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Decentralized Diagnosis and Treatment of Drug-Resistant Tuberculosis in Machakos County, Kenya

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ABSTRACT

Background: Access to drug susceptibility testing (DST) for drug-resistant tuberculosis (DR-TB) diagnosis is challenging. Between 2016-2019, in Machakos county, Kenya, Xpert MTB/RIF was available in 5 sites. Additional DST was done in the national lab. DR-TB treatment was available in 32 clinics.

Methods: This is a cohort study on DR-TB diagnosis, treatment outcomes, and their predictors in Machakos county, between 2016-2019. Rifampicin-resistant TB (RR-TB) was treated with a short treatment regimen (STR). A long regimen was used for patients not eligible for the STR.

Results: Of 85 DR-TB patients, 84 (99%) and 72 (73%) had Xpert MTB/RIF and phenotypic rifampicin DST results, respectively. Of 85, 36 (42%) had rifampicin-susceptible drug-resistant TB (RS/DR-TB); resistance to other first-line drugs than rifampicin) and 49 (58%) had RR-TB. Xpert MTB/RIF and phenotypic DST showed discordant results for rifampicin in 8 patients (7 with RR missed on Xpert MTB/RIF). Of 49 with RR-TB, 45 had second-line DST results. One patient had TB resistant to fluoroquinolone and second-line injectables. Of 36 RS/DR-TB patients, 33 (92%) were treated successfully. Six RR-TB patients died before starting treatment. One RR-TB patient was transferred out. Among the remaining 42 RR-TB patients, treatment success was 50% (11/22) for the STR and 80% (16/20) for the long regimen (p=0.04), with more PLHIV among patients on the STR (70% (14/22) vs 30% (6/20), p=0.03). HIV co-infection (aOR 8.5, 95%CI:1.2-59.2) but not STR use (aOR 1.5, 95%CI:0.3-8.1) predicted having a clinically unfavorable outcome (mortality or treatment failure). Seven patients (all RR-TB and HIV-positive) had severe or life-threatening adverse events, of whom 4 died.

Conclusion: RR-TB treatment success was lower than the 75% World Health Organization target. HIV co-infection and adverse events contributed to unsuccessful treatment outcomes. Decentralization of rapid DST, adverse event monitoring and management, and less toxic RR-TB regimens will be key towards improving outcomes.

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Introduction

Tuberculosis (TB) is the thirteenth leading cause of death worldwide and the second leading cause from an infectious disease, after COVID-19 but ranking higher than HIV/AIDS [1]. Globally in 2019, an estimated 13.1% of all new TB cases and 17.4% of previously treated cases had isoniazid-resistant TB, while 3.3% of new TB cases and 18% of previously treated cases were estimated to have rifampicin-resistant/multi-drug resistant TB (RR/MDR-TB: MDR: resistance to both rifampicin and isoniazid). The World Health Organization (WHO) estimates that there were 500,000 cases with RR/MDR-TB in 2019. The proportion of RR/MDR-TB cases with resistance to any fluoroquinolone was estimated at 20.1% [2].

The emergence of drug-resistant strains of Mycobacterium tuberculosis has complicated tuberculosis control and undermined the objectives of the WHO End TB Strategy (95% reduction in deaths due to TB and a 90% reduction in TB incidence rate by the year 2035 compared to 2015) [3]. The response to this threat has historically been inadequate largely because drug-resistant tuberculosis (DR-TB) is difficult to diagnose and treat. Diagnosis of DR-TB in low resource settings has been challenging due to insufficient modern diagnostics that are available in high income countries. The bulk of TB patients are diagnosed and treated at primary health care level while drug susceptibility testing (DST) is provided at a more central level [4].

In 2019, 692 DR-TB patients were initiated on treatment in Kenya [2]. Machakos county, which is our study area, is among the 10

high TB burden counties of 47 counties from the country. Since 2011, in Kenya Xpert MTB/RIF is used for the diagnosis of TB and also the detection of RR when TB is diagnosed, including in 5 Xpert MTB/RIF sites processing samples from around 140 health facilities in Machakos county. While assuring rifampicin DST for all those eligible requires a lot of logistics, detection of resistance to TB drugs other than rifampicin is even a bigger challenge. Both first-line line probe assays (LPA) and second-line LPA can only be done at the national reference laboratory on smear-positive samples. First-line LPA provides genotypic drug susceptibility testing results for isoniazid and rifampicin resistance, whereas second-line LPA provides DST results for fluoroquinolone and second-line injectable drugs (SLID). Also, culture is performed at national level only. Culture followed by phenotypic DST (pDST) takes weeks to months. Treatment is started while DST results are awaited. Regimens are modified when DST results become available.

Treatment of DR-TB is complicated, very expensive and labour intensive as it requires frequent monitoring by trained and experienced health care workers. First-line TB drugs complemented with a second-line core drug (fluoroquinolone) constitute a 9-month treatment regimen for the patients with rifampicin-susceptible TB but with resistance to one or more of the other first-line drugs (RS/DR-TB). Patients with RR/MDR-TB are treated with either a long (20 months) or a short (9-11 months) RR-TB treatment regimen (STR) [5].

According to WHO, global RR/MDR-TB treatment success rate for RR/MDR-TB was 59% in the cohort started on treatment in 2016 (the large majority being treated with the long RR/MDR-TB regimen). In contrast, the 9-month STR resulted in over 80% treatment success [6]. The efficacy of the injectable-containing STR (9 to 11 months) was non-inferior to the longer treatment regimen (20 months) that followed 2011 WHO recommendations [7]. Adverse events (AE) experienced during treatment pose a threat to adherence and continuation of care. AE may temporally reduce the patients quality of life but may also cause long term disability or be life threatening [8].

Most studies show data for a subgroup of DR-TB patients, either isoniazid-resistant TB, RR/MDR-TB, or (pre-) extensively drug-resistant (XDR) TB (definitions: table 1). To show a more comprehensive view on DR-TB care needs in a high-burden county in Kenya, we show data on treatment success (cure or treatment completion versus death, treatment failure or lost to follow-up) for patients diagnosed with any form of DR-TB, with stratification by resistance profile and treatment regimen. In addition, our study shows data for results from different diagnostic tools (genotypic and phenotypic DST), the delay between diagnosis and treatment initiation, and describes AE and outcomes by DR-TB treatment regimen.

Methods

Study Design and Settings

This was a retrospective cohort study conducted in 32 DR-TB treatment sites within Machakos county, Kenya, including patients notified with DR-TB between 2016-2019. Machakos county borders Nairobi and Kiambu counties to the north, Kitui to the south, Kajiado to the west and Makueni to the east. DR-TB patients were started on treatment after baseline routine investigations and counselling.

Patients with any form of DR-TB submitted a second sample for first-line probe assay and second-LPA, conventional culture and phenotypic DST (pDST) done at the Central Reference Laboratory. For any form of DR-TB monthly follow-up smears, sputum cultures, a full blood count were done and a chest X-ray was done before treatment initiation and at the end of treatment. For RR-TB patients, thus treated with more toxic regimens, additional routine investigations were done on a monthly basis, including sputum cultures, follow-up smears, full blood count, thyroid stimulating hormone, urea, serum potassium and sodium. A chest X-ray was done at the start of treatment, repeated at month six during treatment and after the completion of treatment. Audiometry was done for patients treated with second-line injectable drugs.

Patients with rifampicin-susceptible TB (RS-TB) but with resistance to one or more first-line drugs (RS/DR-TB) were initiated on a regimen with levofloxacin and the four first-line TB drugs (isoniazid, rifampicin, pyrazinamide, and ethambutol) for a duration of 9 months. Patients with RR-TB were started on the STR. The STR was recommended for all patients with rifampicin-resistant pulmonary TB with or without isoniazid resistance including children diagnosed with TB and household contact of any RR-TB case. Patients were excluded from the STR if they were exposed for one month or more to any of the second-line TB drugs that are part of the STR regimen. Patients with confirmed resistance to second-line drugs that are part of the STR or with extrapulmonary RR-TB were also excluded from the STR. The 9-11-month STR included an intensive phase of 4-6 months with high dose isoniazid, kanamycin, moxifloxacin, clofazimine, prothionamide, pyrazinamide and ethambutol and a continuation phase of 5 months with moxifloxacin, clofazimine, pyrazinamide and ethambutol.

Patients not eligible for the STR were treated with a long 20-month standard RR-TB regimen. This long RR-TB regimen consisted of an 8-month intensive phase with capreomycin, prothionamide, cycloserine, levofloxacin, pyrazinamide, para-amino salicylic acid and ethambutol, and a 12-month continuation phase with prothionamide, cycloserine, levofloxacin, pyrazinamide and ethambutol.

A modified long regimen was used for patients not eligible for both the STR and the standard long regimen due to a contra-indication for using second-line injectable drugs. This modified long regimen included a 6-month intensive phase with bedaquiline, clofazimine, cycloserine, levofloxacin, prothionamide and pyrazinamide and a 12-month continuation phase with cycloserine, levofloxacin, prothionamide and pyrazinamide. Another modified long regimen was used for patients with fluoroquinolone-resistant RR-TB. This regimen included an 8-month intensive phase with imipenem, bedaquiline, delamanid, clofazimine, para-amino salicylic acid, pyrazinamide and amoxiclav and a 16-month continuation phase with clofazimine, pyrazinamide, para-amino salicylic acid and amoxiclav. Regimens relied on the 2016 WHO classification of second-line drugs [9].

Study Population and Period

All patients notified with DR-TB in Machakos county, Kenya, between 2016-2019.

Data Collection

Data was collected from DR-TB registers and log books complemented with the TB program electronic data base. The variables of the study included age, sex, HIV status, type of TB, date treatment started, Xpert MTB/Rif results, smear results, culture and DST results, treatment regimen, adverse events and

treatment outcomes (cure and treatment completed defined as treatment success or failure, transfer out, lost to follow-up and died) [2].

Table 1: WHO Definitions Used in Describing the DR-TB Patients by Resistance Pattern

	Definition
Rifampicin resistance	Resistance to rifampicin detected using genotypic or phenotypic methods with or without resistance to other anti-TB drugs
Rifampicin-susceptible/ DR-TB (RS/DR-TB)	Resistance to one or more first-line anti-TB drugs, with susceptibility to rifampicin
Multidrug resistance (MDR)	Resistance to both isoniazid and rifampicin
Pre-extensively drug-resistant tuberculosis (Pre-XDR TB)	MDR-TB with resistance to fluoroquinolones or a second-line injectable (amikacin, kanamycin, or capreomycin), but not both
Extensively drug-resistant TB (XDR TB)	Resistance to isoniazid and rifampicin plus resistance to any fluroquinolone and at least one of the three injectable second-line drugs (i.e., amikacin, kanamycin, or capreomycin)

Statistical Analysis

Data were entered in a password-protected excel data base and analyzed using the R software (R 4.0.3). Categorical variables were summarized using proportions and frequencies. Medians and inter-quartile ranges (IQR) were used to summarize age distribution and the delay between laboratory results became available and the initiation of an appropriate DR-TB treatment regimen. Results were presented in tables stratified by resistance profile. Fisher's exact test was used to test whether the association between categorical variables was significant. A multivariable logistic regression model was used to estimate the association between type of regimen and having a clinically unfavorable outcome (death and treatment failure), adjusted for HIV status, a known predictor of TB mortality.

Ethics Approval

Ethical clearance was obtained from the Institutional Review Board of Institute of Tropical Medicine, Antwerp (1473/21) and the Ethical Review Committee of Mount Kenya University (MKU/ERC/1806). The department of health and emergency services, Machakos county authorized the study.

Results

Baseline Resistance Profile

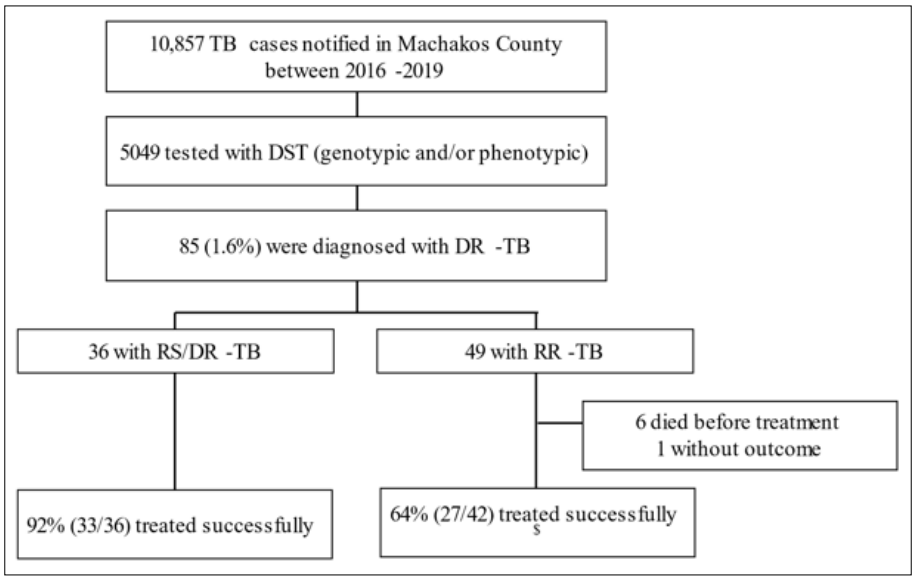

Figure 1: Flow Diagram on TB Cases Diagnosed and Notified from 2016-2019

A total of 10857 TB cases were diagnosed and notified in Machakos County from 2016 -2019, of which 5049 (47%) were tested for DR-TB. Among 5049 screened for DR-TB, 85 (1.6%) were diagnosed with DR-TB. Of 85 DR-TB patients notified, 84 (99%) had an Xpert test result and with 72 (86%) of the 85 DR-TB cases having a rifampicin pDST result.

In 80 (94%) of 84 with an Xpert result, Mycobacterium tuberculosis (MTB) was detected, of which 42 (53%) tested RR (table 2). Of 72 with pDST results, 42 (58%) tested RR. Of 36 with RR on Xpert and a rifampicin pDST result available, 35 (97%) tested RR on pDST. Of 33 with RS on Xpert and a rifampicin pDST result, 7 (21%) had RR on pDST, thus with RR missed by Xpert. Altogether, 49 patients had RR-TB on either Xpert MTB/RIF or pDST. None of four patients with "MTB not detected" on Xpert, pDST showed RR.

Table 2: Xpert MTB/RIF and Phenotypic Rifampicin DST Results of DR-TB Patients from 2016-2019

	Total (n=85)	With rifampicin pDST results	Rifampicin resistance on pDST	(%)
Xpert MTB/RIF result				
MTB detected, RR	42	36	35	(97)
MTB detected, RS	38	33	7	(21)
MTB not detected	4	3	0	
Not done	1	1	0	

DR-TB = drug-resistant tuberculosis; RR = rifampicin resistance; RS = rifampicin susceptible

Of 49 patients with RR, 44 had DST results for isoniazid and second-line drugs on at least one method (table 3). Of 44, 24 (56%) had mono RR, 18 (42%) had MDR and 1 (2%) was diagnosed with XDR-TB. The XDR-TB patient had TB resistant to all four first-line TB drugs, fluoroquinolone and second-line injectable drugs.

Of 36 patients with RS/DR-TB, 32 patients had isoniazid monoresistance and 3 had isoniazid polyresistance, with resistance to both isoniazid and pyrazinamide. Another patient had pyrazinamide monoresistance. Of 36, 7 had fluoroquinolone-susceptible TB on pDST. The other patients had no results for fluoroquinolone DST.

Table 3: Baseline Resistance Profile of DR-TB Patients from 2016-2019

	Total N=85
Any RR	49
Of which mono RR	24
Of which MDR and susceptible to second-line drugs	19
Of which XDR	1
Of which without DST results for other first-line drugs and second-line drugs	5
Any RS/DR-TB [$]	36
Of which INH resistant	32
Of which INH and PZA resistant	3
Of which PZA resistant, susceptible to other first-line TB drugs	1

DR-TB = drug-resistant tuberculosis; RR = rifampicin-resistant; MDR = multidrug-resistant; XDR = extensively drug-resistant; RS = rifampicin susceptible; INH = isoniazid; PZA = pyrazinamide

$ DST for fluoroquinolone was available for 7 of 36 patients with RS/DR-TB and showed susceptibility for all 7.

RS/DR-TB Treatment Outcomes

Of 36 RS/DR-TB patients, 33 (92%) were treated successfully. Two patients were lost to follow-up. One patient died while being treated for cryptococcal meningitis. This patient who died was HIV-positive, underweight and died after 2 months on TB treatment.

RR-TB Treatment Outcomes

Of 49 patients diagnosed with RR-TB, 6 died before starting treatment, all within 10 days after RR-TB diagnosis. Four of 6 were HIV-positive. Four patients had severe lung fibrosis (2 of those 4 were HIV-positive) while 2 were malnourished HIV-positive patients with severe gastroenteritis.

Of 43 started on RR-TB treatment, 27 (63%) were treated successfully. Five patients were LTFU, 9 died, 1 experienced treatment failure, and 1 patient was transferred and remained without reported outcome.

Of 43, 22 (51%) were initiated on the STR and 21 (49%) on a long regimen (table 4). The long regimen was modified for 3 patients: one was a child (injectables not recommended), another patient had initial mild hearing loss (contraindication for injectable drugs), and one patient had XDR-TB. The three patients treated with a modified long regimen were treated successfully. For one patient transferred out to another health facility no outcome was obtained. Treatment success was 50% (11/22) among those treated with the STR and 80% (16/20) among those treated with the long regimen (p=0.04, Fisher's exact test). A larger proportion of those who tested HIV-positive were started on the STR (70% (14/22) vs 30% (6/20), p=0.03, Fisher's exact test). Not considering 5 patients LTFU, clinically unfavorable outcomes (either death or treatment failure) were more frequent among those who tested HIV-positive (47% (9/19) vs 6% (1/18), p=0.005, Fisher's exact test). In a multivariable model that included both HIV status and type of regimen, the odds of having a clinically unfavorable outcomes were higher for those who tested HIV-positive (aOR 8.5, 95%CI:1.2-59.2) but not for those who started on a STR (aOR 1.5, 95%CI:0.3-8.1).

Table 4: Treatment Outcomes by Regimen of DR-TB Patients between 2016-2019

	RR-TB treated with a short regimen N=22		RR-TB treated with a long regimen N=21 #	
	N	(%)	N	(%)
Cured	10	(45)	12	(57)
Treatment completed	1	(5)	4	(19)
Treatment failure	0	(0)	1	(5)
Died	7	(32)	2	(9)
Transfer out	0	(0)	1	(5)
Lost to follow up	4	(18)	1	(5)
HIV negative				
Success $	5	(100)	12	(92)
Clinically unfavorable £	0	(0)	1	(8)
HIV-positive				
Success $	6	(46)	4	(67)
Clinically unfavorable £	7	(54)	2	(33)

RR-TB = rifampicin-resistant tuberculosis
# Included three patients on an individualized (injectable-free) regimen, all three were either cured or completed treatment
$ success = either cure or treatment completion; £ clinically unfavorable: either death or treatment failure

All 9 patients who died while on RR-TB treatment were HIV-positive. Four died within two months on treatment. Seven were on the STR and 2 on the long regimen. Of 7 deaths during the STR, 4 HIV-positive patients died due to AE including renal failure, anemia, hypokalemia and hepatotoxicity, 2 HIV-positive patients died due to pneumocystis carinii pneumonia, and 1 patient was stabbed to death after a quarrel in an entertainment club. Both patients who died during the long regimen were HIV-positive patients with cryptococcal meningitis and also had severe oropharyngeal candidiasis.

Overall, 5 patients were lost to follow-up during RR-TB treatment, of whom 4 on the STR. All 5 were male. One patient on the long RR-TB regimen experienced treatment failure.

Adverse Events

Overall, 57 (72%) of 79 patients treated with a DR-TB treatment regimen experienced at least one AE, 61% (22/36) among those treated with the RS/DR-TB regimen (table 5), and 86% (19/22) and 76% (16/21) among those treated with a short and long RR-TB treatment regimen, respectively (p=0.5, Fisher's exact test for comparison between long and short). The commonest AE were gastro intestinal tract disturbances (nausea, vomiting and diarrhea) and occurred in 14% (5/36) on the RS/DR-TB regimen, 73% (16/22) on the STR, and 48% (10/21) on the long regimen. In one patient the treatment regimen was modified due to the AE. Grade 3-4 AE were reported in 7 (12% of 79) patients and included profound hearing loss, psychosis, hepatotoxicity, severe anemia and hypokalemia. All grade 3-4 AE occurred in HIV-positive patients on the short RR-TB treatment. Of 7, 4 died.

Table 5: Adverse Events by Regimen Among DR-TB Patients Treated from 2016-2019

	RS/DR-TB treated with Lfx/RHZE N=36		RR-TB treated with a short regimen N=22		RR-TB treated with a long regimen N=21	
	N	(%)	N	(%)	N	(%)
No AE	14	(39)	3	(14)	5	(24)
Grade 1-2 AE	22	(61)	12	(54)	16	(76)
Grade 3-4 AE	0	(0)	7	(32)	0	(0)

*Fishers exact test- significant is $\alpha = 0.05$; RR-TB = rifampicin-resistant tuberculosis; DR-TB = drug-resistant tuberculosis; RS/DRTB = rifampicin susceptible/drug resistant tuberculosis; Lfx/RHZE = levofloxacin, rifampicin, isoniazid, pyrazinamide, ethambutol

Discussion

Overall, in Machakos county, Kenya, between 2016-2019, 85 patients were diagnosed with DR-TB: 36 with RS/DR-TB and 49 with RR-TB. Six RR-TB patients died before starting treatment. Treatment success was 92% among those treated for RS/DR-TB and 63% among those treated for RR-TB.

The use of Xpert MTB/Rif was introduced in Kenya in 2011. Among the 85 patients diagnosed with DR-TB, 99% had a Xpert test done. However, in 21% of patients with RS-TB on Xpert, pDST identified RR, thus missed by Xpert. The discordant results could be due to some mutations systematically missed by Xpert or an error in the laboratory during sample processing. The frequency of RR missed by Xpert depends on the setting. In some countries RR-TB is missed up to 30% of RR-TB patients [10]. When RR is missed,

and patient are inadequately treated with a first-line regimen, RR-TB continues to spread. Moreover, in case RR is missed in patients treated with the levofloxacin-strengthened first-line regimen for INHr-TB fluoroquinolone resistance may develop as levofloxacin is not protected, neither by rifampicin or isoniazid [11].

Patients treated for RS/DR-TB had the highest overall successful outcome at 92%. This can be attributed to rifampicin, the most powerful anti-TB drug, used in a regimen strengthened with fluoroquinolone, the most powerful second-line TB drug [9,12].

RR-TB treatment success (63%) was lower than the 75% World Health Organization target [2]. Poor RR-TB treatment outcomes were mainly explained by AE and HIV co-infection. The management of HIV co-infected TB patients is complex as several factors, including the high pill burden arising from both DR-TB and ART treatment regimens, drug-drug interactions, the management of immune reconstitution inflammatory syndrome and HIV opportunistic infections pose a major challenge [13]. Over 50% of the HIV-positive RR-TB patients died. HIV co-infection is a known predictor of mortality among RR-TB patients. Excess unfavorable treatment outcomes among PLHIV have been reported, with mortality up to four times higher compared to the HIV-negative population [14]. However, over 50% mortality is rare. Considering the advanced clinical status of PLHIV with RR-TB in our study, it is important to diagnose RR-TB earlier. Systematic screening for TB and RR-TB in all HIV positive patients should be prioritized to assure early diagnosis and initiation of TB treatment. Moreover, in our study, a quarter of deaths died before they were started on treatment, for instance due to severe lung fibrosis. A study done in Philippines also showed a high mortality rate as a result of advanced TB disease in patients who were not timely put on treatment [15]. We found a median delay of 12 days between diagnosis and treatment start, similar to the therapeutic delay reported by other studies evaluating the performance of Xpert [16]. In our study, the diagnostic delay was probably more extensive. We did not collect data on diagnostic delays. Given the required logistics when sending samples to the national level and the turnaround time of DST, the diagnostic delay between sampling and obtaining the results was probably big. The TB program should aim to reduce diagnostic delays by decentralizing DST and using rapid DST, also for FQ, e.g. with the Xpert MTB/XDR cartridge [17].

We found that unsuccessful outcomes were more frequent among those treated with the STR compared to treatment with a long regimen. In a study done by A.J. Nunn et al, both regimens had a successful outcome of over 78% [7]. A South African study by Farley at al showed similar findings [18]. In our study the higher mortality among patients treated with the STR was mainly explained by the higher proportion of HIV co-infection among those treated with the STR.

The incidence of AE at 67% was similar compared to a meta-analysis which documented that 57.3% of DR-TB patients developed at least one AE [19]. A study done in South Africa reported that 99% of 71 patients developed at least one AE [8]. The commonest AE were gastrointestinal disturbances, including nausea and vomiting. With the introduction of the STR in 2016, WHO anticipated that a shorter duration of treatment with reduced exposure to TB drugs would reduce the proportion of patients experiencing AE [20]. The results of this study demonstrated that contrary to WHO expectations, that over 80% of patients treated with a STR experienced AE. Possibly the high proportion with HIV co-infection among those treated with the STR explains what was observed.

Among HIV co-infected patients, over 60% developed grade 3 and 4 AE, of whom 57% eventually died. This might be explained by combined multiple toxicities associated with second-line TB drugs and ART. Similar findings in Namibia reported that co-infected patients had a four-fold risk of grade 3 to 4 adverse events compared to HIV negative, although this was reported on patients on the long regimen [21]. Death related to AE was documented in patients suffering from severe to life-threatening conditions, including hypokalemia, severe anemia, hepatotoxicity and renal failure. This explains why strict, regular monitoring and reporting of AE during the period when patient is on treatment is crucial. Less toxic RR-TB regimens will be key towards improving treatment outcomes.

This study had several strengths. It relied on routinely collected programme data. Therefore, the findings reflect the reality of the DR-TB program in the county. Moreover, data from all patients with any form or DR-TB were shown. However, the study also had some limitations. Our study used a retrospective study design. It was not designed to compare the effect of different regimens on outcomes, as characteristics between cohorts differed. HIV co-infection among patients treated with the STR was significantly more frequent than among those treated with the long regimen, which hampered the comparison between both regimens. A large proportion of patients was not tested for DR-TB. Considering the regular efforts to update and clean the database, and considering the lack of access to DST, we speculate that DST results were missing in the database when DST was not done, rather than due to a lack of encoding in the database. Some limitations of retrospective studies were mitigated by the use of a prospectively updated database, used for routine reporting. Prospective encoding and the regular use for routine reporting allowed programme staff to complete and clean data by checking the patient cards. As such most study variables were complete. Moreover, the programme was stable throughout the study period. Finally, as the study focused on DR-TB care provision in one county in Kenya, the size of the different DR-TB cohorts was small.

Conclusion

RS/DR-TB treatment outcomes were good, but RR-TB treatment outcomes were below the global target. Advanced TB disease, HIV co-infection and severe AE explain the high frequency of unfavorable outcomes. TB screening in PLHIV should be prioritized. Rapid rifampicin DST should be decentralized further to enhance early diagnosis and treatment initiation with an appropriate treatment regimen. The relatively frequent discordance between Xpert MTB/RIF and phenotypic rifampicin DST shows that there is still an important role for phenotypic DST. To minimize AE less toxic RR-TB treatment regimens are needed.

Author Contributions

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Validation: Tom Decroo
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Writing – review and editing: Francis Makokha, Jonathan Nthusi, Lucy Muregi, Joseph Nzomo

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