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Retreatment TB is a risk factor for multidrug-resistant TB among people with HIV in rural eastern Uganda: A nested case-control study

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ABSTRACT

Rationale: People with human immunodeficiency virus (PWH) have an increased risk of multidrug-resistant TB (MDR-TB) compared to those without HIV.
Objective: To investigate the risk factors for MDR-TB among PWH in rural eastern Uganda.
Methods: We conducted a nested case–control study at Soroti Regional Referral Hospital in rural eastern Uganda. TB records from January 2017 to May 2024 were retrospectively reviewed to identify all PWH. MDR-TB was defined as resistance to at least both Isoniazid and Rifampicin following GeneXpert *Mycobacterium TB* and Rifampicin assay and culture-based drug-susceptible testing. Cases were PWH with MDR-TB, while controls were a random sample of PWH without MDR-TB, in a 1:3 ratio. Multivariable binary logistic regression was used to identify factors independently associated with being a case rather than a control. Adjusted odds ratios (aORs) and 95% confidence intervals (CIs) were reported.
Results: We included 37 cases and 111 controls, and found retreatment TB was associated with being a case rather than a control (aOR 6.97; 95% CI 2.65–19.46). Male sex (aOR: 1.59; 95% CI: 0.67–3.93), clinically diagnosed pulmonary TB (aOR: 0.38; 95% CI: 0.10–1.23) or extrapulmonary TB (aOR: 0.37; 95% CI: 0.05–1.62), and recent anti-retroviral therapy initiation (aOR: 2.07; 95% CI: 0.83–5.28) were insignificantly associated with being a case.
Conclusion: This study showed that retreatment TB is associated with a higher likelihood of MDR-TB among PWH in a referral hospital in rural eastern Uganda. These findings underscore the need for intensified drug resistance surveillance and adherence support among PWH with prior TB treatment.

1. Background

Multidrug-Resistant tuberculosis (MDR-TB) is a major public health threat both globally and regionally [1], complicating efforts to control the TB epidemic. MDR-TB occurs when *Mycobacterium TB*, the organism that causes TB, becomes resistant to at least isoniazid (H) and rifampicin (R), the two most powerful first-line TB drugs [2]. In 2023, an estimated 400,000 people developed MDR-TB globally [1], with a high burden in low- and middle-income countries, particularly in sub-Saharan Africa and Asia. The MDR-TB burden is further exacerbated by the human immunodeficiency virus (HIV) epidemic, with people living with HIV (PWH) having a significantly higher risk of MDR-TB than those without HIV [3]. HIV also negatively affects treatment outcomes among people with MDR-TB [4]. The dual burden of HIV and MDR-TB poses significant challenges to health systems, underscoring the need for integrated approaches to diagnosis, treatment, and care.

Previous studies from sub-Saharan Africa (SSA), including Uganda, have identified several key risk factors for the development of MDR-TB. These include retreatment TB—individuals previously treated for TB [5], smoking [6], contact with people/persons with TB (PWTB) [7], and diabetes mellitus [8], among others. Additional factors include delayed diagnosis, poor adherence to TB treatment, and limited access to diagnostic tools such as drug susceptibility testing [9]. Among these, HIV remains the most significant and consistent risk factor for MDR-TB.

Uganda has a high TB/HIV burden, and available data indicate that 40 % of PWTB have HIV [10]. MDR-TB further complicates the TB/HIV

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syndemic, with estimates suggesting it occurs in 1 % of newly diagnosed TB cases and 12 % of retreatment cases [11]. In contrast, HIV is known as a risk factor for MDR-TB [12], highlighting the need for integrated treatment and prevention strategies to reduce MDR-TB incidence among PWH. In general, PWH face a significantly higher risk of MDR-TB than those without HIV; however, the specific risk factors for MDR-TB in this population remain understudied. While studies have examined MDR-TB in Uganda broadly, limited data exist on retreatment TB and MDR-TB among PWH in rural Eastern Uganda, a region with a high dual burden. We, therefore, investigated the risk factors for MDR-TB among PWH receiving care at a large regional referral hospital in rural eastern Uganda. The study findings contribute to filling a critical evidence gap by identifying context-specific risk factors for MDR-TB among PWH, which can inform targeted interventions and guide integrated care approaches in similar high-burden, resource-limited settings.

2. Methods

2.1. Study setting and data source

This study was conducted at Soroti Regional Referral Hospital (SRRH), located in the Teso sub-region of rural eastern Uganda. Although situated in an urban center, the hospital serves a predominantly rural population, reflecting Uganda's national demographic, where over 80 % reside in rural areas. SRRH was purposively selected as the study site because it is the only MDR-TB treatment facility.

In July 2017, the Uganda Ministry of Health introduced GeneXpert *Mycobacterium TB* and Rifampicin (MTB/RIF) testing at selected health facilities, including SRRH, to improve the diagnosis of pulmonary TB and detect multidrug- and rifampicin-resistant TB [13]. The hospital's TB unit is equipped with GeneXpert MTB/RIF testing and adheres to national TB treatment guidelines, offering comprehensive services including same-day treatment initiation. GeneXpert MTB/RIF testing is offered to all individuals with presumptive TB, allowing the identification of those with drug-susceptible and drug-resistant TB and tailoring of treatment. The MDR-TB unit is staffed by a multidisciplinary team comprising a TB focal person, a Nursing Officer, a Medical Officer, and a Clinical Officer, all experienced in TB care. This team ensures adherence to standardized protocols and delivery of consistent TB messages, contributing to improved TB control in the region. For this study, between March 15, 2025, and June 6, 2025, we retrospectively abstracted TB data for all PWH from the TB Unit Register at SRRH, including demographic and clinical factors. Eligible individuals were PWH aged $\geq$ 18 years who received GeneXpert MTB/RIF testing and had documented MDR-TB results. People with MDR-TB had resistance to at least both Isoniazid and Rifampicin based on GeneXpert MTB/RIF assay and culture-based phenotypic drug-susceptible testing. We excluded individuals with unknown HIV status, aged $<$ 18 years, and those who had substantial missing data.

2.2. Study design

The study employed a nested case-control design to assess the risk factors for MDR-TB among PWH. The design was based on a retrospective review of records for PWH who underwent GeneXpert MTB/RIF testing and received TB treatment at SRRH between January 2017 and May 2024. This design is suitable for studying rare outcomes within a defined retrospective cohort, minimizes bias, and preserves temporal and methodological rigor. The case-to-control ratio was 1:3.

2.3. Study variables and measurements

The dependent variable was MDR-TB, defined as a binary outcome (yes/no). A participant was classified as having MDR-TB if infected with *Mycobacterium tuberculosis* that showed resistance to both isoniazid (H) and rifampicin (RIF), with or without resistance to other first-line anti-TB drugs. Cases were defined as PWH with MDR-TB confirmed using GeneXpert MTB/RIF assay, while controls were a random sample of PWH with drug-susceptible TB (without MDR-TB). Independent variables included socio-demographic characteristics such as age, sex, residence, and clinical features like ART treatment history at the time of TB diagnosis (known to have HIV and receiving ART vs. newly diagnosed with HIV and not started on ART), disease classification, and TB treatment history (new vs. retreatment).

2.4. Sample size and data analysis

We retrieved all available records for PWH who had TB, were documented in the TB unit register, and underwent GeneXpert MTB/RIF testing between January 2017 and May 2024. We screened the records based on the study's eligibility criteria and retained only records that met the criteria. We descriptively summarized numerical data like age using means and standard deviation (SD) for normally distributed variables or medians and interquartile range (IQR) for skewed distributions. Categorical variables such as sex were summarized using frequencies and percentages. In the bivariate analysis, we cross-tabulated each variable with the outcome (cases vs. controls) and performed appropriate statistical tests. Differences between cases and controls for categorical variables were assessed using the Chi-square test for cell counts $\geq$ 5 and Fisher's exact test for counts $<$ 5. Mean differences for numerical variables were assessed using the Student's *t*-test if normally distributed, or the Mann–Whitney *U* test if skewed. Multivariable conditional logistic regression was used to identify factors independently associated with MDR-TB, adjusting for clinically relevant and statistically significant variables. Adjusted odds ratios (aORs) and 95 % confidence intervals (CIs) were reported.

3. Results

3.1. Study profile

Of the 579 records retrieved, 500 met the eligibility criteria and were included in the analysis. Of the 79 records excluded, 6 had unknown HIV serostatus, 69 were for individuals aged under 18 years, and 4 had incomplete data. Among the 500 eligible records, 37 represented people with MDR-TB (cases), and 463 were for those without MDR-TB. From the 463 non-MDR-TB records, 111 were randomly selected to serve as controls (Fig. 1).

3.2. Distribution of socio-demographic and clinical factors by MDR-TB status among PWH at the Soroti Regional Referral Hospital

Table 1 presents the distribution of socio-demographic and clinical characteristics by MDR-TB status among PWH. The mean age was similar between cases and controls, 40.0 $\pm$ 12.5 vs. 41.2 $\pm$ 11.4, respectively ($p = 0.589$). A statistically significant difference was observed only in TB treatment history—whether the individual was newly diagnosed or retreated for TB ($p < 0.001$). No significant differences were observed between cases and controls for the other variables (all $p > 0.05$).

3.3. Risk factors for MDR-TB among PWH at the Soroti Regional Referral Hospital

Table 2 shows the risk factors for MDR-TB among PWH. In the unadjusted analysis, retreatment TB was the only factor significantly associated with higher odds of MDR-TB among PWH (unadjusted odds ratio [OR]: 6.97; 95 % CI: 2.65–19.46). Male sex (unadjusted OR [OR]: 2.16; 95 % CI: 0.99–4.95) and TB diagnosis and treatment during the COVID-19 pandemic (OR: 2.61; 95 % CI: 1.00–7.71) also showed trends toward a higher likelihood of MDR-TB, but were not statistically significant. Conversely, people with clinically diagnosed pulmonary TB

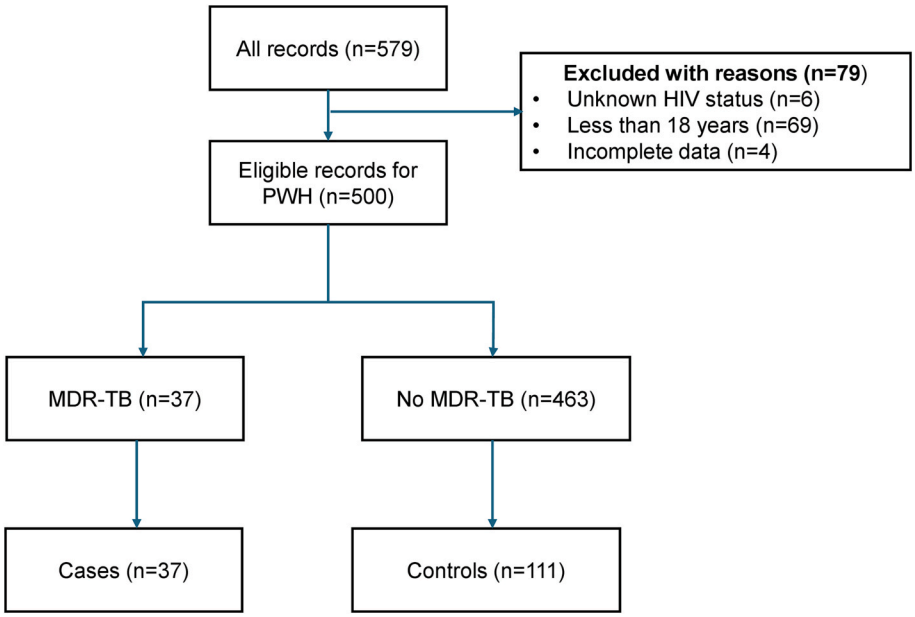

Fig. 1. Study profile of PWH with MRD-TB (cases) versus without MDR-TB (controls) in a 1:3 ratio.

(OR: 0.42; 95 % CI: 0.11–1.19) and extrapulmonary TB (OR: 0.34; 95 % CI: 0.05–1.32) also showed a trend toward lower odds of MDR-TB compared to bacteriologically confirmed pulmonary TB, though these associations were not statistically significant.

In the adjusted analysis, retreatment TB remained as the only independent and statistically significant factor associated with MDR-TB (adjusted OR [aOR]: 6.39; 95 % CI: 2.23–19.65).

Other factors, including male sex (aOR: 1.59; 95 % CI: 0.67–3.93), clinically diagnosed pulmonary TB (aOR: 0.38; 95 % CI: 0.10–1.23), extrapulmonary TB (aOR: 0.37; 95 % CI: 0.05–1.62), and recent ART initiation (aOR: 2.07; 95 % CI: 0.83–5.28), showed non-significant associations with MDR-TB. The adjusted model was parsimonious and demonstrated the best fit, with the lowest Akaike Information Criterion (AIC) of 160.1. It showed good discriminatory ability, with a C-statistic (area under the curve, AUC) of 73.6 %. The Hosmer-Lemeshow goodness-of-fit test indicated adequate model specification, as the null hypothesis of correct model specification was not rejected (Chi-square = 5.66, df = 8, P = 0.685).

3.4. Drug resistance patterns among PWH and MDR-TB at SRRH

Rifampicin and isoniazid both showed the highest resistance rates of 100 %, highlighting them as the most commonly resisted first-line anti-TB drugs. Both Streptomycin and Ethambutol showed resistance rates of 8 %. Susceptibility was 32.4 % for Ethambutol and Amikacin, and 27.0 % for Cycloserine (Supplementary Table 1).

4. Discussion

Our study, which exclusively involved PWH, reveals that PWH with a history of previous TB treatment (retreatment TB), namely those classified as treatment failure, relapse, or lost to follow-up, were significantly more likely to develop MDR-TB compared to those who were newly diagnosed with TB or had no prior TB treatment. Our result agrees with a systematic review and *meta*-analysis of global TB data [14] and observational studies in Uganda [15], Kenya [16], Ethiopia [17–19], the Central African Republic [20], Cameroon [21], Nepal [22], and China [23], among others. Retreatment TB is also a risk factor for rifampicin resistance, one of the cornerstone drugs used in TB treatment [24]. This finding emphasizes the central role of previous TB treatment outcomes in shaping the risk of drug resistance among PWH. From a programmatic perspective, this finding highlights systemic challenges in the management of TB among PWH. Retreatment TB is a well-documented risk factor for MDR-TB, yet access to drug susceptibility testing (DST) using GeneXpert MTB/RIF before initiation of TB treatment remains suboptimal in many high-burden settings. In rural eastern Uganda, where this study was conducted, a previous study reported that just 30 % of people with retreatment TB received GeneXpert MTB/RIF testing [25], which is low. Inadequacies in integrated TB and HIV care may also be another plausible reason, leading to fragmented care, poor retention, and missed opportunities for timely diagnosis and effective treatment of drug-resistant TB. Furthermore, retreatment cases are often managed empirically, which risks the use of ineffective regimens if resistance is not promptly detected. Our findings suggest that retreatment TB should serve as a strong clinical indicator for MDR-TB risk in PWH. Programmatically, GeneXpert MTB/RIF should be implemented as the primary diagnostic test for people with presumed TB to enable rapid detection of drug resistance and timely initiation of appropriate therapy for people with MDR-TB. Additionally, GeneXpert MTB/RIF testing should be routinely offered to all people undergoing retreatment for TB as part of MDR-TB surveillance, to promptly identify drug resistance and guide appropriate management.

Although not statistically significant, we observed a U-shaped association between age groups and the likelihood of MDR-TB. Compared to individuals aged $\leq$ 24 years, the likelihood of MDR-TB was highest among individuals aged 25–34 years, declined slightly among those aged 35–44 years, and peaked again among individuals aged $\geq$ 45 years. A study in Lesotho found that individuals aged $\geq$ 26 years had a lower likelihood of MDR-TB compared to those aged $<$ 26 years [26], in contrast to our findings.

A study in Kenya also reported that older age was associated with an increased likelihood of MDR-TB among presumptive TB patients [16], which contrasts with our findings. Additionally, the Global Burden of Disease data (1990–2021) show that the burden of MDR-TB is highest among older populations and individuals in lower socioeconomic regions [27], with risk factors varying substantially across regions and age groups. This discrepancy may be due to differences in study populations; while our study focused exclusively on PWH, who are at a higher risk of MDR-TB, the previous studies included both individuals with and without HIV.

This study found that men tended to have a higher likelihood of MDR-TB than women, although the association was not statistically

Table 1
Distribution of socio-demographic and clinical factors by MDR-TB status among PWH at the Soroti Regional Referral Hospital.

Variables	Levels	Controls (n = 111)	Cases (n = 37)	P-value
Age group (years)	≤24	10 (9.0)	3 (8.1)	0.607
	25–34	26 (23.4)	8 (21.6)	
	35–44	40 (36.0)	10 (27.0)	
	45 and over	35 (31.5)	16 (43.2)	
	Mean (standard deviation)	40.0 (12.5)	41.2 (11.4)	0.589
Sex	Female	53 (47.7)	11 (29.7)	0.085
	Male	58 (52.3)	26 (70.3)	
Baseline weight (kgs)	Mean (Standard deviation)	50.8 (11.3)	54.1 (10.1)	0.121
Time of TB diagnosis	Before COVID-19	35 (31.5)	6 (16.2)	0.164
	During COVID-19	29 (26.1)	10 (27.0)	
	After COVID-19	47 (42.3)	21 (56.8)	
TB disease type	BC-PTB	74 (66.7)	31 (83.8)	0.137
	CD-PTB	23 (20.7)	4 (10.8)	
	EPTB	14 (12.6)	2 (5.4)	
Types of persons with TB	Newly diagnosed with TB	103 (92.8)	24 (64.9)	<0.001
	Retreatment TB	8 (7.2)	13 (35.1)	
ART treatment history at the time of TB diagnosis	Known to have HIV, been on ART	76 (68.5)	22 (59.5)	0.422
	Newly diagnosed with HIV, recently started on ART	35 (31.5)	15 (40.5)	
Household TB contact	No	14 (12.6)	2 (5.4)	0.359
	Yes	97 (87.4)	35 (94.6)	

Note: ART: Anti-retroviral Therapy; BC-PTB: Bacteriologically confirmed pulmonary TB; CD-PTB: Clinically diagnosed pulmonary TB; COVID-19: Coronavirus Disease 2019; EPTB: Extrapulmonary TB.

Table 2
Risk factors for MDR-TB among PWH at the Soroti Regional Referral Hospital.

Variables	Levels	Unadjusted analysis	Adjusted analysis
		OR (95 % CI)	**OR (95 % CI)**
Age categories (years)	≤24	1	1
	25–34	1.03 (0.24–5.39)	1.28 (0.24–8.15)
	35–44	0.83 (0.21–4.22)	1.21 (0.25–7.38)
	45 and over	1.52 (0.40–7.48)	2.68 (0.55–16.71)
	Mean (standard deviation)	1.01 (0.98–1.04)	
Sex	Female	1	1
	Male	2.16 (0.99–4.95)	1.59 (0.67–3.93)
TB disease type	BC-PTB	1	1
	CD-PTB	0.42 (0.11–1.19)	0.38 (0.10–1.23)
	EPTB	0.34 (0.05–1.32)	0.37 (0.05–1.62)
TB treatment history	Newly diagnosed with TB	1	1
	Retreatment TB	**6.97*** (2.65–19.46)**	**6.39** (2.23–19.65)**
ART treatment history	Known to have HIV, been on ART	1	1
	Newly diagnosed with HIV, recently started on ART	1.48 (0.68–3.18)	2.07 (0.83–5.28)
Household TB contact	No	1	
	Yes	2.53 (0.66–16.60)	
Time of TB diagnosis	Before COVID-19	1	
	During COVID-19	2.61 (1.00–7.71)	
	After COVID-19	2.01 (0.67–6.54)	

Note: ART: Anti-retroviral Therapy; BC-PTB: Bacteriologically confirmed pulmonary TB; CD-PTB: Clinically diagnosed pulmonary TB; COVID-19: Coronavirus Disease 2019; EPTB: Extrapulmonary TB; Statistical significance at 5 % level: *P < 0.05; ***P < 0.001; Bolded figures indicated significant results.

significant. This finding agrees with previous studies in Nigeria [28] and the Central African Republic [20]. Our findings may be explained by a greater risk of TB disease in men, including the presence of several risk factors for multidrug- or rifampicin-resistant TB that are more prevalent. Resultantly, male individuals with TB may face a higher risk of MDR/RR-TB than their female counterparts [29].

The risk of MDR-TB appeared higher during and after the COVID-19 pandemic compared to the pre-pandemic period, although the differences were not statistically significant. This trend may reflect pandemic-related disruptions in TB and HIV services, including reduced access to diagnosis and treatment [30–32], which extended into the recovery period. However, these findings should be interpreted with caution, given their unadjusted and non-significant nature.

5. Strengths and limitations

Our study exclusively focused on PWH and the factors associated with MDR-TB, compared to previous studies, hence eliminating the confounding effect of HIV through specification or restriction. The findings, therefore, provide evidence for targeted interventions among PWH. The study had some limitations. It was conducted in a predominantly rural setting, so the findings may not apply to PWH in urban areas due to varying socioeconomic profiles. The study also relied on existing medical records, which may be incomplete or contain inaccuracies. While the design is suitable for studying rare outcomes, the relatively small sample of people with MDR-TB may have limited the statistical power to detect associations with other risk factors. Future research with larger samples or pooled multi-site data is needed to validate and strengthen these findings. Moreover, our study included only PWH tested with GeneXpert MTB/RIF, which may have underestimated the true MDR-TB burden and limited the generalizability of the findings.

Unmeasured confounders such as CD4 count, viral load, socioeconomic status, and treatment adherence may have influenced the results and should be considered when interpreting the findings. The lack of qualitative data on the perspectives of PWTB and healthcare providers regarding MDR-TB should also be considered as a potential limitation. These limitations should be considered when interpreting the results.

6. Conclusion and recommendation

Our study showed that retreatment TB is associated with a higher likelihood of MDR-TB among PWH at Soroti Regional Referral Hospital in rural eastern Uganda. Targeted interventions for patients with retreatment TB, including early resistance testing and tailored adherence support, are essential to reduce the burden of MDR-TB among PWH in rural eastern Uganda and similar settings.

Ethical statement

Ethical approval was obtained from the Mbale Regional Referral Hospital Research Ethics Committee (Ref: MRRH-2023–600, dated: March 10, 2025). Given the retrospective nature of the study, a waiver of informed consent was granted by the ethics committee. No personal identifiers were collected, and administrative clearance was obtained from Soroti Regional Referral Hospital (the study site).

CRediT authorship contribution statement

Godfrey Opolot: Writing – review & editing, Writing – original draft, Visualization, Validation, Methodology, Investigation, Data curation, Conceptualization. **Peter Olupot-Olupot:** Writing – review & editing, Visualization, Validation, Methodology, Data curation, Conceptualization. **Samuel Okware:** Writing – review & editing, Writing – original draft, Visualization, Validation, Supervision, Methodology, Investigation, Data curation, Conceptualization. **Jonathan Izudi:** Writing – review & editing, Writing – original draft, Visualization, Validation, Supervision, Methodology, Investigation, Data curation, Conceptualization.

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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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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jctube.2025.100562.

References

[1] World Health Organization. Global TB Report 2024. Geneva: Switzerland; 2024.
[2] Gandhi NR, Nunn P, Dheda K, Schaaf HS, Zignol M, van Soolingen D, et al. Multidrug-resistant and extensively drug-resistant tuberculosis: a threat to global control of tuberculosis. Lancet (London, England). 2010;375(9728):1830-43. Epub 2010/05/2doi: 10.1016/s0140-6736(10)60410-PubMed PMID: 20488523.
[3] Sultana ZZ, Hoque FU, Beyene J, Akhlak-Ul-Islam M, Khan MHR, Ahmed S, et al. HIV infection and multidrug resistant tuberculosis: a systematic review and meta-analysis. BMC Infect Dis 2021;21(1):51. https://doi.org/10.1186/s12879-020-05749-2.
[4] Song Y, Jin Q, Qiu J, Ye D. A systematic review and meta-analysis on the correlation between HIV infection and multidrug-resistance tuberculosis. Heliyon 2023;9(11):e21956. https://doi.org/10.1016/j.heliyon.2023.e21956.
[5] Omona K, Opiyo AM. Assessment of risk factors associated with multi-drug resistant tuberculosis (MDR-TB) in Gulu regional referral hospital. African health sciences. 2023;23(3):343-57. Epub 2024/02/1doi: 10.4314/ahs.v23i3.41. PubMed PMID: 38357137; PubMed Central PMCID: PMCPMC10862605.
[6] Wagnew F, Alene KA, Kelly M, Gray D. Impacts of body weight change on treatment outcomes in patients with multidrug-resistant tuberculosis in Northwest Ethiopia. Scientific reports. 2024;14(1):508. Epub 2024/01/05. doi: 10.1038/s41598-023-51026-y. PubMed PMID: 38177234; PubMed Central PMCID: PMCPMC10767082.
[7] Wu L, Chen N, Xia D, Jiang X. Risk factors for multidrug resistance in pulmonary tuberculosis patients with diabetes mellitus. Frontiers in medicine. 2025;12:151620Epub 2025/02/1doi: 10.3389/fmed.2025.151620PubMed PMID: 39958828; PubMed Central PMCID: PMCPMC11825338.
[8] Baya B, Achenbach CJ, Kone B, Toloba Y, Dabitao DK, Diarra B, et al. Clinical risk factors associated with multidrug-resistant tuberculosis (MDR-TB) in Mali. International journal of infectious diseases : IJID : official publication of the International Society for Infectious Diseases. 2019;81:149-55. Epub 2019/02/1doi: 10.1016/j.ijid.2019.02.004. PubMed PMID: 30772470; PubMed Central PMCID: PMCPMC6481646.
[9] Vyawahare C, Mukhida S, Khan S, Gandham NR, Kannuri S, Bhaumik S. Assessment of risk factors associated with drug-resistant tuberculosis in pulmonary tuberculosis patients. Indian Journal of Tuberculosis 2024;71:S44–51. https://doi.org/10.1016/j.ijtb.2023.07.007.
[10] Oga-Omenka C, Tseja-Akinrin A, Sen P, Mac-Seing M, Agbaje A, Menzies D, et al. Factors influencing diagnosis and treatment initiation for multidrug-resistant/rifampicin-resistant tuberculosis in six sub-Saharan African countries: a mixed-methods systematic review. BMJ global health. 2020;5(7). Epub 2020/07/04. doi: 10.1136/bmjgh-2019-002280. PubMed PMID: 32616481; PubMed Central PMCID: PMCPMC7333807.
[11] Akalu TY, Clements ACA, Gebreyohannes EA, Xu Z, Bai L, Alene KA. Risk factors for diagnosis and treatment delay among patients with multidrug-resistant tuberculosis in Hunan Province, China. BMC Infect Dis 2024;24(1):159. https://doi.org/10.1186/s12879-024-09036-2.
[12] Okethwangu D, Birungi D, Biribawa C, Kwesiga B, Turyahabwe S, Ario AR, et al. Multidrug-resistant tuberculosis outbreak associated with poor treatment adherence and delayed treatment: Arua District, Uganda, 2013–2017. BMC Infect Dis 2019;19(1):387. https://doi.org/10.1186/s12879-019-4014-3.
[13] Republic of Uganda. Consolidated guidelines for the prevention and treatment of HIV and AIDS in Uganda. Kampala, Uganda: Ministry of Health; 2022.
[14] Batte C, Namusobya MS, Kirabo R, Mukisa J, Adakun S, Katamba A. Prevalence and factors associated with non-adherence to multi-drug resistant tuberculosis (MDR-TB) treatment at Mulago National Referral Hospital, Kampala, Uganda. African health sciences. 2021;21(1):238-47. Epub 2021/08/17. doi: 10.4314/ahs.v21i1.31. PubMed PMID: 34394303; PubMed Central PMCID: PMCPMC8356628.
[15] Xi Y, Zhang W, Qiao RJ, Tang J. Risk factors for multidrug-resistant tuberculosis: A worldwide systematic review and meta-analysis. PLoS One. 2022;17(6):e0270003. Epub 2022/06/17. doi: 10.1371/journal.pone.0270003. PubMed PMID: 35709161; PubMed Central PMCID: PMCPMC9202901.
[16] Okumu A, Orwa J, Sitati R, Omondi I, Odhiambo B, Ogoro J, et al. Factors associated with tuberculosis drug resistance among presumptive multidrug resistance tuberculosis patients identified in a DRTB surveillance study in western Kenya. Journal of clinical tuberculosis and other mycobacterial diseases. 2024;37:100466. Epub 2024/08/27. doi: 10.1016/j.jctube.2024.100466. PubMed PMID: 39188352; PubMed Central PMCID: PMCPMC11345928.
[17] Admassu F, Abera E, Gizachew A, Sedoro T, Gari T. Risk factors of multidrug resistant tuberculosis among patients with tuberculosis at selected multidrug resistance treatment initiative centres in southern Ethiopia: a case-control study. BMJ Open 2023;13(1):e061836. https://doi.org/10.1136/bmjopen-2022-061836.
[18] Wotale TW, Lelisho ME, Negasa BW, Tareke SA, Gobena WE, Amesa EG. Identifying risk factors for recurrent multidrug resistant tuberculosis based on patient's record data from 2016 to 2021: retrospective study. Sci Rep 2024;14(1):23912. https://doi.org/10.1038/s41598-024-73209-x.
[19] Desissa F, Workineh T, Beyene T. Risk factors for the occurrence of multidrug-resistant tuberculosis among patients undergoing multidrug-resistant tuberculosis treatment in East Shoa, Ethiopia. BMC Public Health 2018;18(1):422. https://doi.org/10.1186/s12889-018-5371-3.
[20] de Dieu LJ, Woromogo SH, Tekpa G, Diemer H-S-C, Gando H, Djidéré FA, et al. Risk factors for multidrug-resistant tuberculosis in the Central African Republic: a case-control study. J Infect Public Health 2023;16(9):1341–5. https://doi.org/10.1016/j.jiph.2023.06.007.
[21] Cecile DIS, Alex NN, Joëlle ND, Cedric NS, Noemy CT, Irene WG, et al. Risk Factors Associated to Multidrug-Resistant Tuberculosis in patients Attending the Deido District Hospital of Douala – Cameroon. the. International Journal of Mycobacteriology 2022;11(4).
[22] Acharya P, Bhattarai N, Kunwar BR, Sharma KR, Khanal VK, Yadav BK. Risk Factors of Multi-Drug Resistant Tuberculosis among Tuberculosis Patients in Province 3, Nepal: A case-control study. medRxiv. 2024:2024.06.16.24309002. doi: 10.1101/2024.06.16.24309002.
[23] Wu L, Cai X, Jiang X. Risk factors for multidrug-resistant tuberculosis: a predictive model study. Frontiers in medicine. 2024;11:1410690. Epub 2024/10/14. doi: 10.3389/fmed.2024.1410690. PubMed PMID: 39399107; PubMed Central PMCID: PMCPMC11466792.
[24] Le X, Qian X, Liu L, Sun J, Song W, Qi T, et al. Trends in and Risk Factors for Drug Resistance in Mycobacterium tuberculosis in HIV-Infected patients. Viruses [Internet] 2024;16(4).
[25] Izudi J, Tamwesigire IK, Bajunirwe F. Surveillance for multi-drug and rifampicin resistant tuberculosis and treatment outcomes among previously treated persons with tuberculosis in the era of GeneXpert in rural eastern Uganda. Journal of clinical tuberculosis and other mycobacterial diseases. 2020;19:100153. Epub 2020/03/04. doi: 10.1016/j.jctube.2020.100153. PubMed PMID: 32123755; PubMed Central PMCID: PMCPMC7038458.
[26] Yahaya JY. Sociodemographic determinants of multidrug-resistant tuberculosis in Lesotho: A case-control study. PLOS global public health. 2025;5(7):e0004075. Epub 2025/07/10. doi: 10.1371/journal.pgph.0004075. PubMed PMID: 40638609.
[27] Wang X, Shang A, Chen H, Li J, Jiang Y, Wang L, et al. Global, regional, and national disease burden of multidrug-resistant tuberculosis without extensive drug resistance, 1990–2021: Findings from the Global Burden of Disease Study 2021. Drug Resist Updat 2025;82:101265. https://doi.org/10.1016/j.drup.2025.101265.

[28] Madaki S, Mohammed Y, Rogo LD, Yusuf M, Bala YG. Age and gender in drug resistance tuberculosis: a cross-sectional case study at a national tuberculosis reference hospital in Nigeria. Journal of Global Antimicrobial Resistance 2024;39:175–83. https://doi.org/10.1016/j.jgar.2024.09.002.

[29] McQuaid CF, Horton KC, Dean AS, Knight GM, White RG. The risk of multidrug- or rifampicin-resistance in males versus females with tuberculosis. Eur Respir J. 2020;56(3). Epub 2020/05/21. doi: 10.1183/13993003.00626-2020. PubMed PMID: 32430421.

[30] Bbuye M, Muyanja SZ, Sekitoleko I, Padalkar R, Robertson N, Helwig M, et al. Patient level barriers to accessing TB care services during the COVID-19 pandemic in Uganda, a mixed methods study. BMC Health Serv Res 2024;24(1):52. https://doi.org/10.1186/s12913-023-10513-8.

[31] Palattiyil G, Kisaakye P, Mwenyango H, Katongole S, Mulekya F, Sidhva D, et al. Access to HIV/AIDS or TB care among refugees in Kampala, Uganda: exploring the enablers and barriers during the COVID-19 pandemic. Journal of Migration and Health 2022;5:100098. https://doi.org/10.1016/j.jmh.2022.100098.

[32] Jackson PD, Muyanja SZ, Sekitoleko I, Bbuye M, Helwig M, Padalkar R, et al. Risk factors for disruptions in tuberculosis care in Uganda during the COVID-19 pandemic. PLOS global public health. 2023;3(6):e0001573. Epub 2023/06/02. doi: 10.1371/journal.pgph.0001573. PubMed PMID: 37267249; PubMed Central PMCID: PMCPMC10237487.