Epidemiology and Burden of Drug-Resistant Tuberculosis in OR Tambo District Municipality, Eastern Cape, South Africa: A Retrospective Cross-Sectional Study

Yanga Somjobo , Lindiwe Modest Faye , Mojisola Clara Hosu *

Posted Date: 4 June 2026

doi: 10.20944/preprints202606.0374.v1

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 doi:10.20944/preprints202606.0374.v1

Article

Epidemiology and Burden of Drug-Resistant Tuberculosis in OR Tambo District Municipality, Eastern Cape, South Africa: A Retrospective Cross-Sectional Study

Yanga Somjobo, Lindiwe Modest Faye, and Mojisola Clara Hosu *

Tuberculosis and Antimicrobial Resistance Intervention Platform (TARIP), Tuberculosis Research Group, School of Pathology, Faculty of Medicine and Health Sciences, IYunivesithi Walter Sisulu, Mthatha 5100, South Africa

* Correspondence: mhosu@wsu.ac.za

Abstract

Background: Tuberculosis (TB) remains a major global health concern, particularly in low- and middle-income countries, due to its high prevalence, mortality, and economic impact. The emergence of drug-resistant tuberculosis (DR-TB) has intensified this burden, posing significant challenges to disease control and management. Understanding the epidemiology of DR-TB is crucial for improving prevention strategies, guiding treatment interventions, and informing public health policies aimed at reducing its spread and impact. **Methods:** A retrospective cross-sectional study was conducted using medical records of patients diagnosed with DR-TB between January 2020 and December 2024 at DR-TB Clinics in the O.R. Tambo District Municipality, Eastern Cape, South Africa. Data on demographic, clinical, and treatment outcome variables were collected using a structured abstraction tool. Data was analyzed using SPSS. **Results**: A total of 385 participants were included in the study, with a mean age of 38.6 years. Males accounted for 62.3% of cases. Most participants (94.3%) resided in rural areas, and 62% were HIV-coinfected. Rifampicin-resistant TB was the most common type (51%), followed by MDR-TB (38%). A significant association was observed between age and HIV status ($p = 0.001$). Treatment outcomes showed that 40.8% of patients were cured, while 11.7% died, with mortality highest among older and HIV-positive patients. Comorbidities reported included hypertension and diabetes mellitus. **Conclusions**: DR-TB in O.R. Tambo District disproportionately affects young adults, males, and HIV-positive individuals, with suboptimal treatment outcomes and a substantial comorbidity burden. Strengthened integrated TB/HIV care, early diagnosis, and targeted rural interventions are needed to improve DR-TB outcomes in this setting.

Keywords: drug-resistant tuberculosis; multidrug-resistant tuberculosis; epidemiology; tuberculosis burden; TB/HIV coinfection; O.R. Tambo District Municipality; Eastern Cape

1. Introduction

Tuberculosis (TB) is a contagious disease caused by *Mycobacterium tuberculosis*, primarily affecting the lungs, and is characterized by a prolonged incubation period and easy transmission. It remains a significant global public health challenge despite improvements in treatment and prevention [1,2]. According to the 2025 WHO global report, there were approximately 10.7 million new TB cases globally, with 54% men, 35% women, and 11% children. In the same year, an estimated 1.23 million deaths were recorded, with a case fatality rate of 11.5% [3]. TB continues to disproportionately affect low- and middle-income countries (LMICs), particularly in sub-Saharan Africa, where poverty, overcrowding, malnutrition, HIV co-infection, and limited healthcare access perpetuate disease transmission and poor treatment outcomes [4,5].

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Drug-resistant tuberculosis (DR-TB) has emerged as a major public health challenge, threatening progress toward the global End TB Strategy targets [6]. DR-TB occurs when *Mycobacterium tuberculosis* develops resistance to one or more first-line anti-tuberculosis drugs, primarily due to inadequate treatment adherence, poor-quality medications, delayed diagnosis, interrupted drug supply, and ongoing transmission of resistant strains within communities [6–8]. The most concerning forms include rifampicin-resistant TB (RR-TB), multidrug-resistant TB (MDR-TB), pre-extensively drug-resistant TB (pre-XDR-TB), and extensively drug-resistant TB (XDR-TB). In 2024, approximately 0.40 million cases were MDR/RR-TB, with an estimated 0.15 million deaths, underscoring the persistent challenge of DR-TB in global TB control efforts [3]. Although the global burden of MDR/RR-TB has gradually declined since 2015, DR-TB remains a significant challenge in resource-limited settings because of prolonged treatment regimens, adverse drug reactions, low treatment success rates, and increased healthcare costs. The economic burden of DR-TB is substantial, with more than 81% of affected households facing catastrophic healthcare expenses for treatment [9].

The African region continues to bear a disproportionately high burden of TB. According to the WHO African Regional Office, about 57,000 people in Africa developed MDR/RR-TB in 2024, accounting for nearly 15% of global DR-TB cases [10]. That year, roughly 390,000 TB cases in the region were linked to HIV infection, representing about one-third of all TB cases there [10]. The concurrent spread of TB and HIV poses significant challenges for disease control, especially in countries like South Africa, where HIV-induced immunosuppression heightens vulnerability to TB infection and progression to active disease [11,12].

South Africa remains among the 30 countries with the highest TB burden globally and faces significant challenges related to TB/HIV co-infection and DR-TB. According to the WHO Global Tuberculosis Report 2025, despite substantial investments in prevention and treatment, South Africa still has one of the world's highest TB incidence rates [3]. The country has made progress by expanding rapid molecular diagnostics, such as GeneXpert MTB/RIF, and adopting shorter, all-oral DR-TB treatment regimens [13]. Nonetheless, DR-TB continues to impede TB control efforts because of persistent transmission, delayed case detection, socioeconomic disparities, and challenges with treatment adherence.

National surveillance data from the South African District Health Information System (DHIS) indicate that the Eastern Cape Province remains among those with persistently high TB notification rates and a substantial DR-TB burden [14]. The province is marked by widespread poverty, unemployment, inadequate housing, and limited access to healthcare services, all of which contribute to ongoing TB transmission [15–17]. Within the Eastern Cape, the O.R. Tambo District Municipality has consistently been identified as a high-burden district for TB and DR-TB. The district experiences considerable socioeconomic deprivation, high HIV prevalence, and healthcare resource constraints, which together increase vulnerability to TB infection and lead to poor treatment outcomes.

Despite ongoing TB control efforts at the national and provincial levels, detailed district-level data on the distribution, trends, and burden of DR-TB remain scarce in many rural and underserved areas of South Africa. Such localized epidemiological information is vital for guiding targeted public health actions, strengthening surveillance, optimizing resource allocation, and improving treatment outcomes in affected communities [1,18]. Additionally, identifying demographic and clinical factors associated with DR-TB at the district level is crucial for developing strategies to reduce transmission and achieve the country's TB elimination goals.

2. Materials and Methods

2.1. Study Design

This study used a retrospective cross-sectional design, reviewing records of patients diagnosed with DR-TB between January 2020 and December 2024.

 doi:10.20944/preprints202606.0374.v1

2.2. Study Setting

The Eastern Cape Province ranks fourth among South Africa's nine provinces, with a population of 6.67 million, representing 11.1% of the country's total population. The Eastern Cape's share of national GDP was 7.6% [15]. The O.R. Tambo District covers approximately 12,095.1 km2. The district is designated a Category C2 Municipality, indicating it is predominantly rural. The study was conducted at selected healthcare facilities in the O.R. Tambo District Municipality in the Eastern Cape Province. These facilities provided primary and district-level anti-TB services and served as the region's rural health care delivery system.

2.3. Data Collection

Data was extracted from patient files using a structured data abstraction tool. Variables collected included demographics, clinical information, comorbidities, treatment details, and outcomes. Data was captured in Excel, cleaned, and exported into SPSS for statistical analysis.

2.4. Data Analysis

Data was entered into Microsoft Excel and analyzed using SPSS version 30 (IBM Corp., Armonk, NY, USA). All descriptive statistics are presented as frequencies and percentages. A p-value of < 0.05 was considered statistically significant.

2.5. Operational Definitions

Multidrug-resistant TB (MDR-TB) is caused by *Mycobacterium tuberculosis* strains resistant to both isoniazid and rifampin. Pre-extensively drug-resistant TB (pre-XDR-TB) refers to MDR/RR-TB strains that are also resistant to fluoroquinolones. Extensively drug-resistant TB (XDR-TB) involves MDR/RR-TB strains that, in addition to fluoroquinolone resistance, are resistant to at least one Group A drug, such as levofloxacin, moxifloxacin, bedaquiline, or linezolid.

3. Results

3.1. Demographic Characteristics of Study Participants

A total of 385 participants were included in the analysis. Over 60% of the population were males, with almost 60% in the 18-39 age bracket. The mean age of participants was 38.6 years (SD = ±14.2), with a median age of 37 years. The age distribution ranged from 25 years at the 25th percentile to 48 years at the 75th percentile (Table 1).

Table 1. Demographic characteristics of the study population.

Demographic	All (N=385), n (%)	HIV positive (N=238), n (%)	HIV negative (N=145), n (%)	p-value
Gender				0.20
Male	240 (62.3)	142 (59.7)	96 (66.2)	
Female	145 (37.7)	96 (40.3)	49 (33.8)	
Age				<0.001
<=24	49 (12.7)	13(5.5)	36 (24.8)	
25-39	178 (46.2)	124 (52.1)	53 (36.6)	
40-53	100 (26.0)	74 (31.1)	26 (17.9)	
54+	58 (15.1)	27 (11.3)	30 (20.7)	
Residence				0.23
Peri-urban	22 (5.7)	8 (3.4)	14 (9.7)	
Rural	363 (94.3)	230 (96.6)	131 (90.3)	

3.2. Patterns of Drug-Resistant TB

The distribution of patients by DR-TB type showed that RR-TB accounted for 51% of cases, followed by MDR-TB (38%), Pre-XDR-TB (5%), and XDR-TB (0.8%) (Table 2). Across all resistance

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types, the 25–39-year age group remained the most affected. RR-TB and MDR-TB cases peaked within this group (47.5% and 46.9%, respectively). Pre-XDR-TB was more frequent among older adults aged 40–53 years (40%), while all XDR-TB cases occurred in individuals aged 25–39 years. Overall, 61.8% of participants were HIV-positive. HIV co-infection rates increased with higher levels of resistance.

Table 2. Distribution of DR-TB and HIV coinfection in the study population.

Variables	ALL (N=385), n (%)	RR (N = 196), n (%)	MDR (N= 145), n (%)	Pre-XDR (N= 20) n (%)	XDR (N = 3), n (%)
Age					
<=24	49 (12.7)	24 (12.2)	21 (14.5)	1 (5.0)	0 (0)
25-39	178 (46.2)	93 (47.5)	68 (46.9)	7 (35.0)	3 (100)
40-53	100 (26.0)	50 (25.5)	34 (23.5)	8 (40.0)	0 (0)
54+	58 (15.1)	29 (14.8)	22 (15.2)	4 (20.0)	0 (0)
Gender					
Male	240 (62.3)	127 (64.8)	87 (60.0)	10 (50)	1 (33.3)
Female	145 (37.7)	69 (35.2)	58 (40.0)	10 (50)	2 (66.7)
HIV status					
HIV positive	238 (61.8)	120 (61.2)	90 (62.1)	13 (65.0)	3 (100)
HIV negative	145 (37.7)	76 (38.8)	54 (37.2)	7 (35.0)	0 (0)

3.3. Treatment Outcomes and Associated Factors

Treatment outcomes among the 385 participants revealed that 157(40.8%) were cured, 91 (23.6%) completed treatment, 35 (9.1%) were lost to follow-up (LTFU), 11 (2.9%) experienced treatment failure, 45 (11.7%) died, and 38 (9.9%) were transferred out (Table 3).

Table 3. Treatment outcomes of the study population.

Variables	All N=385	Cured N=157, n (%)	Tx Complete N=91, n (%)	LTFU N=35, n (%)	Tx Failed N=11, n (%)	Died N=45, n (%)	Transferred out N=38, n (%)
Age							
<=24	49 (12.7)	22 (14.0)	17 (18.7)	4 (11.4)	3 (27.3)	1 (2.2)	2 (5.3)
25-39	178 (46.2)	76 (48.4)	40 (44.0)	23 (65.7)	5 (45.5)	14 (31.1)	17 (44.7)
40-53	100 (26.0)	42 (26.8)	22 (24.2)	5 (14.3)	2 (18.2)	12 (26.7)	12 (31.6)
54+	58 (15.1)	17 (10.8)	12 (13.2)	3 (8.6)	1 (9.1)	18 (40.0)	7 (18.4)
Gender							
Male	240 (62.3)	107 (68.2)	47 (51.7)	24 (68.6)	3 (27.3)	29 (64.4)	23 (60.5)
Female	145 (37.7)	50 (31.9)	44 (48.3)	11 (31.4)	6 (72.7)	16 (35.6)	15 (39.5)
Comorbidities							
Hypertension	37 (9.6)	17 (10.8)	8 (8.8)	2 (5.7)	0 (0)	5 (11.1)	5 (13.2)
Diabetes	9 (2.3)	3 (1.9)	3 (3.3)	0 (0)	0 (0)	1 (2.2)	0 (0)
Epilepsy	8 (2.1)	5 (3.2)	0 (0)	0 (0)	0 (0)	3 (6.7)	0 (0)
Mental Illness	3 (0.8)	2 (1.3)	0 (0)	1 (2.9)	0 (0)	0 (0)	0 (0)
Hearing Loss	2 (0.5)	0 (0)	1 (1.10)	0 (0)	0 (0)	0 (0)	0 (0)
Allergies	3 (0.8)	3 (1.9)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
HIV status							
HIV positive	238 (61.8)	107 (68.2)	53 (58.2)	22 (62.9)	8 (72.7)	24 (53.3)	22 (57.9)

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HIV negative	145 (37.7)	49 (31.2)	38 (41.8)	13 (37.1)	3 (27.3)	21 (46.7)	16 (42.1)
Regimen type							
Long	55 (14.3)	16 (10.2)	14 (15.4)	5 (14.3)	0(0)	9 (20)	11 (29.0)
Short	329 (85.5)	141 (89.8)	77 (84.6)	30 (85.7)	11 (100)	36 (80)	27 (71.1)
Type of DR-TB							
RR	196 (50.9)	74 (47.1)	50 (55.0)	21 (60)	0 (0)	29 (64.4)	18 (47.4)
MDR	145 (37.7)	61 (38.9)	37 (40.7)	10 (28.6)	9 (81.8)	12 (26.7)	13 (34.2)
Pre-XDR	20 (5.2)	5 (3.2)	3 (3.3)	2 (5.6)	2 (18.2)	2 (4.4)	6 (15.8)
XDR	3 (0.7)	0 (0)	0 (0)	2 (5.7)	0 (0)	0 (0)	1 (2.6)

4. Discussion

The present study demonstrated that DR-TB in the O.R. Tambo District Municipality predominantly affected young economically active adults, with a mean age of 38.6 years and 59% of participants aged 18–39 years. Similar demographic patterns have been widely reported in South Africa and other high-burden settings globally. In a recent DR-TB hotspot study in the O.R. Tambo District, the mean age was 37.5 years, with the majority of patients aged 20–59 years [19]. Comparable findings have also been documented in Ethiopia, Nigeria, and Zimbabwe, where DR-TB disproportionately affects young adults who are socially and economically active [20–22]. A study by Bonsa et al. [23] in Ethiopia reported that almost half of the MDR-TB patients were between 25 and 44 years old, reflecting increased exposure, mobility, and HIV prevalence among younger adults. Similarly, studies from India and Central Asia have consistently shown that MDR/RR-TB prevalence is higher among middle-aged individuals, suggesting that DR-TB remains largely a disease of economically productive populations [24,25]. These patterns suggest ongoing community transmission among mobile, working-age populations, with important implications for household transmission, productivity loss, and health-system burden.

In this study, males accounted for 62.3% of cases, consistent with other South African and international research. WHO reports consistently indicate that TB is more common in men than in women globally [3,26]. Male dominance in DR-TB cases has been repeatedly observed in cohorts from South Africa, Nigeria, and Ethiopia [19,20,27]. Consistent with our study findings, Faye et al. [19] observed that 56.1% of participants were male, whereas Ogunsina et al. [28] reported that 67.6% were male and 32.4% were female. Gender differences in TB are linked to occupational exposure and behavioral factors such as delayed healthcare seeking, smoking, alcohol use, and poor treatment adherence among men [29–31]. Men's occupational mobility increases the risk of treatment interruption and the development of DR-TB, while family and community support promote treatment adherence and reduce this risk [32]. Active, young working men, often away from family and community, face a higher risk of DR-TB. These patterns are more prominent in men than in women [29]. In Asia, male migration primarily drives disease spread, whereas in sub-Saharan Africa, a high female HIV burden due to structural vulnerabilities influences disparities. These regional differences highlight how socioeconomic and demographic factors shape gender differences in public health [33–36].

The overwhelming majority of participants lived in rural areas, underscoring the rural burden of DR-TB in the Eastern Cape Province. Despite decentralization efforts, DR-TB service delivery in the O.R Tambo District remains constrained by geographic and socioeconomic barriers, leading to poor adherence and treatment interruptions [37]. Globally, an alarming health disparity persists between urban and rural populations [38]. Rurality has been linked to delayed diagnosis, limited treatment access, transportation barriers, and interrupted continuity of care in several African countries [17,39]. Studies from rural KwaZulu-Natal and Mozambique report that patients frequently experience diagnostic delays and poorer treatment outcomes due to limited healthcare infrastructure and inadequate access to specialized DR-TB services [40–42]. These findings underscore the urgent

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need to strengthen rural health systems and expand access to timely DR-TB diagnosis and treatment to reduce the rural burden of the disease.

The HIV co-infection rate observed in this study reflects the persistent overlap between the TB and HIV epidemics in South Africa. The significant association between age and HIV status further underscores the influence of HIV on DR-TB epidemiology among younger and middle-aged adults. Similar HIV co-infection rates have been documented in KwaZulu-Natal and the Eastern Cape, where HIV prevalence among DR-TB patients often exceeds 50% [43,44]. Studies from Lesotho and Eswatini have likewise reported extremely high HIV prevalence among MDR/RR-TB patients [45,46]. HIV is a recognized risk factor for unfavorable DR-TB outcomes, even among patients on antiretroviral therapy (ART). [47,48]. Enhancing integrated care and patient support remains crucial to improving outcomes for this vulnerable population [49,50]. Ensuring adherence to TB and ART regimens is critical to improving outcomes for co-infected individuals, especially in a predominantly rural setting like the Eastern Cape.

Our study found that RR-TB is the predominant form of drug resistance. This pattern closely mirrors findings from retrospective cross-sectional studies in Limpopo [51,52]. Previous studies have shown that RR-TB is a reliable surrogate marker for MDR-TB because rifampicin resistance is often accompanied by isoniazid resistance [53]. Consequently, rapid detection of RR-TB using molecular diagnostic tools enables early identification and treatment of probable MDR-TB cases, thereby reducing management delays and limiting community transmission.

The treatment outcomes in this study raise concerns. The cure rate observed is notably lower than the figures reported in the WHO global 2025 report and another South African study [3,51]. These disparities may be due to factors such as the rural setting of O.R. Tambo, high HIV co-infection rates, socioeconomic challenges, and potential gaps in treatment support. The mortality rate, especially among HIV-positive individuals, aligns with data from high HIV-burden areas in sub-Saharan Africa [51,54]. HIV-positive patients face a heightened risk of death due to drug interactions, delayed ART initiation, immunosuppression, opportunistic infections, and treatment complications [55].

The presence of hypertension and diabetes as comorbidities is clinically significant because non-communicable diseases (NCDs) may complicate DR-TB treatment, increase pill burden, and worsen outcomes. Similar findings have been reported in KwaZulu-Natal and among public primary care patients in South Africa, where hypertension, diabetes mellitus, cardiovascular disease (CVD), and other NCDs were associated with poorer TB and DR-TB treatment outcomes, increased mortality, and greater treatment complexity [56–58]. The dual burden of infectious and NCDs in the Eastern Cape, therefore, necessitates integrated screening and management at the primary healthcare level, particularly for patients initiating TB treatment.

Implications for Public Health Practice

These findings have practical value for public health. First, they support stronger integration of TB and HIV services, especially for older adults and rural patients, who appear to be at higher risk of poor outcomes. Second, the predominance of RR-TB underscores the need for rapid diagnosis, prompt linkage to treatment, and routine follow-up resistance testing to ensure regimens match resistance patterns early. Third, the high rural burden highlights the need for decentralized care, community follow-up, transport support, and stronger tracing systems to reduce delays and treatment interruptions. Fourth, men should be prioritized for early screening and support for retention. Finally, district TB programs should strengthen routine surveillance so that local trends in mortality, cure, and resistance patterns can guide timely decisions on staffing, outreach, and drug supply. These priorities align with South Africa's current RR-TB clinical guidance and TB recovery strategy.

Limitations of the study

This study has several limitations. First, the retrospective cross-sectional design relied on routinely recorded data, which may have been missing or incomplete. Second, the study could describe patterns and associations but could not establish cause-and-effect relationships. Third, the analysis was limited to variables available in patient records, so important factors such as the timing of ART initiation, adherence, socioeconomic hardship, distance to clinic, and resistance to second-

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line drugs may not have been fully captured. Fourth, the findings come from one district and may not be directly generalizable to all settings in South Africa. Finally, treatment outcome categories were summarized at a single point in time, so longer-term relapse or post-treatment survival could not be assessed.

5. Conclusions

DR-TB in the O.R. Tambo District remains a significant public health concern, especially among young adult males, rural populations, and those coinfected with HIV. While the demographic and resistance patterns align broadly with other South African studies, the cure rate is notably lower than both national and global benchmarks. This issue is compounded by barriers to rural healthcare access and the persistent intersection of TB and HIV. These insights highlight the need for enhanced rural DR-TB surveillance, earlier use of molecular diagnostics, integrated HIV and TB care, support for treatment adherence, screening for comorbidities, and targeted strategies for men and economically active adults.

Author Contributions: Conceptualization, Y.S. and M.C.H.; methodology, Y.S.; L.M.F.; and M.C.H.; validation, LM.F., and M.C.H.; formal analysis, Y.S. and M.C.H.; investigation, Y.S.; data curation, Y.S., L.M.F., and M.C.H.; writing—original draft preparation, Y.S.; writing—review and editing, L.M.F. and M.C.H.; supervision, M.C.H.; project administration, M.C.H. All authors have read and agreed to the published version of the manuscript.

Funding: This research received no external funding, and the APC was funded by IYunivesithi Walter Sisulu.

Institutional Review Board Statement: The study was conducted in accordance with the Declaration of Helsinki, and approved by the Walter Sisulu Health Sciences Research Ethics Committee (protocol code WSU HREC 114/2025 and date of approval 03 July 2025).

Informed Consent Statement: The study reviewed medical records of DR-TB patients and had no contact with patients; therefore, consent was not required. All data were anonymized, and no identifiable information was included in the analysis or reporting of results.

Data Availability Statement: Data are contained within the article.

Acknowledgments: The authors are grateful to the healthcare facility managers for granting access to patients' records.

Conflicts of Interest: The authors declare no conflicts of interest.

Abbreviations

The following abbreviations are used in this manuscript:

ART	Antiretroviral therapy
CVD	Cardiovascular disease
DHIS	District Health Information System
DR-TB	Drug-resistant tuberculosis
LMICS	Low- and middle-income countries
LTFU	Loss to follow up
MDR-TB	Multidrug-resistant tuberculosis
NCDs	Non-communicable diseases
Pre-XDR-	Pre-extensively drug-resistant tuberculosis
RR-TB	Rifampicin-resistant tuberculosis
TB	Tuberculosis
WHO	World Health Organization
XDR-TB	Extensively-drug resistant tuberculosis

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