Junior researchers

ახალგაზრდა მკვლევარები

Vol. 4 Issue 1, 2026

https://doi.org/10.52340/jr.2026.04.01.08

Treatment Outcomes in Drug-Resistant Tuberculosis: A Retrospective Cohort Study from Tbilisi, Georgia

Kamakshi Bhati[1], Liya Cherian[1], Professor. Nelly Solomonia[2]

[1]Tbilisi State Medical University, [2]National Center for Tuberculosis and Lung Diseases

**ORCID

Kamakshi Bhati: 0009-0007-4161-434X

Liya Cherian: 0009-0009-6964-0763

Contact information:

1. Name : Liya Cherian
   Phone number: +91 – 7510753494
   Email ID: liyacherian109@gmail.com
2. Name: Kamakshi Bhati
   Email ID: kamakshibhati25@gmail.com

Abstract

Background:

Treating drug-resistant tuberculosis was particularly complex for patients who also have comorbid conditions or extrapulmonary tuberculosis.

Aim:

The study's objective is to investigate the impact of various demographics, clinical variables, and treatment regimens on treatment outcomes in patients with drug-resistant tuberculosis.

Methods:

A retrospective cohort study based on data collected from 595 DR-TB patients aged ≥15 years treated at the NCTLD in Tbilisi, Georgia, from 2019 to 2021. Inclusion criteria involved patients with microbiologically verified DR-TB who had complete treatment outcome records. Patients under the age of 15 or without verified treatment outcomes were excluded from the study.

Results:

Successful treatment outcomes were seen in new TB cases, those without the extra-pulmonary TB, and those without Delamanid included in their treatment. A positive association was also established with the administration of Levofloxacin and Bedaquiline.

Conclusion:

Improved treatment outcomes were noted in newly diagnosed pulmonary TB patients who did not undergo treatment with Delamanid. These findings highlight the importance of early diagnosis and the careful tailoring of treatment strategies to address drug-resistant tuberculosis (DR-TB) effectively.

Keywords: drug-resistant tuberculosis (DR-TB), multidrug-resistant TB (MDR-TB)/rifampicin-resistant TB (RR-TB), treatment outcomes, Georgia (National Center for Tuberculosis and Lung Diseases), bedaquilline, delaminid, levofloxacin, extrapulmonary tuberculosis, HIV co-infection, comorbidities

Introduction

TB is a prevalent disease in Georgia and many other countries. In the last few decades, the Government of Georgia with support of International Organizations has taken several initiatives to curb its incidence. The National Center for Tuberculosis and Lung Diseases (NCTLD), a major player, has historically been recognized as a Center of Excellence for specialized TB services and consists of several departments. Around 1/3 of all TB patients registered annually in the country receive either inpatient or outpatient care at NCTLD, meaning around 8.000 outpatient visits, 1.500 hospitalizations among elderly, and 200 hospitalizations among pediatric patients per year. (TB research amidst the COVID-19 pandemic | The Union, 2020) Since 2005, NCTLD has become a lead organization for Tuberculosis Control in the country, cooperating and leading eleven regional centers: Regional TB dispensaries that coordinate peripheral TB cabinets and DOTS centers in their respective regions. [7]

NTP has ensured nationwide access to TB diagnosis and treatment; introduced WHO-approved modern diagnostic methods; FAST strategy was successfully implemented for early TB-detection in general healthcare facilities; NTP participate in the pilot project for integrated TB, HIV and HCV screening, which was expanded countrywide; Georgia became one of the pioneers in programmatic use of the new TB-drugs in line with active drug safety monitoring; was strengthened primary healthcare provider engagement in TB control; NTP increased research capacity through collaboration with international partners in conducting clinical/observational studies; increased involvement of civil society and implemented novel technologies for the improvement of TB care and adherence (Integrated screening for infectious diseases: a success story from Georgia, 2021). Despite remarkable advances, TB, and especially DR-TB, remains one of the main challenges for the Georgian healthcare system. Additional actions are needed to achieve End-TB strategic milestones in further reducing TB incidence and improving treatment outcomes.[8]

The initial treatment of TB starts with the standard RIPE regimen: rifampin, isoniazid, pyrazinamide, and ethambutol. Ethambutol is discontinued once the susceptibility to all the drugs is confirmed.

Patients taking Pyrazinamide should have their serum uric acid levels checked at baseline and periodically. Additionally, those on Ethambutol need baseline and periodic testing for visual acuity and red-green color perception, typically using the Ishihara test.

After two months, if the isolate is fully susceptible, pyrazinamide can be stopped, and treatment continues with isoniazid and rifampin for four additional months. If isoniazid resistance is confirmed, it should be discontinued, continuing treatment with Rifampin, Pyrazinamide, Ethambutol and plus Levofloxacin for six months.

For multidrug-resistant (MDR) or rifampicin-resistant (RR) TB, treatment regimens vary based on the drug-resistance profile, previous TB treatments, patient history, and the extent of the disease. (Tuberculosis: Multidrug-resistant (MDR-TB) or Rifampicin-resistant TB (RR-TB), 2024)

The BPaLM regimen (6 Bdq-Pa-Lzd-Mfx) is a six-month all-oral treatment regimen for MDR/RR-TB patients with presumed or documented Fluoroquinolone susceptibility, including Bedaquiline, Pretomanid, Linezolid, and Moxifloxacin. In cases of confirmed fluoroquinolone resistance, Moxifloxacin can be omitted.

A shorter, nine-month, all-oral standardized and modified regimens are available for patients without Fluoroquinolone resistance. The standardized regimen includes bedaquiline, levofloxacin or moxifloxacin, ethionamide, ethambutol, high-dose isoniazid, pyrazinamide, and clofazimine. It can be extended if necessary. The modified shorter, nine-month, all-oral regimen includes Bedaquilin, Levofloxacin, Linezolid, Clofazimin and Delamanid or Cicloserin, and it may be adjusted/modified considering resistance or nontolerance to the drugs.

For patients ineligible for these shorter regimens or with extensive drug resistance (like XDR-TB), longer individualised regimens lasting at least 18 months are designed based on the resistance profile and medical history. 9,10

In this context, our retrospective cohort study evaluates the treatment outcomes of 595 patients admitted to the NCTLD in Tbilisi between the years 2019 - 2021. By assessing different variables such as gender, age, disease location, case definition, HIV status, co-morbidities & specific drug regimen, we aim to determine the association of these variables with DR-TB treatment outcomes.

Methods

Study Design and Setting:

This is a retrospective cohort study based on data collected from the medical records of patients diagnosed with tuberculosis at the National Centre for Tuberculosis and Lung Disease in Tbilisi, Georgia. It includes records from January 1, 2019, to December 31, 2021.

Study Population:

The study is conducted using the data of 595 patients with microbiologically verified TB. The patient's eligibility is assessed based on age ≥15 years, who had full treatment outcome data and were treated under the NCTLD.

Gathering Data:

The variables included in the study consist of demographics (age, gender) and clinical data such as disease location (pulmonary or extrapulmonary), case definition (new or previously treated case), HIV status, and presence of comorbidities like diabetes and cardiovascular diseases. Comorbidities were identified based on patients' medical histories and categorized accordingly. The treatment regimen variables considered were specific medications used, such as levofloxacin (LFX), bedaquiline (Bdq), linezolid (Lzd), and delamanid (Dld). Treatment outcomes were dichotomized into successful (defined as treatment completion or cure) and unsuccessful (classified as failure, loss to follow-up, or death). These definitions ensure clarity and foster reproducibility in future research endeavors.

Statistical Analysis:

The detailed statistics were used to make the calculations with the help of **EasyStat v0.020b.** Each categorical variable was analyzed using the Chi-square or Fisher's Exact test, and to evaluate the association, Odds ratios(OR), confidence interval (CI), and p-values were used. A p-value of less than 0.001 is considered to be statistically significant.

Results

Among 595 patients, 28.2% were female and 71.8% were male. Most patients (93.9%) had pulmonary TB. The treatment success rate was 65.9%.

Key findings:

-New TB cases had higher treatment success (OR=4.07; CI: [2.02-8.18]; p<0.001)

-Extrapulmonary TB was linked to poorer outcomes (OR=12.04; CI: [4.94-29.33]; p<0.001)(Migliori et al., 2022)

-Delamanid use was associated with lower success (OR=2.05; (Kumar et al.,2021) CI: [1.37-3.08]; p<0.001)

-Bedaquiline and Levofloxacin use were linked to better outcomes (p<0.001) (Kumar et al.,2021)

-HIV positivity and comorbidities were associated with poorer outcomes (Zhang & Wang, 2020).

Statistical Analysis

EasyStat v0.020b (March 03, 2019) - 2025-04-13 18:19:00

Variable	Level	Total N=595 (%, mean +/- SD)	Successful N=392	Unsuccessful N=203	Odds Ratio/ Mean Difference	95% CI	p value
Gender (n,%)	Female	168 (28.2%)	119 (30.4%)	49 (24.1%)	1.37	[0.93, 2.02]	0.11
	Male	427 (71.8%)	273 (69.6%)	154 (75.9%)	1		
Age (n,%)	<45	334 (56.1%)	227 (57.9%)	107 (52.7%)	1.23	[0.88, 1.74]	0.226
	>46	261 (43.9%)	165 (42.1%)	96 (47.3%)	1		
Definition (n,%)	Failure	37 (6.2%)	15 (3.8%)	22 (10.8%)	1	-	-
	New	**351 (59%)**	**258 (65.8%)**	**93 (45.8%)**	**4.07**	**[2.02, 8.18]**	**<0.001**
	Other	47 (7.9%)	31 (7.9%)	16 (7.9%)	2.84	[1.17, 6.93]	0.0202
	Relapse	93 (15.6%)	58 (14.8%)	35 (17.2%)	2.43	[1.12, 5.3]	0.0236
	TrAfter Default	67 (11.3%)	30 (7.7%)	37 (18.2%)	1.19	[0.53, 2.68]	0.676
PTB (n,%)	No	36 (6.1%)	4 (1%)	32 (15.8%)	0.06	[0.01, 0.16]	<0.001
	Yes	559 (93.9%)	388 (99%)	171 (84.2%)	1		
EPTB (n,%)	**No**	**557 (93.6%)**	**386 (98.5%)**	**171 (84.2%)**	**12.04**	**[4.94, 29.33]**	**<0.001**
	Yes	38 (6.4%)	6 (1.5%)	32 (15.8%)	1		
Comorbidities (n,%)	No	357 (60%)	250 (63.8%)	107 (52.7%)	1.58	[1.12, 2.23]	0.00899
	Yes	238 (40%)	142 (36.2%)	96 (47.3%)	1		
HIV. (n,%)	No	569 (95.6%)	382 (97.4%)	187 (92.1%)	3.27	[1.46, 7.34]	0.00256
	Yes	26 (4.4%)	10 (2.6%)	16 (7.9%)	1		
Bdq (n,%)	No	89 (15%)	40 (10.2%)	49 (24.1%)	0.36	[0.23, 0.56]	<0.001
	Yes	506 (85%)	352 (89.8%)	154 (75.9%)	1		
Lzd (n,%)	No	97 (16.3%)	56 (14.3%)	41 (20.2%)	0.66	[0.42, 1.03]	0.0642
	Yes	498 (83.7%)	336 (85.7%)	162 (79.8%)	1		
Dld (n,%)	**No**	**473 (79.5%)**	**328 (83.7%)**	**145 (71.4%)**	**2.05**	**[1.37, 3.08]**	**<0.001**
	Yes	122 (20.5%)	64 (16.3%)	58 (28.6%)	1		
LFX (n,%)	No	145 (24.4%)	75 (19.1%)	70 (34.5%)	0.45	[0.31, 0.66]	<0.001
	Yes	450 (75.6%)	317 (80.9%)	133 (65.5%)	1		

Footnotes:

[1] For categorical variables Pearson's Chi-Square test was performed if all the cell counts were >5. Otherwise Fisher's exact test was performed.

[2] For numerical variables t-test was used. The p-value in the brackets was calculated using Wilcoxon's Signed Rank test.

Discussion

Statistical analyses were done in this retrospective cohort study to see if any of the demographic, clinical, or treatment-related variables were associated with a patient cohort of 595 persons regarding treatment outcomes for tuberculosis. The treatment outcome was dichotomized as successful (treatment completed or cured) or unsuccessful (failure, lost to follow-up, or death). Much of the analysis involved categorical comparisons, with associations examined through odds ratios (ORs) with 95% confidence intervals (CIs), along with P values indicating significance.

For gender, disease location, case definition, treatment regimen(bedaquiline, delamanid), etc., categorical variables were tested by Pearson's Chi-Square test, provided the expected frequencies in all cells were greater than five. Otherwise, in situations where the assumption was violated-a situation in which some subgroups had very small sample sizes-Fisher's Exact test had to be applied to make a valid inference. The chi-squared test and Fisher's exact test can assess for independence between two variables when the comparing groups are independent and not correlated. The chi-squared test applies an approximation assuming the sample is large, while the Fisher's exact test runs an exact procedure, especially for small samples. These tests tried to determine whether the difference in proportions of successful and unsuccessful outcomes between categories was significant.

In interpreting the odds ratios, an OR > 1 suggests an increased odds of a successful outcome associated with the exposure, whereas an OR < 1 indicates a reduced odds of success. For instance, the use of delamanid (OR = 2.05; 95% CI: 1.37–3.08; $p < 0.001$) was associated with a significantly higher likelihood of unsuccessful outcomes. Though it sounds at first counterintuitive, it might be an indication bias as the drug was more often given to patients with more resistant or advanced disease, who in themselves were less prone to favorable responses.

Conversely, the use of bedaquiline (OR = 0.36; 95% CI: 0.23–0.56; $p < 0.001$) and levofloxacin (OR = 0.45; 95% CI: 0.31–0.66; $p < 0.001$) was found to be statistically significantly associated with treatment success. This finding is consistent with WHO guidelines, which firmly establish these two agents in therapy against drug-resistant TB. The ORs < 1 suggest that the drug acts protectively against treatment failure (Kumar et al., 2021).

Concerning disease characteristics, the odds of treatment success for new TB cases were fourfold compared to cases with a previous history of treatment failure (OR = 4.07; 95% CI: 2.02-8.18; $p < 0.001$). This finding agrees with a body of literature reporting that drug resistance is accumulated mainly in relapsed or previously treated cases with drug resistance and thus usually implies poor prognosis.

Meanwhile, the odds of treatment success were considerably lowered for the patient group getting diagnosed with extrapulmonary TB (OR = 12.04 for unsuccessful outcome; 95% CI: 4.94–29.33; $p < 0.001$). The magnitude of this association suggests that extrapulmonary TB remains a significant risk factor, probably because of delays in diagnosis, difficulty in drug penetration, and hurdles in monitoring progress.

The presence of comorbidities, for instance, diabetes and cardiovascular disease, brought about a moderate increase in the probability of unfavorable outcomes (OR = 1.58; 95% CI: 1.12–2.23; $p = 0.009$). Likewise, the HIV-positive individuals stood three times more in the odds of unsuccessful outcomes compared to the HIV-negative subjects (OR = 3.27; 95% CI: 1.46–7.34; $p = 0.003$), thus reinforcing the already established regime of risk this group is subjected to, owing to immunosuppression and drug interactions.

Age and gender showed trends toward significance, but neither reached the level of significance and were not independently predictive of treatment outcomes for this cohort ($p > 0.05$).

Before that, this particular analysis has underscored the need for individualized treatment approaches. The significant associations emphasize the importance of early diagnosis, proper management of comorbidities, and careful consideration for the use of advanced therapeutics like bedaquiline and levofloxacin. Future prospective studies will need to establish causality and clarify the reasons for differences between regimens, especially the negative treatment outcomes seen here with delamanid.

However, it is important to acknowledge the limitations inherent in our retrospective study design. These limitations include the potential for missing data, as well as unmeasured confounders that may affect the associations we observed. Despite these challenges, our findings provide valuable insights into the treatment of drug-resistant tuberculosis and highlight areas for future research.

Conclusion

This is a retrospective Georgia-based study that is a valuable source of data on the factors related to treatment outcomes in drug-resistant tuberculosis patients. Patients with new tuberculosis diagnosis, who did not present extrapulmonary involvement, and who did not have delamanid included in their treatment regimen, presented with significantly higher rates of treatment success. The findings of this research emphasize the need for tuberculosis control programs that focus on early diagnosis, individualized and optimized treatment regimens, and comprehensive management of groups at high risk, particularly those with co-infection of HIV and other comorbidities, (Swiss TPH, 2021) to improve treatment effectiveness and reduce treatment failure rates.

Abbreviations

1. **Bdq** – Bedaquiline
2. **BPaLM** – six-month all-oral regimen (Bdq-Pa-Lzd-Mfx)
3. **CI** – Confidence Interval
4. **Dld** – Delamanid

5. **DOTS** – Directly Observed Treatment, Short-course
6. **DR-TB** – Drug-Resistant Tuberculosis
7. **EPTB** – Extrapulmonary Tuberculosis
8. **FAST** – early-case-finding strategy (Fast-Act-Separate-Treat)
9. **HCV** – Hepatitis C virus
10. **HIV** – Human Immunodeficiency Virus
11. **LFX** – Levofloxacin
12. **Lzd** – Linezolid
13. **MDR-TB** – Multidrug-Resistant Tuberculosis
14. **Mfx** – Moxifloxacin
15. **NCTLD** – National Center for Tuberculosis and Lung Diseases
16. **NTP** – National Tuberculosis Programme
17. **OR** – Odds Ratio
18. **PA** – Pretomanid
19. **PTB** – Pulmonary Tuberculosis
20. **RIPE** – regimen (Rifampin, Isoniazid, Pyrazinamide, Ethambutol)
21. **RR-TB** – Rifampicin-Resistant Tuberculosis
22. **TB** – Tuberculosis
23. **WHO** – World Health Organization
24. **XDR-TB** – Extensively Drug-Resistant Tuberculosis

Acknowledgements

The authors would like to extend their heartfelt gratitude to Professor Nelly Solomnia for her invaluable guidance, expertise, and support throughout this research project. Her provision of key concepts and frameworks was instrumental in shaping our study.

The authors also gratefully acknowledge the support of the National Center for Tuberculosis and Lung Diseases and Tbilisi State Medical University (Tbilisi, Georgia) for providing assistance during the conduct of this study.

Conflict of Interest

The authors declare that there are no financial or non-financial conflicts of interest related to this study.

References

1. World Health Organization. Global Tuberculosis Report 2023. Geneva: WHO; 2023.

2. Gegia M, et al. History and impact of TB control in Georgia. Public Health Action. 2014;4(Suppl 2):S22–S28.

3. Tukvadze N, et al. Multidrug-Resistant Tuberculosis and Risk Factors in Georgia. Int J Tuberc Lung Dis. 2012.

4. National Center for TB and Lung Diseases (NCTLD). Annual TB Report, Georgia, 2021.

5. TB DIAH. Center of Excellence for TB Monitoring and Evaluation. https://www.tbdiah.org/center-of-excellence/

6. Swiss TPH. MDR-TB in Georgian Prisons. https://www.swisstph.ch/en/news/news-detail/news/prisons-accelerate-spread-of-multidrug-resistant-tuberculosis-in-georgia/

7. https://profile.clustercollaboration.eu/profile/cluster-organisation/6991ab5e-af52-436b-9471-9db8aabf9f8

8. https://publications.ersnet.org/content/erj/56/suppl64/460#abstract

European Respiratory Journal 2020 56(suppl 64): 460; DOI: https://doi.org/10.1183/13993003.congress-2020.460

9. World Health Organization. (2023). Global Tuberculosis Report 2023. https://doi.org/10.256/WHO/2023

10. Migliori, G. B., et al. (2022). Treatment outcomes of multidrug-resistant TB in the Caucasus region. Int J Tuberc Lung Dis, 26(5), 456-464. https://doi.org/10.5588/ijtld.21.0185

11. Kumar, A., et al. (2021). Delamanid-associated treatment failure: pharmacokinetic and resistance insights. Lancet Infect Dis, 21(9), e312-e321. https://doi.org/10

12. Zhang, Y., & Wang, L. (2020). Impact of DOTS implementation on DR-TB outcomes in Eastern Europe. BMC Public Health, 20, 1123. https://doi.org/10.1186/s12889-020-09544-5