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Research article

Predictors of poor treatment outcomes among drug-resistant tuberculosis patients in Hunan province, China

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ABSTRACT

Background: Drug-resistant tuberculosis (DR-TB) is a significant public health concern, often resulting in poor treatment outcomes. This study aims to identify predictors of poor treatment outcomes among patients with DR-TB in Hunan Province, China.

Methods: A retrospective cohort study was conducted in Hunan Province using data collected between 2013 and 2018 among patients with DR-TB treatment. Univariable and multivariable parametric survival analyses were performed using a shared frailty survival model with a Weibull distribution and Gamma frailty to identify determinants of poor treatment outcomes. Adjusted hazard ratios (AHR) with a 95 % confidence interval (CI) were calculated for the best-fitted model. The goodness of fit for the model was assessed using the Cox-Snell residual test.

Results: A total of 1384 bacteriologically confirmed DR-TB patients were included in the analysis. Of these, 9.97 % (95 % CI: 8.05–11.67 %) experienced poor treatment outcomes. The hazard of poor treatment outcomes was significantly higher among patients with a history of previous TB treatment compared to those with new TB (AHR = 1.82, 95 % CI: 1.27–2.61). Additionally, each one-day delay in diagnosis was associated with a slightly increased hazard of poor treatment outcomes (AHR = 1.00034, 95 % CI:1.000041–1.00064). Patients who received medication supervision and consistent treatment follow-up (i.e., systematic management) had a significantly lower hazard of poor treatment outcomes than those without systematic management (AHR = 0.08, 95 % CI: 0.05–0.14).

Conclusion: A substantial proportion of DR-TB patients in Hunan Province experience poor treatment outcomes, with prior TB treatment and delays in diagnosis being key predictors. Early diagnosis and systematic management, including medication supervision and consistent follow-up, significantly reduce the risk of poor treatment outcomes. Focused interventions for previously treated TB cases are crucial to improving treatment outcomes and mitigating the risk of long-term physical sequelae among DR-TB survivors.

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1. Introduction

Drug-resistant tuberculosis (TB) is a form of TB resistant to standard TB drugs and is responsible for thousands of deaths every year. According to the World Health Organization (WHO) Report, an estimated 410,000 people developed drug-resistant (DR)-TB in 2022, with the highest burden of DR-TB (46 %) reported in Southeast Asia regions including China. The proportion of DR-TB among new cases was 3.3 % and among previously treated TB cases was 17 % [1].

Poor treatment outcomes among DR-TB patients remain a major challenge for achieving the global End-TB Strategy targets [2]. DR-TB treatment takes a longer duration (6 months–24 months), is more toxic, less potent, and carries an increased risk of transmission, and higher mortality rates [2]. Recently, shorter-duration regimens with less toxicity and better treatment outcomes were introduced to treat DR-TB [3]. The global treatment success rate of DR-TB remains low at 63 % in 2020 [4]. In China, the reported treatment success rate falls below the global average at 54 % [4]. The underlying reasons for this lower treatment outcome in China have yet to be thoroughly investigated. Understanding the predictors of poor DR-TB treatment outcomes in high-burden countries such as China would be valuable for clinical management improvement, public health interventions, and resource allocations. While there was a study conducted in Hunan province to assess the factors contributing to the suboptimal treatment success rates, the study was limited to the period of 2011–2014 and did not include important clinical and demographic factors including drug-resistant patterns, ethnicity, residence, patient follow-up and management, and severity of illness [5]. Therefore, this study aims to identify determinants of poor treatment outcomes including death, loss of follow-up, and treatment failure among DR-TB patients in Hunan province.

2. Methods and materials

2.1. Study design and area

A retrospective cohort study was conducted in Hunan province, China. The data were obtained from Hunan Chest Hospital, the largest and the only chest hospital in the province, located in the provincial capital of Changsha City. Since its establishment in 2011, the hospital has provided diagnostic and treatment services for both Drug-susceptible (DS)-TB and DR-TB, with over 600 in-patient beds [6]. All patients diagnosed with DR-TB who completed their treatment (i.e., cured, completed, died, experienced treatment failure, or lost to follow-up) regardless of age were included in our study.

2.2. Microbiological analysis and DST for diagnosis of DR-TB

In Hunan Province, the diagnosis of DR-TB is confirmed using molecular diagnostic tests such as GeneXpert MTB/RIF and culture-based methods with drug susceptibility testing (DST). However, culture was carried out by 32 counties out of 131 counties in Hunan Province. DST covers several first-line drugs (rifampicin, isoniazid, ethambutol, and streptomycin) as well as some second-line drugs (kanamycin and ofloxacin).

2.3. Treatment regimen and management

The study included DR-TB patients treated at Hunan Chest Hospital, comprising both those hospitalized and those receiving outpatient care. Patients diagnosed with bacteriologically confirmed DR-TB were admitted to Hunan Chest Hospital for comprehensive treatment and management. An individualized regimen, comprising a minimum of four drugs selected based on DST results and the patient's prior TB treatment history, was utilized. The treatment regimen typically included injectable drugs (such as Amikacin, Kanamycin, and Capreomycin), a quinolone (Levofloxacin, Gatifloxacin, or Moxifloxacin), Para-aminosalicylic acid, Prothionamide, Pyrazinamide, Clarithromycin, Cycloserine, or Ethambutol.

Each patient received hospitalization lasting one to two months, receiving directly observed treatment short courses (DOTs) from trained healthcare providers. During their stay, patients received psychological support and counselling from professional nurses. Upon achieving clinical stability, patients transitioned to outpatient care, returning monthly for medication refills, and receiving support from trained family members and community supervisors. Follow-up sputum smear and culture tests were performed monthly for the first two months, followed by testing every other month until treatment completion.

2.4. Data sources and variables

The analysis encompassed all patients diagnosed with DR-TB and treated in Hunan Province from 2013 to 2018. Exclusions comprised patients reporting adverse effects only, those transferred out, and individuals whose diagnoses changed. Data were sourced from an internet-based TB management information system, the TB control institute of Hunan Province, DR-TB medical records, and DST registration books. A post hoc power analysis, with an assumption of alpha (0.05), power (0.8), hazard ratio (1.82), event probability (0.0997), and withdrawal probability (0.0195), indicated that a minimum sample of 178 was required. However, our study included all 1381 patients who met the inclusion criteria, exceeding the minimum required sample size.

Patient information from these varied sources was integrated using individual identification. Socio-demographic variables such as gender, age, ethnicity, occupation, residence, detainees, and patient source, along with clinical variables including treatment category (new vs. re-treatment cases), year of enrolment, diagnosing institution, diagnosis delay, treatment delay, systemic management, and treatment outcomes, were utilized for the analysis. Treatment outcomes were categorized as cure, completion, death, loss to follow-up,

and treatment failure. The definitions of treatment outcomes and other important variables are available in Supplementary Table S1.

2.5. Data analysis

Descriptive analyses were conducted to compare demographic and clinical variables by treatment outcomes. The Kaplan-Meier failure curve was used to describe the cumulative hazard ratio of poor treatment outcomes over time.

For variable selection, we applied a systematic approach, starting with univariate analyses of potential predictors. Variables with a p-value <0.25 were used for inclusion in the multivariable model, ensuring that important predictors were not excluded prematurely. We applied multivariable survival regression to identify predictors of poor treatment outcomes among DR-TB patients, using a shared

Table 1
Baseline demographic and clinical characteristics of patients with DR-TB in Hunan Hospital, China, 2013–2018.

Variables	Cured	Treatment completed	Death	Treatment failure	Lost follow-up	Total
	N = 964; n (%)	N = 282; n (%)	N = 35; n (%)	N = 76; n (%)	N = 27; n (%)	N = 1384; n (%)
Age (in years)						
15–64	757 (69.07)	233 (21.26)	20 (1.82)	62 (5.66)	24 (2.19)	1096 (100.00)
≥65	207 (71.88)	49 (17.01)	15 (5.21)	14 (4.86)	3 (1.04)	288 (100.00)
Gender						
Female	221 (71.29)	67 (21.61)	3 (0.97)	14 (4.52)	5 (1.61)	310 (100.00)
Male	743 (69.18)	215 (20.02)	32 (3.00)	62 (5.78)	22 (2.02)	1074 (100.00)
Occupation						
Student	22 (57.89)	12 (31.58)	0 (0.00)	4 (10.53)	0 (0.00)	38 (100.00)
Government employed.	15(57.69)	7 (26.92)	0 (0.00)	4 (15.39)	0 (0.00)	26 (100.00)
Farmers and migrants	765 (70.51)	223 (20.55)	28(2.58)	50 (4.61)	19 (1.75)	1085 (100.00)
Housekeeping	73 (70.19)	26 (25.00)	0 (0.00)	5 (4.81)	0 (0.00)	104 (100.00)
Private employed	14 (66.67)	2 (9.52)	0 (0.00)	4 (19.05)	1 (4.76)	21 (100.00)
Retired	43 (67.19)	11 (17.19)	6 (9.38)	4 (6.25)	0 (0.00)	64 (100.00)
Others*	32 (69.57)	1 (2.17)	1 (2.17)	5 (10.87)	7 (15.22)	46 (100.00)
Year of enrolment						
2013	66 (79.52)	12 (14.46)	1 (1.20)	4 (4.82)	0 (0.00)	83 (100.00)
2014	73 (71.57)	15 (14.71)	5 (4.90)	2 (1.96)	7 (6.86)	102 (100.00)
2015	120 (67.42)	48 (26.97)	1 (0. 56)	4 (2.25)	5 (2.8)	178 (100.00)
2016	218 (69.42)	71 (22.61)	0 (0.00)	16 (5.10)	9 (2.87)	314 (100.00)
2017	215 (70.49)	65 (21.31)	9 (2.95)	12 (3.93)	4 (1.32)	305 (100.00)
2018	272 (67.66)	71 (17.67)	19 (4.73)	38 (9.45)	2 (0.49)	402 (100.00)
Ethnicity						
Han	917 (69.84)	266 (20.26)	33 (2.51)	69 (5.26)	27 (2.13)	1313 (100.00)
Other minorities	47 (65.28)	16 (22.22)	2 (2.78)	7 (9.72)	0 (0.00)	72 (100.00)
Treatment category						
New	757 (69.20)	261 (23.86)	16 (1.46)	46 (4.20)	14 (1.28)	1094 (100.00)
Retreatment	207 (71.38)	21 (7.24)	19 (6.56)	30 (10.34)	13 (4.48)	290 (100)
Diagnosis institution						
CDC	790 (69.91)	240 (21.24)	28 (2.48)	45 (3.98)	27 (2.39)	1130 (100)
General hospital	151 (67.11)	37 (16.44)	6 (2.67)	31 (13.78)	0 (0.00)	225 (100)
TB dispensary	19 (76.00)	5 (20.00)	1 (4.00)	0 (0.00)	0 (0.00)	25 (100)
Current residency						
Hong Kong, Macau, Taiwan	23 (74.19)	8 (25.81)	0 (0.00)	0 (0.00)	0 (0.00)	31 (100)
inter-city flowing	905 (70.26)	251 (19.49)	34 (2.64)	71(5.51)	27 (2.10)	1288 (100)
Inter-province flowing	34 (54.84)	22 (35.48)	1 (1.61)	5 (8.07)	0 (0.00)	62 (100)
Local	2 (66.67)	1(33.33)	0 (0.00)	0 (0.00)	0 (0.00)	3 (100)
Patient source						
Health check	12 (57.14)	4 (19.05)	2 (9.52)	2 (9.52)	1(4.77)	21 (100.00)
Referral	344 (70.20)	99 (20.20)	9 (1.84)	27 (5.51)	11 (2.25)	490 (100.00)
Seeking consultation	311 (74.76)	67 (16.11)	10 (2.40)	19 (4.57)	9 (2.16)	416 (100.00)
Tracing	297 (64.99)	112 (24.51)	14 (3.06)	28 (6.12)	6 (1.32)	457 (100.00)
Severely ill						
No	906 (69.43)	268 (20.54)	33 (2.53)	74 (5.67)	24 (1.83)	1305 (100.00)
Yes	58 (73.42)	14 (17.72)	2 (2.53)	2 (2.53)	3 (3.80)	79 (100.00)
Treatment management						
Full process management	21(30.00)	41(58.57)	5 (7.14)	3 (4.36)	0 (0.00)	70 (100.00)
Full process supervision	926 (79.42)	122 (10.46)	29 (2.49)	62 (5.32)	27 (2.31)	1166 (100 %)
Intensive phase supervision	13 (9.49)	112 (81.75)	1 (0.73)	11 (8.03)	0 (0.00)	137 (100.00)
Self-administered medication	4 (36.36)	7 (63.64)	0 (0.00)	0 (0.00)	0 (0.00)	11 (100.00)
Systemic management						
No	5 (15.63)	6 (18.75)	4 (12.50)	7 (21.88)	10 (31.24)	32 (100.00)
Yes	959 (70.93)	276 (20.41)	31(2.29)	69 (5.10)	17 (1.27)	1352 (100.00)

Government employees: teacher, healthcare worker, and cadre/civil servant.
Private employees: Catering and food industry, commercial service, and seaman and long-distance driver.
Others*: Unknown.

frailty model with a Weibull distribution and Gamma frailty to account for both fixed and random effects. The analysis incorporated a wide range of socio-demographic and treatment-related variables.

Initially, we assessed the proportional hazards assumption for the Cox model using a visual inspection of Schoenfeld residuals and a global test. To determine the best fit, we compared the Cox model to several parametric survival models (Exponential, Weibull, and Lognormal). We then applied a univariate Frailty survival model and a shared frailty survival model with prefecture as a random effect to address heterogeneity across prefectures. The goodness of fit was evaluated using Akaike Information Criteria (AIC), and the model with the lowest AIC value was selected. Parameter estimation was performed using maximum likelihood methods, and the model fit was further assessed with the Cox-Snell residual test. Adjusted hazard ratios (AHRs) with 95 % confidence intervals (CIs) were calculated to quantify the impact of each predictor on the risk of poor treatment outcomes.

3. Results

A total of 1384 bacteriologically confirmed DR-TB patients were analyzed in this study. The median age of the study participants was 51 years, with more than two-thirds (77.60 %; n = 1074) being male. Most participants were farmers and migrants (78.39 %; n = 1085) and belonged to the Han ethnic group (94.87 %; n = 1313). Nearly one-fifth of the study participants (20.95 %, n = 290) had a history of previous TB treatment (Table 1).

3.1. Poor treatment outcomes

The prevalence of poor treatment outcomes among DR-TB patients was 9.97 % (95 % CI: 8.05–11.67). Of the patients, 964 (69.65 %) were cured, 282 (20.38 %) completed treatment, 35 (2.53 %) died, 76 (5.49 %) experienced treatment failure, and 27 (1.95 %) were lost to follow-up. The rate of poor treatment outcomes in Hunan Province was also included at a prefecture level to address the unobserved heterogeneity (Supplementary file: Table S2). The rate of poor treatment outcomes fluctuated from 5.62 % in 2015 to 14.68 % in 2018, with a linear increase in recent years (Fig. S1). Similarly, the trends for death, treatment failure, and loss to follow-up varied between 2013 and 2018 (Fig. S2). Survival analysis for treatment outcomes showed that over 94 % of poor treatment outcomes occurred during the continuation phase (i.e., after 6 months of treatment initiation). The probability of experiencing poor DR-TB treatment outcomes was 5.61 % at 6 months and 19.67 % at 12 months. The study had a total follow-up time of 267,824 days at risk. The median time to experience a poor DR-TB treatment outcome was 13 months with an IQR of one month (37 days) (Fig. 1).

3.2. Predictors of poor treatment outcomes among DR-TB patients

The final multivariable analysis identified several clinical variables as predictors of poor treatment outcomes among DR-TB patients. Specifically, previously treated TB patients had an 82 % increased hazard of poor treatment outcomes compared to newly diagnosed DR-TB patients (AHR = 1.82, a 95 % CI:1.28–2.61). Each additional day of diagnosis delay increased the hazard of poor treatment outcomes by approximately 0.024 % (AHR = 1.00024, a 95 % CI: 1.00002–1.00053). Patients receiving medication supervision and consistent treatment follow-up (systemic management) experienced a 99.9 % reduction in the hazard of poor treatment outcomes compared to those without such systemic management (AHR = 0.074, a 95 % CI: 0.045–0.121) (Table 2). The Cox-Snell residual test confirmed the adequacy of the fitted model (Fig. 2), and detailed model diagnostics are provided in the appendix (Table S2, Fig S1, and Fig S2).

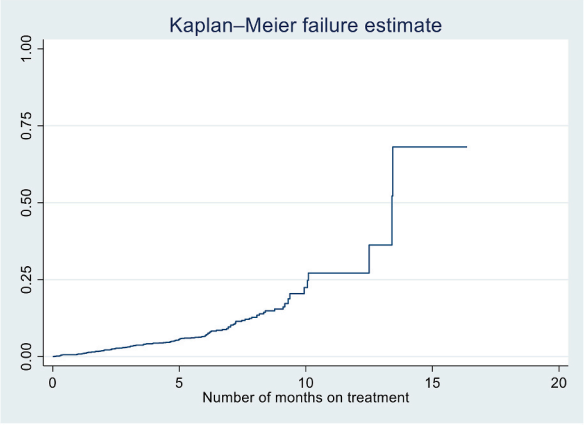

Fig. 1. Cumulative hazard of poor treatment outcomes among patients treated for DR-TB, Hunan Province, China, 2013–2018.

Table 2
A shared frailty survival model with a Weibull distribution and Gamma frailty among DR-TB patients in Hunan Province, 2013–2018.

Variables	COR (95 % CI)	P-value	AOR with 95 % CI	P-value
Gender				
Female	1		1	
Male	1.49 (0.95–2.36)	0.085	1.27 (0.80–2.02)	0.3.07
Ethnicity				
Han	1			
Other minorities*	1.30 (0.66–2.55)	0.450	**NA**	
Age				
<65 years	1		NA	
≥65 years	1.23 (0.83–1.83)	0.307		
Current diagnosis institution				
CDC	1		1	
Hospital & TB dispensary	1.90 (1.30–2.78)	0.001	1.43 (0.91–2.23)	0.120
Current residence				
Local county	1			
Others**	0.67 (0.30–1.52)	0.342	**NA**	
Occupation				
Employed	1		1	
Farmers and migrants	0.49 (0.25–0.97)	0.040	0.55 (0.27–1.01)	0.091
Housemaid	0.27 (0.09–0.81)	0.020	0.35 (0.12–1.07)	0.065
Others***	1.14 (0.53–2.42)	0.728	1.01 (0.47–2.18)	0.978
Patient source				
Seeking consultation due to symptoms	1			
Referral and tracing	1.12(0.78–1.61)	0.535	**NA**	
Year of enrolment				
2013	1		1	
2014	2.46 (0.89–6.84)	0.084	2.25 (0.81–6.25)	0.120
2015	1.01(0.34–2.95)	0.987	0.98 (0.34–2.89)	0.976
2016	1.45 (0.55–3.78)	0.452	1.29 (0.49–3.39)	0.604
2017	1.48 (0.57–3.88)	0.420	1.22 (0.46–3.20)	0.691
2018	2.81 (1.12–7.01)	0.027	1.87 (0.72–4.86)	0.198
Severely ill				
No	1			
Yes	0.84 (0.39–1.80)	0.656	**NA**	
Treatment category				
New treatment category	1		1	
Retreatment category	1.71 (1.16–2.52)	0.007	1.82 (1.27–2.61)	0.001
Diagnosis delay (in days)	1.0003 (1.00002–1.0006)	0.038	1.00034(1.000041–1.00064)	0.026
Treatment delay (in days)	1.0005 (0.995–1.006)	0.551	NA	
Systemic management				
No	1		1	
Yes	0.08 (0.05–0.14)	0.000	0.14 (0.08–0.22)	0.000
ln_p	**0.35 (0.20–0.52)**			0.000

Others Dong, Miao, Tujia, Yao, Bai, Buyi, 3=Dai, Gelao, Hani, Hui, Jingpo, Kazakh, Kirgiz, Korean, Lahu, Li, Lisu, Manchu, Mongolian, Salar, She, Tibetan, Tu, Uighur, Wa, Yi, Zhua*
Others** Local city another county, local province another county, and another province.
Government employees (teachers, health care workers, cadre/civil servants).
Private employees (catering and food industry, waiting for people in a public place, commercial service, fisherman,/boat people, seaman, and long-distance driver).
Farmers and migrants: farmers, workers, migrants, and herdsmen.
Other*** Children, students, unemployed, and retired.
NA: Not applicable for the multivariable model as the p-value was >0.02 in the univariable model.
ln_p = 0.35 indicates the hazard of poor treatment outcomes is increasing over time.

4. Discussion

Poor treatment outcomes pose a significant challenge to achieving the targets of the end-TB strategy. This study aimed to determine the burden, trend, and predictors of poor treatment outcomes among DR-TB patients in Hunan province from 2013 to 2018. Our findings revealed that 10 % of DR-TB patients experienced poor treatment outcomes, with a linear increase observed in recent years. The rate of poor treatment outcomes in our study is lower compared to studies conducted in Pakistan [7], China [8], and Papua New Guinea [9]. However, it is notably higher than the 2 % poor treatment outcome rate reported for DS-TB patients in Hunan Province [10]. This finding suggests that poor treatment outcomes are more prevalent among DR-TB patients than DS-TB patients. The more complex treatment regimens, longer durations, and higher drug resistance associated with DR-TB contribute to greater treatment challenges and poorer outcomes.

Our study also identified a history of previous TB treatment as a predictor of poor treatment outcomes among DR-TB patients. This finding is in line with previous studies conducted in Indonesia [11,12], Vietnam [13], India [14], and another province of China [15].

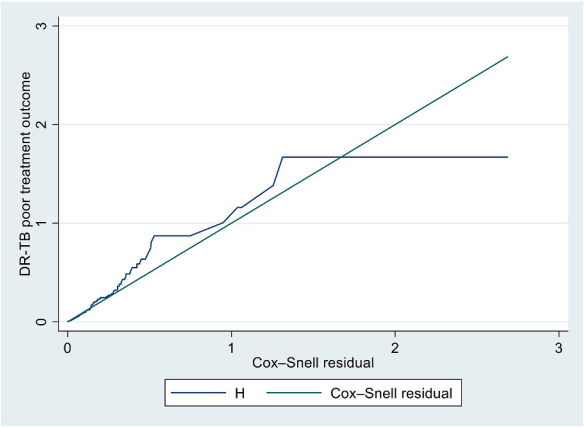

Fig. 2. Goodness of fit test for shared frailty model with a Weibull distribution and Gamma frailty model among DR-TB patients in Hunan province, 2013-2018.

Patients with a history of TB treatment may develop resistance to specific drugs [16], complicating subsequent treatment efforts [17]. Such resistance often spans multiple drugs, limiting treatment options and increasing the risk of poor treatment outcomes [18]. Additionally, restricted treatment options can result in longer durations, increased toxicity, and reduced success rates [19]. Another potential explanation is that patients with a history of poor DR-TB treatment outcomes may have underlying health conditions affecting drug metabolism, immune function, and overall health, which can impact treatment effectiveness [12].

Diagnosis delay was also associated with an increased risk of poor treatment outcomes among DR-TB patients. This finding is consistent with a previous study conducted in China [20]. Delayed diagnosis allows DR-TB to progress, enabling bacterial multiplication and spread throughout the body [21]. This progression can lead to more extensive damage to the lungs and other organs [22], complicating treatment [23]. Additionally, delays in diagnosis increase the risk of transmission to close contacts, further exacerbating the burden of DR-TB and impacting WHO End-TB strategies [24],

Patients undergoing systemic management for DR-TB experienced a lower risk of poor treatment outcomes. Systemic management of DR-TB involves a multidisciplinary approach that includes comprehensive strategies for diagnoses, care, monitoring, and prevention of disease transmission [10]. One key component is Directly observed therapy (DOTs), which is widely implemented in China to ensure adherence to treatment, minimize relapse risk, provide thorough patient education and counselling [25]. For instance, a modelling study in China showed that maintaining the DOTs strategy could reduce TB incidence by 42 % and TB mortality by 41 % between 2015 and 2035 [26]. Despite these benefits, there remains a lack of evidence on which specific intervention strategies are most effective for improving treatment outcomes in DR-TB patients.

The study has several important limitations. First, due to the secondary nature of the data, key variables potentially influencing poor treatment outcomes, such as behavioral factors (smoking and chronic alcohol use), psychological factors (depression, anxiety, and stress), comorbidities (diabetes mellitus and HIV co-infection status), and nutritional status, were not assessed. This omission may limit the generalizability of the findings. However, the study aimed to address determinants of poor treatment outcomes among DR-TB patients using readily available socio-demographic and clinical variables. Second, nearly one-third of DR-TB patients were transferred out, and their treatment outcomes could not be determined, leading to their exclusion from the study. This could potentially result in an underestimation or overestimation of the actual burden of poor treatment outcomes among DR-TB patients and may not fully represent the situation in Hunan province. Lastly, stratified analysis for specific outcomes such as death, treatment failure, and loss of follow-up could not be performed due to the limited number of cases.

5. Conclusion

Poor treatment outcomes among DR-TB patients continue to be a significant concern in Hunan province, highlighting the urgent need for sustained efforts to mitigate treatment failures and associated mortality. The study demonstrates the critical importance of timely diagnosis, the implementation of systematic management approaches, and the need to address the challenges faced by patients with a history of previous TB treatment. Addressing these factors is essential to reduce the risk of poor treatment outcomes and prevent long-term physical sequelae among DR-TB survivors.

CRediT authorship contribution statement

Temesgen Yihunie Akalu: Writing – review & editing, Writing – original draft, Visualization, Validation, Software, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Archie C.A. Clements:** Writing – review & editing, Visualization, Validation, Supervision, Data curation, Conceptualization. **Zuhui Xu:** Writing – review & editing, Supervision. **Liqiong Bai:** Writing – review & editing, Supervision. **Kefyalew Addis Alene:** Writing – review & editing, Validation, Supervision, Software, Resources,

Project administration, Methodology, Investigation, Funding acquisition, Data curation, Conceptualization.

Ethical approval and consent to participate

The Curtin University Human Research Ethics Committee granted ethical approval, and the Hunan TB Control Institute obtained written informed consent from all study participants. However, due to the retrospective nature of the data, obtaining consent directly from study subjects was not feasible. Therefore, the ethics committee of Hunan research ethics waived the requirement for informed consent. To ensure patient confidentiality, the medical records of study participants were de-identified and password-protected. The study was conducted by the principles outlined in the Declaration of Helsinki."

Consent for publication

Not required.

Availability of data and material

Due to privacy and ethics considerations related to the sensitive nature of DR-TB, we have not deposited the data into a publicly available repository. However, the data is available upon request from the corresponding author.

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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.heliyon.2024.e40391.

References

[1] Global Tuberculosis Report 2023, World Health Organization, Geneva, 2023. https://www.who.int/.../tb-reports/global-tuberculosis-report-2023.
[2] WHO. Global Tuberculosis Control SURVEILLANCE, PLANNING, FINANCING, WHO Press, Switzerland, 2008.
[3] WHO Consolidated Guidelines on Drug-Resistant Tuberculosis Treatment, World Health Organization, 2019. Report No.: Report No.: 924155052X.
[4] World Health Organization, Global Tuberculosis Report, 2020.
[5] K.A. Alene, H. Yi, K. Viney, E.S. McBryde, K. Yang, L. Bai, et al., Treatment outcomes of patients with multidrug-resistant and extensively drug resistant tuberculosis in Hunan Province, China, BMC Infect. Dis. 17 (2017) 1–11.
[6] Z. Amin, H. Mitiku, D. Marami, T. Shume, F. Weldegebreal, Magnitude of multidrug resistance and associated factors of pulmonary tuberculosis among adult smear positive patients in eastern Ethiopia, Infect. Drug Resist. 14 (2021) 4493–4500.
[7] A.A. Malik, U. Khan, P. Khan, A. Anwar, N. Salahuddin, S. Khowaja, et al., Drug-resistant tuberculosis treatment outcomes among children and adolescents in Karachi, Pakistan, Trop Med Infect Dis 7 (12) (2022).
[8] Lecai J, Mijiti P, Chuangyue H, Qian G, Weiguo T, Jihong C. Treatment Outcomes of Multidrug-Resistant Tuberculosis Patients Receiving Ambulatory Treatment in Shenzhen, China: a Retrospective Cohort Study. (2296-2565 (Electronic)).
[9] J. Foster, D. Mendez, B.J. Marais, D. Peniyamina, E.S. McBryde, Predictors of unfavourable treatment outcome in patients diagnosed with drug-resistant tuberculosis in the Torres Strait/Papua New Guinea border region, PLoS One 17 (12) (2022) e0266436.
[10] B. Gilmour, Z. Xu, L. Bai, K.A. Alene, A.C. Clements, Risk factors associated with unsuccessful tuberculosis treatment outcomes in Hunan Province, China, Trop. Med. Int. Health 27 (3) (2022) 290–299.
[11] D. Arlinda, R.M. Indah, A. Yulianto, A.D. Harso, A.K. Syarief, M. Karyana, Poor tuberculosis treatment outcomes associated with older age, previous treatment, HIV and drug resistance at seven hospitals in Indonesia, Jurnal Penelitian dan Pengembangan Pelayanan Kesehatan (2020) 61–68.
[12] S. Soedarsono, N.M. Mertaniasih, T. Kusmiati, A. Permatasari, W.K. Ilahi, A.T. Anggraeni, Characteristics of previous tuberculosis treatment history in patients with treatment failure and the impact on acquired drug-resistant tuberculosis, Antibiotics 12 (3) (2023) 598.

[13] L.H. Van, P.T. Phu, D.N. Vinh, V.T. Son, N.T. Hanh, L.T.H. Nhat, et al., Risk factors for poor treatment outcomes of 2266 multidrug-resistant tuberculosis cases in Ho Chi Minh City: a retrospective study, BMC Infect. Dis. 20 (2020) 1–10.
[14] M.M. Parmar, K.S. Sachdeva, P.K. Dewan, K. Rade, S.A. Nair, R. Pant, et al., Unacceptable treatment outcomes and associated factors among India's initial cohorts of multidrug-resistant tuberculosis (MDR-TB) patients under the revised national TB control programme (2007–2011): evidence leading to policy enhancement, PLoS One 13 (4) (2018) e0193903.
[15] J. Lecai, P. Mijiti, Treatment outcomes of multidrug-resistant tuberculosis patients receiving ambulatory treatment in Shenzhen, China: a retrospective cohort study, Front. Public Health 11 (2023) 1134938.
[16] N-n Tao, Y-f Li, W-m Song, J-y Liu, Q-y Zhang, T-t Xu, et al., Risk factors for drug-resistant tuberculosis, the association between comorbidity status and drug-resistant patterns: a retrospective study of previously treated pulmonary tuberculosis in Shandong, China, during 2004–2019, BMJ Open 11 (6) (2021) e044349.
[17] M. Pv Shekhar, Drug resistance: challenges to effective therapy, Curr. Cancer Drug Targets 11 (5) (2011) 613–623.
[18] WHO G, Global tuberculosis report 2020, Glob Tuberc Rep. 2020 (2020).
[19] A.S. Albanna, D. Menzies, Drug-resistant tuberculosis: what are the treatment options? Drugs 71 (7) (2011) 815–825.
[20] Y. Chen, Z. Yuan, X. Shen, J. Wu, Z. Wu, B. Xu, Time to multidrug-resistant tuberculosis treatment initiation in association with treatment outcomes in Shanghai, China, Antimicrob. Agents Chemother. 62 (4) (2018), 10.1128/aac. 02259-17.
[21] M. Suneja, S.E. Beekmann, G. Dhaliwal, A.C. Miller, P.M. Polgreen, Diagnostic delays in infectious diseases, Diagnosis 9 (3) (2022) 332–339.
[22] A. Allué-Guardia, J.I. García, J.B. Torrelles, Evolution of drug-resistant Mycobacterium tuberculosis strains and their adaptation to the human lung environment, Front. Microbiol. 12 (2021) 612675.
[23] K.T. Tefera, N. Mesfin, M.M. Reta, M.M. Sisay, K.S. Tamirat, T.Y. Akalu, Treatment delay and associated factors among adults with drug resistant tuberculosis at treatment initiating centers in the Amhara regional state, Ethiopia, BMC Infect. Dis. 19 (2019) 1–8.
[24] D. Liebenberg, B.G. Gordhan, B.D. Kana, Drug resistant tuberculosis: implications for transmission, diagnosis, and disease management, Front. Cell. Infect. Microbiol. 12 (2022) 943545.
[25] J. Volmink, P. Matchaba, P. Garner, Directly observed therapy and treatment adherence, Lancet 355 (9212) (2000) 1345–1350.
[26] G.H. Huynh, D.J. Klein, D.P. Chin, B.G. Wagner, P.A. Eckhoff, R. Liu, et al., Tuberculosis control strategies to reach the 2035 global targets in China: the role of changing demographics and reactivation disease, BMC Med. 13 (2015) 1–17.