PUBLIC HEALTH & PRIMARY CARE | RESEARCH ARTICLE

Association of MDR-TB treatment outcomes and HIV status in Zimbabwe: A retrospective study

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Abstract: MDR-TB has created an additional burden in TB control due to limited treatment options and the generally poor treatment outcomes. We investigated association of MDR-TB treatment outcomes and HIV status in Zimbabwe. The study was a retrospective cohort study of case records from National TB Surveillance System of MDR-TB patients (>16 years) who were culture proven at diagnosis and started treatment between January 2013 and December 2016. Cox proportional hazard regression models were used to assess risk factors associated with mortality. Kaplan–Meier curves were used to determine whether survival probabilities differed for HIV-co-infected and HIV-negative MDR-TB patients. 201 case records were considered for study; 174 cases (87%) started MDR-TB treatment; 11% died before treatment initiation, and 2% did not start treatment. Among 174 cases who were analyzed, 92 were HIV-positive and 82 were HIV-negative. Sixty-three (36%) died during follow up. Number of deaths was not significantly different in patients with or without HIV infection (p = 0.17). Age (25–59 years) (hazard ratio 2.58, 95% CI 1.44–6.77, p = <0.0001) and previous TB treatment (hazard ratio 4.52, 95% CI 1.94–14.2, p = 0.001) were independent predictors of death. Fewer deaths occurred in HIV-infected MDR-TB patients on highly active antiretroviral treatment than those who were not given this therapy (p = 0.01). Treatment outcomes for MDR-TB are likely to be negatively affected by untreated HIV, individual factors and health system factors. National TB control programmes need to be tailored at improving these determinants of MDR-TB and HIV diagnosis and treatment, to improve treatment outcomes.

ABOUT THE AUTHOR

The authors have a strong flair for HIV/AIDS research, as well as research on HIV-co-infection with tuberculosis; HIV-NCDs Comorbidity, and other related key determinants which are likely to negate the gains already made in controlling HIV/AIDS. The present study complements these research interests, since uncontrolled TB is known to be a leading cause of mortality in HIV-positive people, with a great potential to negate the gains already achieved in treating HIV/AIDS through antiretroviral therapy (ART).

PUBLIC INTEREST STATEMENT

The present study, “Association of MDR-TB treatment outcomes and HIV status in Zimbabwe: A retrospective study”, sought to establish factors affecting treatment outcomes for multiple drug resistant tuberculosis, and whether outcomes for HIV negative people with MDR-TB differed to HIV positive people with MDR-TB. The findings show that HIV infection was not an important predictor of death in people diagnosed with MDR-TB. People facing greater risk of death were found to be those of economically active age group of 25 to 59 years (possibly caused by missed treatment appointments due to work commitments); those over the age of 59 years (due to possible co-infection with other diseases caused by advanced age and compromised immunity); and those previously treated for TB. This implies that comprehensive TB management and full compliance to treatment is important for better treatment outcomes.
1. Introduction

Globally, tuberculosis (TB) causes an estimated 1.8 million case fatalities yearly, with approximately 80% of these deaths coming from 22 high-burden countries which include Zimbabwe (Noppert et al., 2015). TB is the second leading cause of mortality as a result of a single infectious agent both globally and in Zimbabwe, after human immunodeficiency virus (HIV) (Citizens Health Watch [CHW], 2015). Treatment failure, unsuccessful disease control programmes, coupled with continued transmission have resulted in emergence and spread of multidrug-resistant tuberculosis (MDR-TB), (that is, TB resistant to at least rifampicin and isoniazid drugs) (Dheda et al., 2010).

Approximately 5% of TB cases worldwide developed MDR-TB in 2013—where 3.5% of these were new cases and 20.5% were formerly treated TB cases (Alene et al., 2017). Drug resistance surveillance data reveal that around 480,000 persons developed MDR-TB globally in 2013, from which there were approximately 210,000 fatalities (Kibret et al., 2017).

MDR-TB continues to present a global challenge to TB control efforts. Cure rates for MDR-TB are very low globally, ranging from 40% to 70% compared to the corresponding cure rates for drug susceptible TB that range from 75% to 95% in well-run TB control programmes (Anderson et al., 2013). MDR-TB cure rates are lowest in Africa (mean 48%), particularly Sub-Saharan Africa where HIV prevalence is also highest (Musa et al., 2017). Unsuccessful treatment of MDR-TB may lead to more adverse forms of drug resistant TB that are more difficult and expensive to treat and manage. Treatment for MDR-TB and XDR-TB was shown to often pose serious and adverse side effects that in some circumstances may lead to non-adherence to treatment, which further makes the drug resistant forms of TB more difficult to treat (Htun et al., 2018).

MDR-TB can occur among both people living with HIV and those without HIV, threatening treatment outcomes including survival rates. However, little is known about the association of MDR-TB treatment outcomes and HIV status in Zimbabwe.

The study sought to determine if the survival probabilities of MDR-TB patients vary by HIV status and to investigate further risk factors to mortality in MDR-TB patients under treatment.

It is important to identify the factors associated with low treatment rates of MDR-TB and to assess whether HIV status and use of anti-retroviral treatment in HIV co-infected MDR-TB patients have significant effect on the treatment outcomes of MDR-TB, in order to make appropriate recommendations.

2. Methods

2.1. Study population

All MDR-TB patients of at least 16 years of age, who were diagnosed in Zimbabwe from between January 2013 to December 2016 and recorded in the MDR-TB national surveillance system were considered for the study. These were all retrieved from the national surveillance system of Zimbabwe. Data was collected from 2013, since extensive data collection and surveillance of patient level MDR-TB treatment outcomes started in 2013 in Zimbabwe.

All culture proven MDR-TB patients aged at least 16 years; who had commenced treatment for MDR-TB; with known HIV status and known MDR-TB treatment outcome were included in the study. The exclusion criteria were based on any one of the following: MDR-TB patient below the age of 16; unknown HIV status; unknown MDR-TB treatment outcome; patients with a positive false positive sputum culture sample; and patients with data indicating culture conversion before initiation of treatment.
MDR-TB treatment outcomes were based on WHO standard definitions with broad outcomes being favorable and unfavorable treatment outcomes (Falzon et al., 2011; World Health Organization, 2017). Detailed information on these outcomes is given in Table 1:

| Favorable Treatment Outcomes | Unfavorable Treatment Outcomes |
|------------------------------|--------------------------------|
| (1) **Cured** is defined as someone who completed treatment without evidence of treatment failure and who had two or more consecutive negative cultures taken at least 30 days apart, after the intensive phase. | (1) **Treatment failure** is defined as treatment terminated or a need for permanent regimen change of at least two anti-TB drugs due to an adverse drug reaction, or lack of culture conversion by the end of the intensive phase, or bacteriological reversion in the continuation phase after conversion to negative after intensive phase, or evidence of additional acquired resistance to fluoroquinolones or second-line injectable drugs. |
| (2) **Treatment completed** is defined as a patient who had completed treatment but did not meet the definition for cured due to a lack of bacteriological results. | (2) **Default/Lost to follow-up** is defined as a patient whose treatment was interrupted for two consecutive months or more. |
| (3) **Death** is defined as mortality for any reason during the course of treatment. | |

2.2. **Study design and sample size**
This was a retrospective cohort study of patients meeting the eligibility criteria and registered in the National TB Surveillance System of Zimbabwe from January 2013 to December 2016. Treatment outcomes for all years were collected in 2018. All patients were followed-up for at least 18 months after commencement of treatment (treatment duration for MDR-TB). MDR-TB recorded cases are relatively few in Zimbabwe; hence, the study included all the diagnosed cases (culture proven).

A similar study by Dheda et al. (2010) observed a death rate of 19% among HIV-negative patients diagnosed with MDR-TB, compared to a death rate of 41% among HIV-positive patients diagnosed with MDR-TB. With reference to these values, the minimum required sample size with 80% study power and 5% level of significance was 152 participants. A total of 174 MDR-TB patients who were initiated on treatment were finally analyzed.

2.3. **Data collection**
Ethical approval was obtained from Medical Research Council of Zimbabwe (MRCZ) and approval to access data was obtained from the Ministry of Health and Child Care, Department of Epidemiology and Disease Control, and from the National AIDS and TB Unit.

Demographic and clinical characteristics of patients were obtained from the National TB Surveillance System for Zimbabwe. Covariates consistently used in published literature include HIV status, age, sex, BMI, any co-morbidity, number of drugs used for treatment (in a treatment regimen), previous TB treatment and previous treatment with second line drugs (Johnston et al., 2009). Of these, only age, sex, BMI, HIV status and previous TB treatment (treatment history) were present in the National TB surveillance system, hence included in the statistical model.

All the surveillance data for MDR-TB patients in the National Surveillance System were aggregated (categorised). Age was categorised into youth (16–24 years), adults (25–59 years) and elderly (>59) elderly. BMI was categorized into under-weight (<18.5 kg/m²) and normal weight ≥ (18.5 kg/m²). Other classes of BMI that include overweight and obese were not included as there were no MDR-TB patients on treatment who fell under those classes.
2.4. Statistical analysis

Double data entry was employed to guarantee data reliability. Data analysis was performed using Stata V13.1. Descriptive analyses for main study variables, χ² square tests, logistic regression analysis and survival analyses was performed. Logistic regression analysis was also done to explain group differences in terms of dependent variables. Multiple logistic regression analysis was done to allow for identification of significant covariates in determining whether MDR-TB patients fall in the favorable treatment group or the unfavorable treatment outcome group. The Kaplan–Meier method was also used to calculate probabilities of events at different time points, and the log-rank test was used to compare these probabilities by group.

In the analysis, p-values less than 0.05 were considered statistically significant, and 95% level of significant was used.

3. Findings

3.1. Descriptive statistics

A total of 231 case records of MDR-TB patients were assessed for eligibility. Of these, two (2) were immediately excluded as they were less than 16 years of age and a further 16 were also excluded due to unknown HIV status. Further nine participants who had possible false-positive cultures and three who had insufficient data were also excluded, leaving a total of 201 MDR-TB patients as study participants whose data were retrieved from the National TB surveillance System. Of the 201 MDR-TB patients, 174 started treatment for MDR-TB, 23 died before initiation of treatment and 4 did not start treatment for MDR-TB. Therefore, 174 patients who had commenced treatment were included in the final analysis (Table 2 below).

Among the 174 records with full information on treatment outcomes (particularly mortality status and sputum-culture conversion status) and dates of the outcomes, the majority were females (52%).

| Table 2. Descriptive Statistics of Clinical and Demographic Characteristics of MDR-TB patients who initiated treatment (n = 174) |
|---|---|---|---|
| Variable | n | Percentage | Cumulative Percentage |
| Age Categories | | | |
| 16–24 | 33 | 18.96 | 18.96 |
| 25–59 | 115 | 66.10 | 85.06 |
| >59 | 26 | 14.94 | 100 |
| Total | 174 | 100.00 | | |
| Sex | | | |
| Male | 89 | 51.15 | 51.15 |
| Female | 85 | 48.85 | 100 |
| Total | 174 | 100 | | |
| HIV STATUS | | | |
| Positive | 92 | 52.87 | 52.87 |
| Negative | 82 | 47.13 | 100 |
| Total | 174 | 100 | | |
| Treatment History | | | |
| TB new cases | 50 | 28.74 | 28.74 |
| Retreated Cases | 124 | 71.26 | 100 |
| Total | 174 | 100 | | |
| BMI | | | |
| Underweight | 67 | 38.51 | 38.51 |
| Normal | 107 | 61.49 | 100 |
| Total | 174 | 100 | |
Those in the age group 25–59 years, HIV-positive participants and normal BMI category constituted the highest proportions; 66%, 53% and 61%, respectively. Most of the MDR-TB participants on treatment had been previously treated for TB (71%) while the smaller proportion were new cases.

3.2. Analytical statistics of demographic and clinical characteristics (covariates) according to treatment outcomes in patients with MDR-TB (n = 174)

The study mainly focused on two outcomes namely mortality and culture conversion (cure). Table 3 below summarizes clinical and demographic characteristics according to the two outcomes. Since all the covariates were categorical, χ² test, or Fisher’s exact test were used in univariate analyses.

| Table 3. χ² tests and Fisher’s exact test |
|-----------------------------------------|
| **Mortality Status** | **p value** | **Sputum-culture conversion** | **p value** |
| Alive | Dead | | Yes | No |
| Patients | | | | |
| 111(64%) | 63(36%) | | 32(18%) | 142(82%) |
| HIV STATUS | | | | |
| Positive | Negative | | | |
| 63(57%) | 29(46%) | 0.17 | 19(59%) | 73(51%) |
| 48(43%) | 34(54%) | | 13(41%) | 69(49%) | 0.42 |
| Age Category | | | | |
| 16–24 | 25–59 | >59 | | |
| 28(25%) | 50(79%) | 8(13%) | 0.01 | 7(22%) | 26(18%) | 0.89 |
| 65(59%) | 18(16%) | | 21(66%) | 4(12%) | |
| SEX | | | | |
| Male | Female | | | |
| 58(52%) | 31(49%) | 0.70 | 23(72%) | 9(28%) | 66(46%) | 76(54%) | 0.009 |
| 53(48%) | 32(51%) | | 29(82%) | 7(18%) | |
| BMI | | | | |
| Underweight | Normal | | | |
| 46(41%) | 65(59%) | | 11(34%) | 21(66%) | 56(39%) | 86(61%) | 0.60 |
| 21(33%) | 42(67%) | | 21(66%) | | |
| Treatment History | TB new cases Retreated cases | | | |
| 42(38%) | <0.0001 | | 17(53%) | 15(47%) | 33(23%) | 109(77%) | 0.001 |
| 69(62%) | 8(13%) | 55(87%) | 22(16%) | |

3.3. Variables associated with death and sputum culture-conversion (cure) in MDR-TB patients on treatment

Age category (p = 0.01), with the age group 25–59 having the highest proportion of deaths (59%); and treatment history (p < 0.0001), previously treated TB patients having the bigger proportion of deaths (62%) than new cases, were found to be significantly associated with mortality status. Sex and treatment history on the other hand, were also found to be associated with sputum culture-conversion. More males (72%) experienced sputum culture conversion than females while more new cases (53%) were cured than previously treated TB cases. There was no significant difference (p > 0.05) on the number of deaths when outcomes were stratified by HIV status, sex and BMI. There was also no difference (p > 0.05) on the number of cure rates or sputum culture-conversion rates when the outcomes were stratified with HIV status, age category and BMI.

3.4. Logistic regression

Logistic regression sought to find out the factors associated with favorable treatment outcomes and unfavorable treatment outcomes (the binary outcome is thus favorable/unfavorable outcome) as explained in Table 1. Prior to forward selection method on the initial regression model in which all variables with p < 0.25 were retained; the final multivariate regression model retained all five covariates.
3.5. Predictors of unsuccessful treatment outcomes among MDR-TB patients on treatment

The final multivariate logistic regression model identified HIV-positive MDR-TB patients on treatment being at a greater risk of unfavorable treatment outcomes than HIV-negative patients (aOR 3.34, 95% CI 2.21–5.71) \( p = 0.001 \); BMI (aOR 1.52, 95% CI 1.134–2.79) \( p = 0.015 \) with underweight patients more at risk, and re-treated cases (aOR 1.69, 95% CI 1.09–2.27) \( p = 0.032 \), being at more risk to be associated with unfavorable treatment outcomes (see Table 4). Age group, was also found to be associated with treatment outcome, with the 25–59 years age group being at a greater risk of unsuccessful treatment outcome (aOR 2.61 95% CI 1.56–7.26) \( p = 0.034 \), than the 16–24 years age group. The risk of unfavorable treatment outcomes was also significantly greater in >59 years age group compared to the 16–24 years age group (aOR 3.32 95% CI 1.33–4.71; \( p = 0.021 \)).

| Variable                  | MDR-TB n = 174 (n%) | Univariate | Multivariate |
|---------------------------|---------------------|------------|--------------|
| HIV STATUS                |                      |            |              |
| Positive                  | 92(52.9)            | 3.29       | <0.0001      | 3.34 (2.21–5.71) | <0.001 |
| Negative                  | 82(47.1)            |            |              |
| Age Category              |                      |            |              |
| 16–24                     | 33(19.0)            | 1          | 0.047        | 1.69 (1.09–2.27) | 0.034 |
| 25–59                     | 115(66.1)           | 3.36 (1.54–7.32) | 0.037 | 3.21 (1.33–4.71) | 0.021 |
| >59                       | 26(14.9)            | 3.61 (1.02–4.82) |            |              |
| SEX                       |                      |            |              |
| Male                      | 89(51.1)            | 1          | 0.041        | 1.26 (0.87–2.68) | 0.07 |
| Female                    | 85(48.9)            | 2.03 (1.11–3.34) |            |              |
| BMI                       |                      |            |              |
| Underweight               | 67(38.5)            | 1.52 (1.13–2.79) | 0.014 | 1.52 (1.134–2.79) | 0.015 |
| Normal                    | 107(61.5)           | 1          |              |
| Treatment History         |                      |            |              |
| TB new cases              | 50(28.7)            | 1          | 0.016        | 1.69 (1.09–2.27) | 0.032 |
| Retreated cases           | 124(71.3)           | 1.73 (1.18–2.23) |            |              |

3.6. Survival (time-to-event) analyses

The duration from acquisition of the sputum culture samples to the time of commencement of treatment was significantly longer in those who died than those who survived, (79 days, 95% CI 55–101) versus (56 days, 95% CI 48–84), \( p = 0.011 \). After acquisition of sputum samples, 22 patients died before the initiation of treatment. The median time period of follow-up; from the time of commencement of treatment to the time of event (death, conversion or date of censorship) was 7.1 months (95%CI 3.6–11.9). Median duration of treatment was 18.6 months; even in instances where cure/sputum culture-conversion was experienced in less than 18 months of treatment, the treatment policy still requires patients to complete an 18 months treatment course. Fifty-nine (72%) of 82 HIV-infected MDR-TB patients on MDR-TB treatment were also taking highly active antiretroviral therapy. Commencement of treatment resulted in culture-conversion/cure in 32 (18%) of the 174 who started treatment.

3.7. Kaplan Meier (K-M) estimates of death and culture-conversion in MDR-TB patients

There were no significant differences in the probabilities of culture-conversion/cure between the HIV-infected MDR-TB patients and their HIV-non-infected counterparts (\( p = 0.8 \)). Twenty-one (66%) of the 32 that converted had converted by 6 months; by 9 months a cumulative total of 26 (81%) had converted and 29 (91%) had converted by 12 months.
Among the 22 who died before the initiation of treatment, cause of death could not be established. However, the probability and proportion of death was significantly higher in HIV co-infected MDR-TB patients than in non-co-infected patients ($p = 0.02$) (Figure 1).

A total of 63 (36%) patients of the 174 patients who had initiated treatment died during the follow-up period. The proportion of deaths in HIV co-infected 29 (46%) and non-co-infected 34 (54%) was not significantly different among patients who had initiated treatment ($p = 0.17$). Furthermore, the probabilities of death among these groups were not significantly different ($p = 0.07$).

In a sub-analysis involving exclusively HIV co-infected MDR-TB patients on treatment ($n = 82$), the proportion and probability of mortality in patients receiving highly active antiretroviral therapy was significantly lower than of those who were not given this therapy ($p = 0.002$) (Figure 2). The number of deaths in patients receiving highly active antiretroviral therapy was 14 (24%) of the 59 who were given this therapy compared to 15 (65%) of the 23 who were not receiving highly active antiretroviral treatment.

Figure 1. K-M graph for probabilities of death in all patients who died before treatment initiation; stratified by HIV status.

Figure 2. K-M graph for probabilities of death among HIV-positive MDR-TB patients only, stratified according to use of ARV treatment.
3.8. Cox proportional hazard model of factors associated with risk of death in MDR-TB patients on treatment

Having selected the variables through backward selection method and having tested for effect modification on the variables, the final model consisted of only four variables. A Cox proportional hazard model was fitted to assess the factors associated with risk of death in all MDR-TB patients on treatment (HIV co-infected + HIV-negative MDR-TB patients). Another sub analysis to assess the factors associated with risk of death in HIV-positive MDR-TB patients on treatment; in which the Cox model was fitted in for only the co-infected patients was also carried out (Table 5 & Table 6 below).

| Variable               | Multivariate Cox Analysis | p-value |
|------------------------|---------------------------|---------|
|                        | Hazard Ratio (95% CI)     |         |
| HIV Status             | 1.78 (0.83–3.84)          | 0.13    |
| Age Category (25–59 years) | 2.58 (1.44–6.77)          | <0.0001 |
| Sex                    | 1.45 (0.60–3.51)          | 0.40    |
| Treatment History      | 5.21 (1.94–14.2)          | 0.001   |

| Variable               | Multivariate Cox Analysis | p-value |
|------------------------|---------------------------|---------|
|                        | Hazard Ratio (95% CI)     |         |
| Highly-active antiretroviral therapy | 0.37 (0.17–0.79) | 0.01    |
| Age Category           | 0.86 (0.57–1.25)          | 0.43    |
| Sex                    | 1.37 (0.15–13.83)         | 0.81    |
| Treatment History      | 4.52 (0.83–24.81)         | 0.08    |

In a multivariable Cox regression analysis on all MDR-TB patients under treatment, the age group 25–59 years was found to be associated with a greater hazard of death (hazard ratio 2.58, 95% CI 1.44–6.77, p = <0.0001) than the 16–24 years age group. Previous TB treatment was also associated with a greater hazard of death (hazard ratio 4.52, 95% CI, p = 0.001). Significantly more people in the age group 25–59 years died than the people in the 16–24 years age group. There were also a significantly larger number of deaths in the patients who were previously treated for TB than the deaths in new cases.

In a sub group Cox regression analysis involving only HIV-positive patients, being on highly active antiretroviral therapy among the HIV co-infected MDR-TB patients was an independent predictor in the reduction of risk/hazard of death (hazard ratio 0.37, 95% CI 0.17–0.79, p = 0.01).

4. Discussion

Among those who died before MDR-TB treatment initiation, the probability of death was significantly higher in HIV-co-infected MDR-TB patients than in non-co-infected patients. Existing research evidence show that HIV-infected patients are more at risk of developing latent TB activation and resultant unfavorable treatment outcomes, due to their compromised immunity (Htun et al., 2018; WHO, 2017). MDR-TB diagnosed late, or untreated MDR-TB in HIV-positive
people, could negate the net positive effect of ART in HIV-positive people and further weaken immunity leading to possible earlier death than to HIV-negative people. Further, a significant proportion of MDR-TB patients died before treatment initiation. Supporting evidence showed a longer duration from time of acquisition of sputum samples to time of treatment initiation among patients who died compared to those who survived. This indicates delayed/late treatment initiation after MDR-TB diagnosis. Systems should be put in place to facilitate early treatment initiation of MDR-TB to reduce the potential risk of further disease spread and improve treatment success rates. A further inquiry on determinants of MDR-TB treatment delay at both individual and health system levels in Zimbabwe is suggested.

The highest proportion of deaths were observed in the age group 25–59 and >59 years age groups after treatment initiation. The age group of 25–59 years is generally considered to be economically active population (Htun et al., 2018; Zignol et al., 2016, 2007). Individuals in this age range might try to avoid absenteeism at work for fear of lost livelihoods and prioritize working to earn a living, thereby missing or deferring treatment appointments as a result. Possible co-infection with other diseases/conditions due to advanced age and/or compromised immunity might explain the findings observed for individuals in the >59 years age group, and some older adults in the 25–59 age groups, especially those above 50 years. This could then result in worst treatment outcomes in form of the observed treatment failure, default, or death. On the other hand, the large age range makes age category a weak independent predictor of death in MDR-TB patients on treatment, at least to some extent. Use of aggregated data could not permit further analysis of age as a predictor of death to cater for narrow age ranges, for example, five year categories. The National MDR-TB surveillance data need to be further aggregated into narrower age categories or to be disaggregated to enable analysis of the effect of age on mortality. This will direct efforts aimed at identifying possible cause of death due to age, and find appropriate strategies to deal with the issue.

Patients previously treated for TB were found to constitute a higher proportion of death among MDR-TB patients who died after treatment initiation compared to deaths in new cases. Though exact reasons are not known, there are various possible explanations for this finding. It was found that all MDR-TB patients were being treated with a standard regimen which is known to be inadequate for previously treated patients, unlike in other high MDR-TB burden countries that have stronger re-treatment regimens which utilize second-line anti-TB drug (Htun et al., 2018; Musa et al., 2017). Considering that Zimbabwe is a low resourced country, successful treatment outcomes among patients receiving re-treatment could also be hampered by poor screening systems for treatment failure thereby resulting in late diagnosis of MDR-TB among previously treated patients. A further inquiry into factors influencing higher mortality rates among previously treated patients is required to identify exact causes of the problem.

The proportion of deaths among MDR-TB patients on treatment was generally high, but without a significant difference in mortality status when comparing the deaths in HIV-positive and in HIV-negative MDR-TB patients. Possible explanations to this could be proper adherence to antiretroviral treatment (ART) among HIV-positive patients leading to viral suppression, resulting in a net negligible effect of HIV on mortality (Falzon et al., 2011; WHO, 2017). The high proportion of death irrespective of HIV status could also be due to the observed poor prognosis of MDR-TB patients with regards to cure/conversion rates. The very low cure rates could have been due to poor adherence to MDR-TB leading to some reverting back to MDR-TB after cure, as observed. This is further supported by the finding that the greater proportion of MDR-TB patients were previously treated cases where case management is known to be expensive and more difficult (Tesfahunegyn et al., 2015; WHO, 2017). Low efficacy for MDR-TB drugs could be another possible cause for the observed poor prognosis and low cure rates (Htun et al., 2018). More studies are required that will look into causes of treatment adherence among MDR-TB patients and related determinants.
Findings of this study indicated that more males than females experienced sputum culture conversion. Though reasons to this are not clear, gender is a well-known strong determinant of healthcare access in favour of men (Htun et al., 2018; Zignol et al., 2016). Various socio-cultural beliefs, gender roles, economic factors and other structural barriers might make it difficult for women in Zimbabwe to access or adhere to MDR-TB treatment. Such disparities in healthcare access due to gender and other social determinants of health need to be confirmed and addressed to improve treatment outcomes among women.

4.1. Limitations

The major limitation of this study was the use of existing data which was aggregated. As a result, important covariates like participant age which was aggregated on wide intervals did not give sufficient meaning to explain the observed findings, like effect of age on mortality due to MDR-TB. As a result, no conclusive associations could be made on age as an important explanatory variable of mortality in this study.

Fewer variables existing in the national TB surveillance system resulted in some factors important to the study not being included in the analysis as anticipated, thus resulting in the study missing out on important associations. It is recommended that the National TB Surveillance System captures all other important variables on MDR-TB management to allow for data analysis important for assessment and evaluation of progress towards related control efforts.

5. Conclusion

Treatment outcomes for MDR-TB are more likely to be negatively affected by untreated HIV, individual factors and health system factors. Zimbabwe national TB control programmes need to be tailored at improving these determinants of MDR-TB and HIV diagnosis and treatment, to improve MDR-TB treatment outcomes.

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