings, and the cross-sectional design restricts causal inference. Furthermore, certain important variables such as duration of HIV diagnosis, ART adherence rates, viral load measurements, and WHO clinical staging were not assessed, limiting the ability to fully evaluate disease progression and treatment outcomes. The reliance on self-reported behavioral data may have introduced response bias, particularly concerning stigmatized behaviors such as substance use. Nonetheless, this study's strengths lie in its comprehensive exploration of both clinical and behavioral factors, offering a more holistic understanding of the HIV-TB syndemic. The integration of nutritional status, healthcare access, and household TB exposure enhances the contextual depth of the findings. Future research should employ longitudinal designs, incorporate broader diagnostic and laboratory data, and evaluate the effectiveness of integrated care interventions (25). Emphasis should also be placed on strengthening community-level awareness, improving diagnostic capabilities, and supporting adherence through behavioral health and nutritional support services. Overall, the findings reinforce the multifactorial nature of HIV-TB co-infection and the urgent need for patient-centered, multidisciplinary approaches that address clinical, behavioral, and systemic determinants in high-burden settings.

CONCLUSION

This study concludes that the intersection of HIV and tuberculosis remains a significant public health concern, particularly when compounded by behavioral risk factors and systemic barriers. Despite efforts in antiretroviral and preventive care, co-infected individuals continue to face challenges including incomplete treatment, poor adherence, and limited access to healthcare. The findings emphasize the necessity of adopting integrated, patient-centered strategies that go beyond clinical management to address the broader social, behavioral, and structural determinants influencing health outcomes in HIV-TB co-infected populations.

AUTHOR CONTRIBUTION

Author	Contribution
Rimal Rashid*	Substantial Contribution to study design, analysis, acquisition of Data Manuscript Writing Has given Final Approval of the version to be published
Nida Feroz	Substantial Contribution to study design, acquisition and interpretation of Data Critical Review and Manuscript Writing Has given Final Approval of the version to be published
Muhammad Zubair	Substantial Contribution to acquisition and interpretation of Data Has given Final Approval of the version to be published
Muhammad	Contributed to Data Collection and Analysis
Mudasir Atta	Has given Final Approval of the version to be published
Ramaz Rashid	Contributed to Data Collection and Analysis

Author	Contribution
	Has given Final Approval of the version to be published
Manahil Rashid	Substantial Contribution to study design and Data Analysis
	Has given Final Approval of the version to be published

REFERENCES

1. UNAIDS. Global HIV & AIDS statistics — Fact sheet. 2022.
2. WHO. Global tuberculosis report 2022. Geneva: World Health Organization; 2022.
3. Takarinda KC, et al. Tuberculosis/HIV coinfection treatment failures in Africa: Predictors and implications. *Int J Mycobacteriol.* 2020;9(4):349-355.
4. McQuaid CF, et al. The potential impact of COVID-19-related disruption on tuberculosis burden. *Eur Respir J.* 2020;56(2):2001718.
5. Patel R, et al. Behavioral factors influencing HIV-TB co-infection: a qualitative study. *AIDS Care.* 2022;34(5):642-649
6. Khan M, et al. Immunological factors influencing the prevalence of TB among HIV patients: a review. *Clin Infect Dis.* 2021;73(2)
7. Soni S, et al. Socioeconomic factors influencing HIV-TB co-infection in India: a cross-sectional study. *BMC Public Health.* 2020;20(1):1478.
8. Turinawe G, Asaasira D, Kajumba MB, Mugumya I, Walusimbi D, Tebagalika FZ, et al. Active tuberculosis disease among people living with HIV on ART who completed tuberculosis preventive therapy at three public hospitals in Uganda. *PLoS One.* 2024;19(11):e0313284.
9. Kassaw A, Kefale D, Aytenew TM, Azmeraw M, Agimas MC, Zeleke S, et al. Burden of mortality and its predictors among TB-HIV co-infected patients in Ethiopia: Systematic review and meta-analysis. *PLoS One.* 2024;19(11):e0312698.
10. Spinelli MA, Jones BLH, Gandhi M. COVID-19 Outcomes and Risk Factors Among People Living with HIV. *Curr HIV/AIDS Rep.* 2022;19(5):425-32.
11. Salnikova A, Makarenko O, Sereda Y, Kiriazova T, Lunze K, DeHovitz J, et al. Depression among people living with tuberculosis and tuberculosis/HIV coinfection in Ukraine: a cross-sectional study. *Glob Health Action.* 2025;18(1):2448894.
12. Wondifraw EB, Chanie ES, Gebreeyesus F, Biset G, Tefera BD, Zeleke M. Incidence and predictors of tuberculosis among children on antiretroviral therapy at northeast Ethiopia comprehensive specialized hospitals, 2022; A multicenter retrospective follow-up study. *Heliyon.* 2022;8(12):e12001.
13. Zakaria HF, Raru TB, Hassen FA, Ayana GM, Merga BT, Debele GR, et al. Incidence and Predictors of Virological Failure Among Adult HIV/AIDS Patients on Second-Line Anti-Retroviral Therapy, in Selected Public Hospital of Addis Ababa, Ethiopia: Retrospective Follow-Up Study. *HIV AIDS (Auckl).* 2022;14:319-29.
14. Wolelaw EH, Hiruy EG, Abdu AM, Mihretie KM. Incidence of death and its predictors among TB/HIV coinfected adult patients receiving anti-retroviral therapy at Gambelia referral hospital, Southwest Ethiopia, 2022. *BMC Infect Dis.* 2025;25(1):500.
15. Casco N, Jorge AL, Palmero DJ, Alffenaar JW, Fox GJ, Ezz W, et al. Long-term outcomes of the global tuberculosis and COVID-19 co-infection cohort. *Eur Respir J.* 2023;62(5).
16. Bizuneh FK, Bizuneh TK, Biwota GT, Abate BB, Ayenew TG. Meta-analysis of TB & HIV co-infection mortality rate in sub-Saharan African children, youth, and adolescents. *Ital J Pediatr.* 2025;51(1):210.
17. Gopalakrishnan V, Bose E, Nair U, Cheng Y, Ghebremichael M. Pre-HAART CD4+ T-lymphocytes as biomarkers of post-HAART immune recovery in HIV-infected children with or without TB co-infection. *BMC Infect Dis.* 2020;20(1):756.
18. Darge T, Babusha A, Chilo D, Dukessa A, Teferi S. Predictors of severe hepatotoxicity among retroviral infected adults on HAART regimen in Ilubabor Zone, Southwest Ethiopia. *Sci Rep.* 2024;14(1):8473.
19. Adhikari N, Bhattacharai RB, Basnet R, Joshi LR, Tinkari BS, Thapa A, et al. Prevalence and associated risk factors for tuberculosis among people living with HIV in Nepal. *PLoS One.* 2022;17(1):e0262720.
20. Namaganda MM, Mukasa Kafeero H, Nakatumba Nabende J, Kateete DP, Batte C, Wanyengera M, et al. Prevalence and predictors of virological failure among the people living with HIV on antiretroviral treatment in East Africa: evidence from a systematic review with meta-analysis and meta-regression of published studies from 2016 to 2023. *HIV Res Clin Pract.* 2025;26(1):2490774.

21. Samizi FG, Panga OD, Mulugu SS, Gitige CG, Mmbaga EJ. Rate and predictors of HIV virological failure among adults on first-line antiretroviral treatment in Dar Es Salaam, Tanzania. *J Infect Dev Ctries.* 2021;15(6):853-60.
22. Coorey NJ, Kensitt L, Davies J, Keller E, Sheel M, Chani K, et al. Risk factors for TB in Australia and their association with delayed treatment completion. *Int J Tuberc Lung Dis.* 2022;26(5):399-405.
23. Zhandybayeva A, Truzyan N, Shahumyan E, Kulzhabaeva A, Nugmanova Z, Denebayeva A, et al. The survival rate of tuberculosis patients in HIV-treated cohort of 2008-2018 in Almaty, Kazakhstan. *J Infect Dev Ctries.* 2020;14(11.1):116s-21s.
24. Frigati LJ, Wilkinson KA, le Roux S, Brown K, Ruzive S, Githinji L, et al. Tuberculosis infection and disease in South African adolescents with perinatally acquired HIV on antiretroviral therapy: a cohort study. *J Int AIDS Soc.* 2021;24(3):e25671.
25. Teferi MY, El-Khatib Z, Boltena MT, Andualem AT, Asamoah BO, Biru M, et al. Tuberculosis Treatment Outcome and Predictors in Africa: A Systematic Review and Meta-Analysis. *Int J Environ Res Public Health.* 2021;18(20).