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The epidemiology of drug-resistant tuberculosis in Bulawayo and Matabeleland South provinces, Zimbabwe 2017

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ABSTRACT

Objective: To investigate determinants of drug resistance and treatment outcomes among patients with drug-resistant tuberculosis (DR-TB).

Design: This was a cross-sectional study on patients diagnosed with DR-TB in Bulawayo and Matabeleland South provinces, 2015.

Results: A total of 129 participants were identified. DR-TB patients were 3.4 times more likely to have been treated previously for sensitive TB (95% confidence interval 1.3–9.2). Approximately 88.5% of DR-TB patients were diagnosed before completing the sensitive TB course and another 82.1% developed DR-TB within 6 months of completing sensitive TB treatment. The likelihood diminished with increasing time interval, becoming less likely at >12 months post-treatment. Most DR-TB patients (87.5%) were likely to have resided outside Zimbabwe and to have fallen ill there (85.2%). Overall, hearing loss was the most prevalent (70%) medication side effect experienced. Unfavourable interim treatment outcomes were high for patients <6 months on treatment (prevalence odds ratio 2.7, 95% CI 1.2–6.1), becoming 44% less likely after 18 months (95% CI 1.2–11.4).

Conclusions: The majority of DR-TB patients were diagnosed during sensitive TB treatment, suggesting missed DR-TB diagnosis or inadequate treatment. Delays in starting effective TB regimens negatively affect treatment outcomes. Drug sensitivity testing at diagnosis, patient monitoring, and enhanced adherence counselling are recommended.

1. Introduction

Drug-resistant tuberculosis (DR-TB) is a term that describes strains of *Mycobacterium tuberculosis* that demonstrate resistance to one or more of the first-line drugs for tuberculosis (TB) treatment, and encompasses rifampicin-resistant TB (RR-TB), multidrug-resistant TB (MDR-TB), and extensively drug-resistant TB (XDR-TB) (TBFacts.org website, n.d.; WHO/CDC, 2016). DR-TB is emerging as a global public health crisis, threatening to undermine the global TB control achievements made to date (Peitzmeier et al., 2017). The sustainable development goal (SDG) target to end TB by 2030, coupled with the globally endorsed milestones and targets as outlined in the World Health Organization (WHO) End TB Strategy, in combination, aim to mitigate the TB scourge across the globe (World Health Organization, 2014b). These strategies present both a challenge and an occasion for the TB community to change, acclimatize, and embrace every step necessary to reach the vision of a world where no one dies from a curable and preventable disease (World Health Organization, 2014a).

Zimbabwe is ranked the 17th highest TB burden country in the world, and one of the eight countries in Africa belonging to the 30 high burden TB, TB/HIV, and DR-TB countries (World Health Organization, 2017). TB is the second leading cause of severe morbidity and mortality in Zimbabwe (Zimbabwe Ministry of Health and Child Care, 2018a). In a country where HIV drives TB, with high rates of co-infection (80%), TB treatment outcomes remain suboptimal due to the high mortality (Zimbabwe Ministry of Health and Child Care, 2018b).

While TB incidence is on a descending trajectory in Zimbabwe, DR-TB is increasing, with Bulawayo and Matabeleland South provinces bearing a disproportionate overall burden, as illustrated in Figure 1.

If the current DR-TB trend in Zimbabwe is sustained, the country is set to miss the goal of reducing TB incidence by 90% (<10/100 000)

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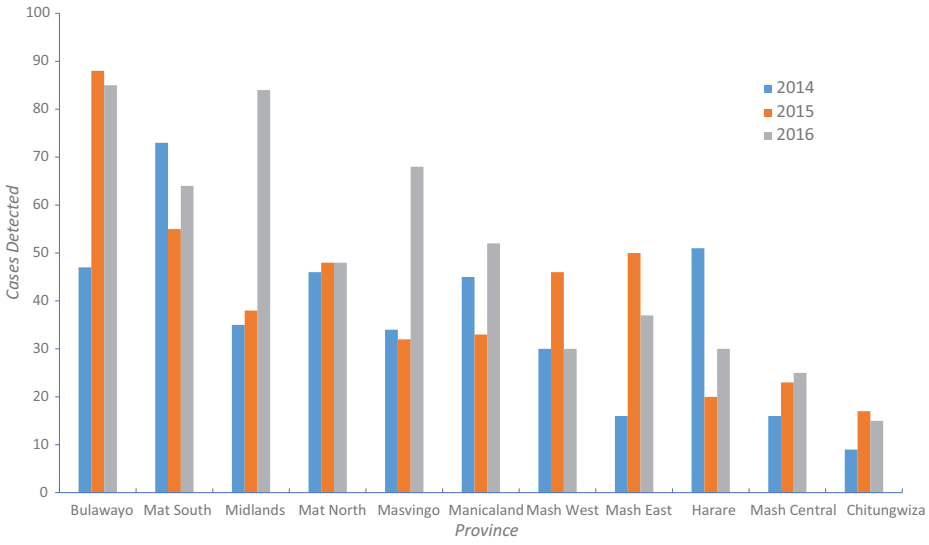

Figure 1. Drug-resistant tuberculosis cases detected, 2014–2016 (National TB Programme data).

by 2035, as espoused in the End TB Strategy (World Health Organization, 2014b). This study was performed to analyse the epidemiology of DR-TB among new and previously treated drug-sensitive clients in the high burden provinces of Zimbabwe (Bulawayo and Matabeleland South provinces), as well as the interim treatment outcomes.

2. Methods

2.1. Study design

A cross-sectional study with an analytical component was used to describe the diagnosis and treatment outcomes of DR-TB in the selected provinces.

2.2. Setting

This study was set in Zimbabwe, located in southern Africa, with a total population of 14.6 million distributed among 10 provinces.

During the period investigated, 'presumptive TB' patients were evaluated at primary and rural health centres where sputum specimens were collected and sent to the reference laboratory in Bulawayo for direct smear microscopy and other tests. The algorithm used at the time did not advocate drug susceptibility testing (DST) for all clients diagnosed with TB. Before 2017, the following groups were prioritized for Xpert MTB/RIF testing, culture, and DST: people with a history of travel to South Africa or Botswana, previously treated TB patients, and those living with HIV. In Zimbabwe, Xpert MTB/RIF was rolled out around 2016 (108 instruments deployed). Drug-resistant, new, and previously treated TB patients received the WHO-recommended standardized 2-year regimen with routine follow-up. The treatment for DR-TB administered was a standardized second-line regimen, comprising an 8-month intensive phase with at least six drugs and a 12-month continuation phase with four drugs, following confirmation of resistance on phenotypic DST. DR-TB patients were admitted to the hospital during the intensive phase of treatment, or for longer, until culture conversion. Patients were referred to proximal primary health care facilities for continuous medication resupply. All treatment was delivered under direct observation (directly observed therapy, DOT) by a health worker. All TB patients were offered HIV testing; those found to be HIV-infected were offered cotrimoxazole preventive therapy (CPT) and antiretroviral therapy (ART) using a first-line regimen consisting of zidovudine/stavudine, lamivudine, and efavirenz. Diagnosis and treatment services were provided free of charge to the patient. Case definitions, outcome categories, recording, and reporting followed national TB programme (NTP) guidelines, which are in accordance with WHO guidelines, and all patient information was captured in manual National TB Registers.

Regarding the study site, Bulawayo and Matabeleland South provinces are located to the south of the country, close to the borders with Botswana and South Africa. Matabeleland South sits at the edge of the Kalahari Desert and has a population of 683 893 spread across seven districts in an area of 54 125 km^2 and a density of 12.636/km^2 (UNDP and Government of Zimbabwe, 2017). Bulawayo is located in the southwest part of the country and has a population of 653 337, covering an area of 39 070 km^2 and has a density of 3389/km^2. Bulawayo is the second largest city in Zimbabwe and is subdivided into five districts. TB services are offered at all 19 health facilities and one infectious diseases hospital in Bulawayo, and a TB focal person oversees service delivery activities. Unlike Bulawayo, Matabeleland South Province has district stationed focal persons that oversee TB service delivery activities. A provincial TB coordinator assumes overall supervision of the district activities and resource distribution.

2.3. Patient population

All laboratory-confirmed DR-TB patients, ≥18 years of age, who were diagnosed with DR-TB during the period January 1 to December 30, 2015 were included. The study was conducted between January and August 2017.

2.4. Data variables, sources of data, and data collection

Information was obtained on the following variables: age, sex, and date of diagnosis for all DR-TB diagnosed patients (defined as the date when the laboratory results were available). The date of treatment initiation, history of previous anti-TB treatment (both first- and second-line anti-TB drugs), HIV status, ART, and TB treatment outcomes were all evaluated. The sources of data were manual clinical records, triangulated with district electronic databases. A pre-tested interviewer-administered questionnaire was used to collect demographic, sociocultural, and treatment-related data from the DR-TB patients. Contact addresses and telephone numbers were used to trace clients who had completed treatment, with the assistance of TB focal persons and village health workers.

2.5. Statistical analysis

Data were cleaned to curtail errors during data entry and analysed using Epi Info Statistical Package version 7 (**Supplementary Material**

Table 1
Demographic characteristics of participants—Bulawayo and Matabeleland South provinces, 2015 (N = 129)

Variable	Category	Bulawayo (n = 90)	Matabeleland South (n = 39)
Sex, n (%)	Female	49 (54.4)	21 (53.8)
	Male	41 (45.6)	18 (46.2)
Age (years), n (%)	18–25	13 (14.4)	6 (15.4)
	25+	77 (85.6)	33 (84.6)
Age (years), median (IQR)		35 (32.5, 43)	37(28.5, 47.5)
Marital status	Single	21 (23.3)	7 (17.95)
	Married	37 (41.1)	17 (43.6)
	Divorced	16 (17.8)	8 (20.5)
	Widowed	16 (17.8)	7 (17.95)
Education level	Never been to school	5 (5.6)	8 (20.5)
	Primary	0 (0)	0 (0)
	Secondary	73 (81.1)	27 (69.2)
	Tertiary	12 (13.3)	4 (10.3)
Religion	Orthodox	31 (34.4)	17 (43.6)
	Pentecostal	26 (28.9)	8 (20.5)
	Apostolic	20 (22.2)	7 (17.95)
	African	9 (10)	7 (17.95)
	Muslim	4 (4.4)	0 (0)

IQR, interquartile range.

Annex S1). A univariate analysis was performed to describe the demographic and clinical characteristics of the DR-TB patients. Interim treatment outcomes were analysed because the recruited population was yet to complete the 2-year treatment regimen. Favourable interim treatment outcomes were grouped to include retention in care with no history of interrupted medication intake and those cured after the regimen. Unfavourable interim treatment outcomes included a history of stopping medication intake, experiencing medication side effects, loss to follow-up, relapse, and death whilst on medication.

A bivariate analysis was performed to examine the factors associated with DR-TB exposure and outcomes. Prevalence odds ratios (PORs) at a 5% significance level were calculated as measures of association. A forward stepwise logistic regression was conducted to adjust for multiple confounders and compute adjusted PORs (aPORs). In addition to age and sex, variables found to be significantly associated in the bivariate analysis (P = 0.1) were included in the model.

3. Results

3.1. Baseline characteristics

Of the 143 documented DR-TB patients diagnosed, 129 (90.2%) were identified and interviewed. Fourteen participants could not be traced through the details provided.

3.2. Demographic characteristics of the participants

The majority of participants in Bulawayo and Matabeleland South provinces were female: 54.4% and 53.9%, respectively. The median age was 35 years (interquartile range 32.5–43 years) for Bulawayo and 37 years (interquartile range 28.5–47.5 years) for Matabeleland South. The majority of participants in each province were married: 41.1% for Bulawayo and 43.6% for Matabeleland South. The most common religion was Pentecostal for Bulawayo participants (28.9%), whilst Orthodox churches were more common in Matabeleland South province (43.6%). Muslim was the least practised form of religion, at 4.4% for Bulawayo and 0% for Matabeleland South (Table 1).

3.3. Income and habitation of study participants

Self-employment was the most common source of livelihood for participants in both Bulawayo and Matabeleland South provinces, at 36.7% and 43.6%, respectively. A small proportion of participants from Matabeleland South (2.6%) and 20% from Bulawayo earned >US$500 monthly. The majority (48.9%) of participants in Bulawayo were renting accommodation, whilst in Matabeleland South, most (41%) participants owned the houses they were residing in (Table 2).

Rifampicin mono-resistance was the most common type of DR-TB for both Bulawayo and Matabeleland South province, at 78.9% (n = 71) and 82% (n = 32), respectively. XDR-TB was least common at 6.7% (n = 6) for Bulawayo and 2.6% (n = 1) for Matabeleland South province.

3.4. Sociocultural factors associated with DR-TB

Most of the DR-TB patients (70%, n = 90) had a history of HIV treatment. Furthermore, DR-TB patients reported a history of residing in South Africa for at least 6 months (87.5%, n = 56), having fallen ill outside Zimbabwe (85.2%, n = 58), a history of alcohol intake (82%, n = 41), and smoking (81.3%, n = 26). Only 17.4% (n = 8) of the DR-TB patients reported receiving a visitor suffering from TB (Table 3).

3.5. Type of TB and risk of DR-TB treatment outcome

Most DR-TB patients, 83.2% (n = 84), had been treated previously for sensitive TB. Among the previously treated, 88.5% (n = 23) were diagnosed before completing the 6-month treatment duration for sensitive TB, whilst 82.4% (n = 42) reported stopping medication intake during the previous treatment period. Participants who experienced medication side effects during previous TB treatment (85.7%, n = 24) constituted the majority of participants diagnosed with DR-TB. Most of the DR-TB patients (82.1%, n = 32) were diagnosed less than 6 months from completion of sensitive TB treatment. This was followed by those who had completed sensitive TB treatment between 6 and 12 months ago and those who had completed it more than 12 months ago, at 80.7% (n = 50) and 57% (n = 4), respectively (Table 4).

3.6. Interim outcomes for DR-TB treatment

Among the DR-TB patients on treatment, those who had taken medication for less than 6 months were 2.7 times more likely to have an unfavourable treatment outcome than those who had received treatment for longer than 6 months (95% CI 1.2–6.1). Adjusted for age and sex in the logistic regression, 70% of DR-TB patients were likely to have received sensitive TB treatment for less than 6 months, before being diagnosed with DR-TB (95% CI 1.5–4.2, P = 0.02) (Table 5).

Among the participants who had an unfavourable treatment outcome, four from Bulawayo (4.4%) and one from Matabeleland South

Table 2
Income and habitation characteristics—Bulawayo and Matabeleland South provinces, 2015 (N = 129)

Variable	Category	Bulawayo (n = 90)	Matabeleland South (n = 39)
Occupation, n (%)	Unemployed	32 (35.6)	17 (43.6)
	Self-employed	33 (36.7)	19 (48.7)
	Formally employed	25 (27.8)	3 (7.7)
Income level (US$), n (%)	<200	54 (60)	32 (82.1)
	201–500	18 (20)	6 (15.4)
	>500	18 (20)	1 (2.6)
Number of persons per room, n (%)	≤3	35 (38.9)	18 (46.2)
	>3	55 (61.1)	21 (53.9)
Ownership status of residence, n (%)	Parents' house	6 (6.7)	12 (30.8)
	House owned	12 (13.3)	16 (41)
	Renting	44 (48.9)	7 (17.9)
	Living with relatives	28 (31.1)	4 (10.3)

Table 3
Sociocultural factors associated with DR-TB—Bulawayo and Matabeleland South provinces, 2015

Exposure	Outcome	
	DR-TB	%
HIV treatment	90	78.3
Diabetes mellitus	5	17.9
Resided in South Africa ≥6 months	56	87.5
Resided in Botswana ≥6 months	5	33.3
Fell ill with TB outside Zimbabwe	58	85.2
Visitor suffering from TB	8	17.4
History of smoking	26	81.3
History of alcohol intake	41	82
History of social drugs use	3	20

DR-TB, drug-resistant tuberculosis.

Table 4
Previous treatment factors associated with DR-TB—Bulawayo and Matabeleland South provinces, 2015

Exposure	Outcome	
	DR-TB	%
Previously treated for TB	84	83.2
Received sensitive treatment <6 months	23	88.5
Stopped medication during previous treatment	42	82.4
Experienced side effects during previous treatment	24	85.7
Time interval from TB treatment to DR-TB diagnosis		
<6 months	32	82.1
6–12 months	50	80.7
>12 months	4	57.1

DR-TB, drug-resistant tuberculosis.

Table 5
Interim outcomes of DR-TB treatment by duration of treatment—Bulawayo and Matabeleland South provinces, 2015

Duration in care	Unfavourable outcome	Favourable outcome	POR	95% CI	P-value
<6 months	19 (38.8)	30 (61.2)	2.7	1.2–6.1	0.007
6–12 months	1 (5.9)	16 (94.1)	0.15	0.01–1.17	0.02
13–18 months	6 (24)	19 (76)	0.9	0.3–2.4	0.39
19–24 months	7 (18.9)	30 (81.1)	0.56	0.2–1.4	0.1

DR-TB, drug-resistant tuberculosis; POR, prevalence odds ratio; CI, confidence interval.

province (2.6%) had a history of defaulting treatment. Five (5.6%) from Bulawayo and 12 (30.8%) from Matabeleland South province died before completing treatment, whilst one per province, 1.1% from Bulawayo and 2.6% from Matabeleland South, were lost to follow-up.

3.7. Side effects experienced whilst on DR-TB treatment

Hearing loss was the most prevalent DR-TB medication side effect reported by Bulawayo (69%) and Matabeleland South (73%) participants, impeding effective communication during interviews. The least prevalent side effect was a loss of appetite at 2.8% (n = 2) reported by Bulawayo participants only (Figure 2).

4. Discussion

Three key findings of this study are highlighted. Firstly, about 70% of all DR-TB patients were diagnosed during treatment for drug-sensitive TB, which indicates missed DR diagnosis or inadequate treatment. This finding may be mitigated by performing routine DST for diagnosis and on all bacteriologically confirmed TB. This will allow early diagnosis and early treatment initiation, and ultimately minimize the development of negative treatment outcomes. Secondly, negative DR-TB treatment outcomes were more likely to occur during the first few months of treatment initiation. This may suggest that there was a delay in diagnosis and initiation of DR-TB treatment, hence the likelihood of negative outcomes. Thirdly, a history of residing in neighbouring countries, particularly South Africa, was closely associated with DR-TB, resulting in the provinces proximal to the border being disproportionately affected.

4.1. Delayed diagnosis resulting in inadequate treatment

A high proportion of patients were switched from sensitive TB treatment before completing the course (88.5%). This characteristically followed sputum-positive results after the removal of ethambutol and pyrazinamide in the continuation phase, exposing the possible undertreatment that would have been masked by combined therapy. Once the two potent drugs are removed, the suppressed rather than eliminated bacilli then flourish with resistance, necessitating therapy switch to the regimen for drug-resistant disease (Blanchard, 1996; Javaid et al., 2017).

Inadequate treatment was further reinforced by the delay in determining DR-TB status, which is a crucial step for patients to enter the DR-TB treatment cascade. The highest proportion of DR-TB participants (82.1%) had a time interval of <6 months, and this diminished as the time interval increased, becoming much less (57.1%) among participants who had a time interval of more than 12 months from previous TB treatment to the development of DR-TB. Developing DR-TB within 12 months of previous treatment is highly suggestive of inadequate treatment arising from either a missed initial diagnosis, inconsistent medication intake, or unadjusted dosages in the event of ≥10% weight change during the treatment course. All three possibilities were likely in the present study. A time interval of above 12 months from previous TB treatment was not associated with DR-TB development. This finding is plausible and suggests a complete resolution of the initial infection, suggesting fresh exposure to the bacilli.

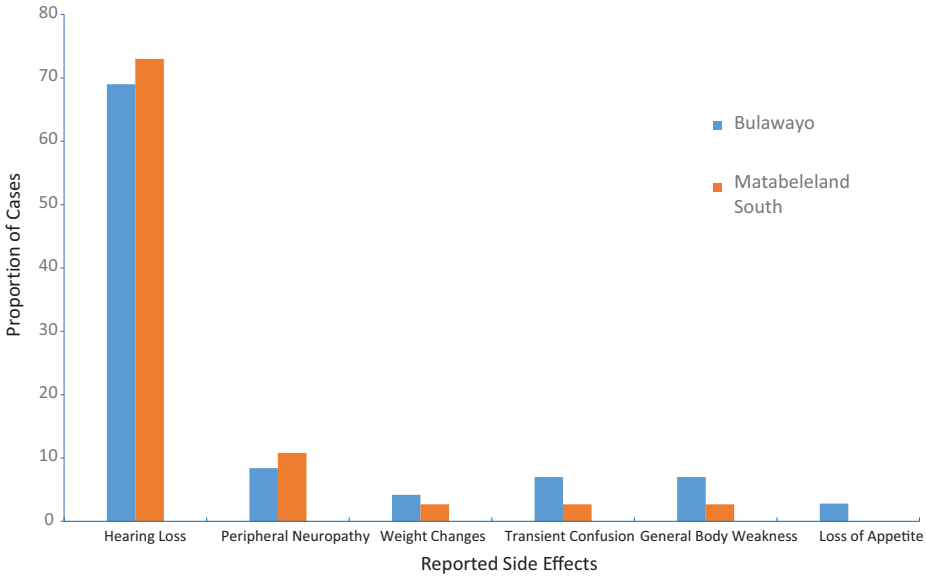

Figure 2. Prevalence of side effects from drug-resistant tuberculosis medication—Bulawayo and Matabeleland South provinces, 2015.

A history of stopping TB drug intake during previous treatment was associated with DR-TB in this study. Stopping medication was prejudiced by two critical issues in this study, which were side effects and feeling better before completing treatment. The likelihood of patients stopping treatment in the face of side effects was apparent. This was an unusual finding, in the context of high patient knowledge levels found in this study. High knowledge levels are usually associated with a better understanding of the condition, which translates to regimen adherence (Nderitu, 2011). The relationship between side effects and abandoning treatment has been confirmed in the literature (Harries et al., 2009; Storla et al., 2008; Tao et al., 2017).

4.2. Low economic standing

The fact that self-employment was the most common source of livelihood for participants from both Bulawayo and Matabeleland South provinces, coupled with the majority earning less than US$200 monthly may have had a bearing on DR-TB. Low socioeconomic status, evidenced by the majority of participants in this study being in the income bracket of less than US$200 monthly, is a known risk factor for DR-TB. DR-TB thrives in poverty, overcrowding, and in those with poor nutritional intake, which lowers immune resistance to TB once exposed as a contact. Low socioeconomic standing has also been shown to be a factor associated with DR-TB in other settings (Skinner and Claassens, 2016). Low educational levels result in a vicious cycle of poverty and disease. This study has already revealed that having some form of self-employment is protective. These people, in turn, may have better access to basic health services and healthier living conditions, which may mitigate against developing MDR-TB.

The same patients with low economic standing are likely unable to afford good housing, have poor access to nutritious food, and limited access to health services due to long distances and a lack of transport money to seek health services. The convergence of these factors results in a high prevalence of TB in resource-constrained settings. This is a true reflection of the economic situation in Zimbabwe, where the majority of the population is not formally employed and is reliant on informal endeavours for sustenance.

4.3. TB and HIV

The association of HIV and all forms of TB is well documented in the literature (Indd et al., 2014). In this study, the majority of DR-TB clients were also infected with HIV and on treatment. A secondary attribute is that HIV-positive patients are regularly screened for TB in Zimbabwe and therefore identified early to start treatment.

Although the country has a generalized HIV epidemic, with HIV prevalence in the 15–49 years age group currently standing at 14%, ART initiation currently stands at 74% for adults and 43% for paediatrics.

The duration of TB treatment is long, and once patients start feeling well, a false sense of wellness may result in treatment interruption seemingly becoming an option, particularly considering the employment and social inconveniences that may be associated with being on treatment. Health workers who display an attitude perceived to be negative by the patients may lead to the development of a negative view of health advice (Mburu et al., 2016; Mehra et al., 2013; Naidoo et al., 2017).

Diabetes lowers the immune system, similar to HIV. In this study, there was no significant association between being diabetic and having DR-TB. This could have been due to the low prevalence of diabetes among study participants. It could also have been due to the low pickup rate of diabetes by clinicians. Most of the participants in both Bulawayo and Matabeleland South provinces were under 50 years of age. This age group is known to be at lower risk of diabetes compared to those >50 years old. Older age is a known risk factor for diabetes. This could explain the low prevalence of diabetes among both TB and DR-TB participants in this study.

4.4. Migration and DR-TB

In this study, those who had a history of migrating to South Africa and Botswana were more likely to have DR-TB compared to those with no history of migration. This is likely to be since the majority of migrants lack proper documentation, which works as an impediment to accessing health facilities when they fall ill. The nature of the jobs obtained by foreigners in these countries does not allow them to afford decent accommodation and sanitation, creating a conducive environment for acquiring infections. Most migrants are known to return home in an advanced stage of disease, thereby influencing negative treatment outcomes.

The majority of patients on DR-TB treatment reported experiencing varying levels of medication side effects, chief among them being hearing loss. This resulted in patients contemplating defaulting treatment. Whilst the client expects to get better on treatment, experiencing side effects requires adequate counselling for the patient to remain motivated and remain on treatment, whilst health workers assume the responsibility of both mitigating the side effects and providing counselling. Pro-

grammatically, this supports the need to switch therapy to the WHO recommended shorter regimen, which has lesser side effects due to the removal of kanamycin.

A statistically significant POR of 2.7 for an unfavourable interim treatment outcome within the first 6 months of being commenced on DR-TB treatment was observed in this study, and this calls for the programme to afford special attention to patients during the initial stages of therapy. The nature of the disease and its prescribed rigid therapy presents adjustment challenges that require support. The longer the duration of treatment, the lesser the chances of non-adherence and inversely the better the treatment outcomes.

It was noted with concern that 36% of DR-TB patients died whilst on treatment, whilst a further 14% died after completion of treatment. The possibility of the cause of death after treatment being unrelated to the treatment phase cannot be ruled out. However, patients dying on treatment is an area that requires further investigation among the cases, in a bid to establish an association between the deaths and the treatment itself, although DR-TB medication-related toxicities are well-documented in the literature. The possibility that patients who died whilst on treatment were not responding to available medication and were, therefore, XDR-TB patients, cannot be ruled out, particularly among those who died within the first 6 to 12 months of treatment (Blanchard, 1996).

4.5. Limitations

This study excluded participants who transferred out of the studied provinces and those who were not traced for an interview. This could have likely reduced the strengths of associations. Recall of previous treatment experiences is dependent on the patient being able to remember what transpired with accuracy. Recall bias cannot be ruled out. The study also depended on the availability and accuracy of clinical records, which was not consistent between facilities, districts, and provinces.

From the findings of this study, it is concluded that programmatic factors were the major causes of DR-TB in the Bulawayo and Matabeleland South provinces. Key among these were inadequate treatment and failure to identify drug-resistant TB at diagnosis. Medication side effects were highly prevalent among DR-TB patients, threatening treatment adherence if not mitigated. Unfavourable treatment outcomes were more likely to occur during the initial adjustment phase of therapy than after more than 6 months of treatment, with a longer treatment duration becoming protective.

4.6. Conclusions

Delayed diagnosis and inadequate previous TB treatment, qualified by switching therapy before treatment completion, and the time interval (<6 months) from previous treatment were associated with DR-TB status and unfavourable treatment outcomes. Strengthening access to drug sensitivity testing at diagnosis, vigilant patient treatment monitoring, and enhanced adherence counselling following treatment initiation are recommended to mitigate the scourge of DR-TB.

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Declarations

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Consent for publication: Not applicable.

Availability of data and material: The dataset used in this study has been provided in Annex S1.

Conflict of interest: The authors declare that they have no competing interests.

Author contributions

HM: conception, design, acquisition, analysis and interpretation of data, and drafting the manuscript. TJ: conception, design, acquisition, analysis and interpretation of data, and drafting the manuscript. JC: conception, design, acquisition, analysis and interpretation of data, and drafting the manuscript. OM: conception, design, data collection, analysis and interpretation, and reviewing several drafts of the manuscript for important intellectual content. NG and GS: conception, design, data collection, analysis and interpretation, and reviewing several drafts of the manuscript for important intellectual content. MT: conception, design, data collection, analysis and interpretation, and reviewing several drafts of the manuscript for important intellectual content. All authors read and approved the final manuscript.

Disclaimer

The contents of this paper do not necessarily reflect the views of the Ministry of Health and Child Care, Zimbabwe, the Matabeleland South and Bulawayo Health Services Department, or The Union.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.ijregi.2022.03.004.

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