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Epidemiology and genetic diversity of multidrug-resistant tuberculosis in East Africa

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SUMMARY

Multidrug-resistant tuberculosis (MDR-TB) is an emerging problem in many parts of the world, and levels of MDR-TB among new TB patients are increasing in sub-Saharan Africa. We reviewed the prevalence and molecular epidemiology of MDR-TB in East Africa, including Burundi, Kenya, Rwanda, Tanzania, and Uganda. In 16 epidemiologic surveys, the prevalence of MDR among new cases ranges from 0.4% in Tanzania to 4.4% in Uganda, and among recurrent cases ranges from 3.9% in Tanzania to 17.7% in Uganda. There is a gap of 5,948 cases between the estimated number of MDR-TB cases in East Africa and the number actually diagnosed. The only confirmed risk factors for MDR-TB are prior treatment for TB and refugee status. HIV has not been reported as a risk factor, and there are no reports of statistical association between spoligotype and drug resistance pattern. Increased capacity for diagnosis and treatment of MDR-TB is needed, with an emphasis on recurrent TB cases and refugees.

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Conflict of interests
The authors have declared that no conflicts of interest exist.

Authors' contributions
BRK Conceived and designed the study; searched, extracted and analyzed data and drafted the manuscript; **LEW S**earched, extracted and analyzed data and drafted the manuscript; **SB** and **RK** Extracted data and edited the manuscript; **SEM, RNP** and **OO** Revised the manuscript critically and approved the final version; **DWF** Conceived and designed the study and revised the manuscript critically and approved the final version.

Keywords

Multidrug-resistant tuberculosis (MDR-TB); prevalence; genetic diversity; risk factors; East Africa

1. Introduction

Multidrug-resistant tuberculosis (MDR-TB), defined as disease caused by *Mycobacterium tuberculosis* resistant to at least isoniazid and rifampicin, is an emerging problem in many parts of the world. In 2011, there were an estimated 630,000 cases of MDR-TB among the world's 12.0 million prevalent cases of TB.[1] The WHO estimates that levels of MDR-TB among new TB patients are increasing in Africa. However, the prevalence, epidemiology, genetic mutations conferring drug resistance and genetic diversity of MDR-TB vary across the continent. Here we review the prevalence and molecular epidemiology of MDR-TB in East Africa.

The East African Community (EAC) was created in 2001 as a free trade union between the countries (population in million) of Burundi (9), Kenya (42), Rwanda (11), Tanzania (46), and Uganda (35).[1,2] The mission of the EAC is to create economic prosperity and political security across the region. The establishment of a free trade and customs union has made these five nations politically and economically intertwined. The inter-dependence between the nations facilitates trade, travel, and migration, creating the potential for the spread of MDR-TB between the nations. Currently, Kenya, Uganda and Tanzania are among the 22 high TB burden countries worldwide. None of the EAC countries are among the 27 high MDR-TB burden countries; however, recent MDR-TB outbreaks in South Africa demonstrate the importance of surveillance and vigilance.[3]

Therefore, this review examines the prevalence, case detection and treatment rates, risk factors, profile of mutations conferring multidrug-resistance, and genotypic diversity of MDR-TB in East Africa.

2. Methods

2.1 Study design

We conducted a systematic literature review for original articles published in English focusing solely on data from January 1997 through the end of December 2012.

2.2 Search strategy

We performed a systematic search of online databases including PubMed/Medline, Embase, Popline, Global Health, Google and Web of Knowledge. We used the search terms beginning with the text string 'tuberculosis' in all possible combinations with 'multidrug resistance', 'drug resistance' 'MDR', and other related keywords including 'genotypes', 'spoligotypes', 'prevalence', 'HIV', 'HIV/AIDS' and 'diagnosis'. Each term was searched separately with the text string 'East Africa' and then with the name of the specific country in East Africa region. Case reports were included. We also reviewed the WHO websites for relevant publications. New links displayed beside the abstracts were followed and retrieved. Finally, the bibliographies of each article were carefully reviewed and relevant articles also retrieved.

2.3 Inclusion and exclusion criteria

We screened titles and abstracts for relevance, and subsequently reviewed the full texts of manuscripts that were potentially pertinent. Only study reports that used original data and had evaluated multidrug-resistant tuberculosis in East Africa were included.

2.4 Data extraction and analysis

Eligible studies were reviewed independently by two authors (BRK and LEW). Due to heterogeneity in study reporting, a structured form for data extraction was created that included: i) exact site and country where the study was conducted; ii) study year and duration; iii) year of publication; iii) study population and setting; iv) number of TB patients recruited; v) type of TB patients involved (new or previously treated cases); vi) procedure for recruitment; vii) study outcome(s) of interest (prevalence of MDR-TB, prevalence of rifampicin resistance, types of mutations conferring resistance, spoligotypes and risk factors for MDR-TB). Extracted data were entered into a Microsoft Excel spreadsheet (Microsoft, Redwoods, WA, USA) for analysis using STATA version 12 (StataCorp LP, College Station, TX, USA). Results were expressed as percentages.

3. Results and Discussion

3.1 Reported and estimated incidence of MDR-TB in East Africa

The total number of TB cases and MDR-TB cases identified in each country of the EAC between 2005 and 2011 is summarized in Table 1. As a proportion of total tuberculosis cases reported, the number of confirmed MDR cases ranged from 6/6,828 (0.09%) in Burundi to 76/6,784 (1.12%) in Rwanda. Additionally, there have been 16 published surveillance studies from East Africa with a well defined patient enrollment criteria reporting levels of MDR-TB; these studies are detailed in Table 2.[4–19] Levels of MDR among new TB patients in the independent surveillance studies ranged from 0.4% in Tanzania to 4.4% in Uganda.[10,15] Levels of MDR among recurrent TB cases ranged from 3.9% in Tanzania to 17.7% in a Uganda.[13,19] Based upon the reported cases and surveillance data, the World Health Organization (WHO) estimated the MDR-TB burden of all new and retreatment cases in 2011 for Burundi, Kenya, Rwanda, Tanzania and Uganda ranging from 1.2% in Tanzania to 4.8% in Rwanda (Table 3).[20–24]

3.2 Cases of confirmed MDR-TB and gaps in MDR-TB testing and treatment

There is a large gap between the numbers of estimated cases of MDR and numbers of confirmed cases of MDR-TB in East Africa. Of the 227,759 notified TB cases in East Africa in 2011, the WHO estimated 6,331 MDR-TB cases (Table 4).[20–24] Only 387 cases of MDR-TB were actually confirmed through diagnostic testing in 2011, and therefore nearly 6,000 cases of MDR-TB are undiagnosed and untreated in East Africa each year.[20–24]

The capacity to diagnose *M. tuberculosis* drug resistance and treat MDR-TB must increase and be considered an essential element of TB care in the EAC. For this potential to be realized, drug resistance testing and MDR-TB treatment must be prioritized by national TB control programs and funding agencies. The introduction of the new GeneXpert MTB/RIF test into the region should facilitate scale-up of testing for MDR.

3.3 Risk factors for MDR-TB

3.3.1 Recurrent tuberculosis—Country-based studies in East Africa found a higher incidence of multidrug-resistance in recurrent cases of tuberculosis than in new cases. In Burundi, a study found that resistance to any anti-TB drug, rifampicin, and at least rifampicin and isoniazid were 16.1%, 2.0%, and 1.4% respectively in new patients.[4] In

recurrent cases, however, resistance rates were much higher at 30%, 15%, and 12% for any anti-TB drug, rifampicin, and at least rifampicin and isoniazid respectively.[4] In Kenya, Ogaro *et al* noted the level of MDR-TB was 0.5% in new TB cases and 8.5% in recurrent tuberculosis cases,[5] while another study in Kenya found MDR-TB in 1.0% of new tuberculosis cases.[6] Umubyeyi *et al* found in Rwanda that the rate of MDR-TB was 3.9% in new patients diagnosed with tuberculosis versus 9.4% in recurrent tuberculosis patients.[8] In Tanzania, Range *et al* examined MDR-TB in new and retreatment TB cases, and found the levels to be 2.0% and 6.3% respectively.[9] Kibiki *et al* also found MDR-TB in 1.8% of new TB patients versus 7.1% of retreatment cases.[11] Another study in Tanzania found MDR-TB in 1.2% of new tuberculosis patients versus 3.9% in retreatment cases.[13] Researchers in Uganda documented the same pattern.[18] Resistance to any drug and MDR-TB were found in 12.1% and 1.1% of new TB cases respectively, versus 28.3% and 11.7% of recurrent TB cases.[18] Recurrent tuberculosis is a risk factor for MDR-TB in East Africa.

3.3.2 HIV Sero-positivity—No studies report a correlation between MDR-TB and HIV in East Africa. There is a clear link between TB and HIV, with 13% (1.1 million) of global TB cases diagnosed in 2011 occurring among individuals also living with HIV.[1] Incidence of HIV-positive TB cases is even higher in Africa; 79% of the HIV-positive TB cases diagnosed in 2011 were from Africa.[1]

However, the relationship between HIV and MDR-TB is less well understood. Reports on associations of HIV co-infection and drug resistance among patients with TB have been contradictory. Some studies outside of East Africa have found strongly increased risks for MDR-TB among patients co-infected with TB and HIV, whereas other studies found no increased risk. [10,15,17,18,25–37] In many of the cases when an association was found, it was related to nosocomical outbreaks in hospital settings. Therefore continued vigilance should be taken in hospital settings where HIV-infected patients may be exposed to MDR-TB.

3.3.3 Refugees—East Africa has seen a large number of refugees due to civil strife and war in the region and in neighboring countries. In a study conducted in North Eastern Kenya, MDR TB prevalence was higher in refugee camp populations than in the nearby non-refugee population.[38] Reports from other parts of the world show that the rates of TB and MDR-TB are higher among refugee populations than non-refugee populations.[39–43] The high level of MDR-TB among refugees in East Africa may be attributed to the disorganization of the health system, concentration of the population, and high default rates in refugee camps. Refugee populations in East Africa should be the focus of screening and treatment for MDR-TB.

3.4 Correlation between rifampicin resistance and MDR

Studies in East Africa demonstrate that resistance to rifampicin is predictive of multidrug-resistance. Studies in Tanzania, Burundi and Uganda found that a high percentage of rifampicin resistant *M. tuberculosis* isolates were also multidrug-resistant (Table 5). [4–6, 8–19] In total, 223/254 (88%) TB isolates tested in East Africa that were resistant to rifampicin were also resistant to isoniazid and were therefore MDR.

3.5 Mutations conferring resistance to rifampicin

Studies have documented that approximately 95% of rifampicin resistant strains possess a mutation on the *rpoβ* gene encoding the β subunit of the RNA polymerase.[44,45] These findings were consistent for MDR-TB throughout East Africa (Table 6).[7,11,17,19,46] In our analysis of the literature from East Africa, all the MDR-TB isolates tested had a mutation in the *rpoβ* gene. Identifying mutations in the short, 81 base pair core region of the *rpoβ* gene is useful in identifying rifampicin resistance and thereby MDR-TB.

3.6 Genetic diversity of MDR-TB

Our analysis showed that the MDR-TB isolates of T2 family were the most common (Table 6).[11,15,17,46–48] There is no statistical association between spoligotype and drug resistance pattern in studies from East Africa. In Kenya, Githui *et al* discovered spoligotype SIT 26 (CAS1) comprised 7/15 (47%) of the 15 MDR isolates.[46] Another 2/15 (13.3%) of the MDR isolates were from the SIT 1 (Beijing). This study is the first in Kenya and the second in sub-Saharan Africa to report the presence of MDR Beijing/W type, yet, no statistical association between spoligotype and drug resistance pattern was found.[46]

A study in Rwanda by Gafirita *et al* found that the T2 family was prevalent among the MDR-TB isolates. Furthermore, 34 of the 64 (53.1%) isolates identified belonged to SIT 52 (T2) and another 8 of the 64 (12.5%) isolates belonged to SIT 125 (T2).[48]

In Tanzania, the three MDR-TB isolates analyzed by Kibiki *et al*, were SIT 21 (CAS1-Kili), SIT 59 (LAM11-ZWE) and SIT 354 (EAI). In this analysis, 7 isolates were *M. tuberculosis* Beijing but none of them were resistant to any anti-TB drugs.[11] Although T2 was the most common drug sensitive isolate, no correlation between type and drug resistance was found.[11]

A study in Uganda showed that there was no significant association between drug resistance and any lineage.[15] A cluster analysis by Asiimwe *et al* of 15 MDR-TB isolates showed that four of 15 MDR isolates were SIT 52 (T2); in addition three MDR isolates were SIT 128 (T2), while SIT 135 (T2-Uganda) had two MDR isolates. The other 6 MDR isolates were distributed as follows: one LAM9 (SIT 42), one UGA7 (T2), one UGA18 and three unique (T2) isolates. Although strains of the T2 family accounted for 13 of the fifteen MDR strains, there was no statistical association between MDR and T2 family.[15]

4. Limitations

Our findings are limited by the relatively small number of studies on MDR-TB conducted in East Africa and the small sample size of most of these studies. However, collectively the 16 epidemiologic studies summarized in Table 2 enrolled more than 6,000 TB patients and provide consistent findings on MTB drug resistance in the region. This allows us to draw some important conclusions which may guide public health policy in East Africa.

5. Conclusions

- The estimated MDR-TB prevalence in East Africa ranges from 0.4 – 4.4% in new patients and from 3.9 – 17.7% in recurrent TB patients.
- There is a large gap between the estimated number of MDR-TB cases and the number actually diagnosed and treated. Approximately 6,000 MDR-TB cases go undiagnosed and untreated each year.
- Recurrent tuberculosis and refugee status are established risk factor for MDR-TB.
- The most common spoligotypes in East Africa are SIT 52 (T2), SIT 125 (T2) and SIT 26 (CAS1), but there have been no statistical associations between spoligotype and drug resistance patterns reported.
- All MDR isolates tested have a mutation in the *rpoβ* gene; therefore new molecular diagnostics for MDR should be effective in East Africa.
- Increased capacity for diagnosis and treatment of MDR-TB is needed, with an emphasis on recurrent TB cases and refugees.

- More studies with large sample size are warranted in MDR-TB in East Africa.

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Table 1

Epidemiology and Number of Confirmed MDR-TB Cases in East Africa as Reported by the WHO: 2005 – 2011[a]

East African Country	2005	2006	2007	2008	2009	2010	2011
Burundi							
Population in million	7	8	8	8	8	8	9
TB cases notified	6,585	6,114	6,284	6,808	7,277	7,719	6,828
Confirmed MDR-TB cases[†]	-	0	26	17	0	24	6
% of TB cases that is MDR	-	0	0.41	0.25	0	0.31	0.09
Kenya							
Population in million	36	37	38	39	40	41	42
TB cases notified	102,680	108,342	106,438	99,941	102,997	106,083	103,981
Confirmed MDR-TB cases[†]	44	89	82	102	150	112	166
% of TB cases that is MDR	0.04	0.08	0.08	0.10	0.15	0.11	0.16
Rwanda							
Population in million	9	9	9	10	10	11	11
TB cases notified	7,220	8,117	7,638	7,472	7,251	7,065	6,784
Confirmed MDR-TB cases[†]	35	-	102	79	78	90	76
% of TB cases that is MDR	0.48	-	1.34	1.06	1.08	1.27	1.12
Tanzania							
Population in million	39	40	41	42	44	45	46
TB cases notified	61,022	59,282	59,371	60,490	71,643	63,453	61,148
Confirmed MDR-TB cases[†]	10	13	169	24	24	34	68
% of TB cases that is MDR	0.02	0.02	0.28	0.04	0.03	0.05	0.11
Uganda	-	-	-	-	-	-	
Population in million	29	30	31	32	33	33	35
TB cases notified	41,040	40,782	40,909	42,178	41,703	45,546	49,018

East African Country	2005	2006	2007	2008	2009	2010	2011
Confirmed MDR-TB cases†	46	-	-	26	57	93	71
% of TB cases that is MDR	0.11	-	-	0.06	0.14	0.20	0.14

[a] These are the numbers of cases confirmed and reported by national tuberculosis (TB) programs to the World Health Organization (WHO).[20–24,49]

† Confirmed multi-drug resistant tuberculosis (MDR-TB) are those newly diagnosed with resistance to at least isoniazid and rifampicin.

Table 2

Country-Specific Surveillance Studies Detailing *M. tuberculosis* Multi Drug Resistance (MDR) in East Africa[a]

Country, Study	Population	New TB	Recurrent TB
		% MDR (# resistant/total TB cases)	% MDR (# resistant/total TB cases)
Burundi			
Sanders *et al*[4]	All smear-positive, new and retreatment patients were enrolled consecutively in the study over a period of 15 months from 2002–2003. Patients were recruited from seven diagnostic centers of Bujumbura, Burundi, together registering one third of all cases in the country.	1.4 (7/496)	11.6 (8/69)
Kenya			
Ogaro *et al*[5]	All smear-positive, new and previously treated pulmonary TB patients aged 14 years and older were enrolled consecutively between February and August 2010 from 16 diagnostic and treatment facilities in Nairobi, Kenya.	0.5 (2/369)	8.5 (17/199)
Ndung'u *et al*[6]	All sputum culture or smear positive, newly diagnosed pulmonary TB patients aged 18 years and older were enrolled systematically between April and December 2010 from five hospitals and TB clinics in and around Nairobi, Kenya.	1.0 (3/286)	-
Rwanda			
Umubyeyi *et al*[7]	All smear-positive, new and previously treated pulmonary TB patients were recruited between January 2002 to September 2005 from 4 provinces of Rwanda (Kigali, Butare, Ruhengeri, and Rwamagana).	10.8[b] (69/638)	
Umubyeyi *et al*[8]	All smear-positive, new and retreatment pulmonary TB cases registered between November 2004 and February 2005 with the National Tuberculosis Control Program of Rwanda were eligible for inclusion.	3.9 (24/616)	9.4 (8/85)
Tanzania			
Range *et al*[9]	All newly diagnosed and relapse pulmonary TB patients, aged 15 years or older were consecutively enrolled between August 2001 and July 2002 from Sekou Toure Regional Hospital, Bugando Medical Center, Butimba and Buzuruga Health Centers and Magu District Hospital. Tuberculosis was confirmed through clinical examination smear microscopy, culture, and/or chest x-ray.	2.0 (9/455)	6.3 (3/48)
Urassa *et al*[10]	All smear positive patients who had no history of use of anti-TB drugs exceeding 4 weeks in the previous 12 months, and were aged 19 to 65 years old were invited to participate in the study. The TB isolates for the study were collected between 2001 and 2004 from five of the 14 out-patient Tb treatment clinics in Dares Salaam, Tanzania.	0.4[c] (1/280)	-
Kibiki *et al*[11]	All smear-positive patients prior to initiation of TB treatment (mean age of 37 years) were recruited between April and September 2005 from Kibong'oto National Tuberculosis Referral Hospital (KNTH) and Kilimanjaro Christian Medical center (KCMC) of the Kilimanjaro region of northern Tanzania.	2.1 (2/97)	7.1 (1/14)
Matee *et al*[12]	All smear positive, newly diagnosed pulmonary TB patients were consecutively enrolled between October 2005 and August 2006 from the Temeke district of Dar es Salaam.	1.3 (3/226)	-
Chonde *et al*[13]	All sputum smear-positive, new and previously treated TB patients were eligible for enrolment between July 2006 to August 2007 from 40 diagnostic centers that are a representative sample of all diagnostic centers in Tanzania.	1.2 (11/909)	3.9 (5/127)
Uganda			
Temple *et al*[14]	All AFB smear-positive, new and retreatment tuberculosis patients aged 18 years or older were consecutively enrolled between July 2003 and November 2006 from the National Tuberculosis and Leprosy Programme (NTLP) clinic at Mulago Hospital in Kampala, Uganda.	12.7 (52/409)	

Country, Study	Population	New TB	Recurrent TB
		% MDR (# resistant/total TB cases)	% MDR (# resistant/total TB cases)
Asiimwe *et a1*[15]	All smear-positive, newly-presenting patients aged 18 years or older were consecutively enrolled between February and November 2006 from four main TB clinics in Rubaga, Uganda.	4.4 (15/339)	0 (0/5)
Jones-López *et al*[16]	All AFB smear-positive, retreatment tuberculosis patients age 18 years or older were consecutively enrolled between July 2003 and January 2007 from an inpatient TB ward of the National Tuberculosis and Leprosy Programme (NTLP) Chemotherapy Centre at Mulago Hospital in Kampala, Uganda.	-	6.3 (18/288)
Bazira *et a1*[17]	All smear-positive newly diagnosed and retreatment TB patients aged 18 years or older were enrolled consecutively between May 2007 and April 2008 from clinics in the former greater Mbarara region in South Western Uganda.	1.7 (2/116)	0 0/9
Lukoye *et al*[18]	All smear-positive TB patients who were registered for treatment and aged 18 years or older were enrolled between August 18 and December 19, 2008 following a rotational fashion from health care facilities in Kampala, Uganda. All health care facilities in Kampala were enrolled following a rotational fashion from so that each facility participated for the same amount of time in the study.	1.1 (5/473)	11.7 (7/60)
Albert *et al*[19]	All sputum smear-positive, retreatment tuberculosis patients were consecutively enrolled between attending the Mulago National Referral Hospital TB Unit in Kampala, Uganda.	-	17.7[d] (20/113)

[a] We include in this table 16 published surveillance studies from East Africa with a well defined patient enrollment criteria reporting levels of multidrug resistant-tuberculosis (MDR-TB); MDR-TB is defined as resistance to at least isoniazid and rifampicin.

[b] The total number of new and recurrent TB cases was not specified.

[c] Patients in the study had no history of use of anti-TB drugs exceeding 4 weeks in the previous 12 months and therefore, exclude most of the retreatment population.

[d] Combined prevalence determined by either line probe assay or Mycobacterium growth index tube drug susceptibility test (MGIT DST).

Table 3

WHO Estimated Number and Proportion of MDR-TB Cases in East Africa: 2011[a]

Country of East Africa	New TB Number multi-resistant/ Total new TB cases (% MDR)	Recurrent TB Number multi-resistant/ Total recurrent TB cases (% MDR)	All TB Number multi-resistant/ Total all TB cases (% MDR)
Burundi	202/6,513 (3.1)	32/315 (10.2)	234/6,828 (3.4)
Kenya	2,913/93,964 (3.1)	1,000/10,017 (10.0)	3,913/103,981 (3.8)
Rwanda	248/6,370 (3.9)	79/414 (19.1)	327/6,784 (4.8)
Tanzania	641/58,278 (1.1)	106/2,870 (3.7[b])	747/61,148 (1.2)
Uganda	630/45,004 (1.4)	480/4,014 (12.0)	1,110/49,018 (2.3)
Total	4,634/210,129 (2.2)	1,697/17,630 (9.6)	6,331/227,759 (2.8)

[a]The World Health Organization (WHO) estimates the number and proportion of new and retreatment cases of MDR-TB using country-level information. For countries that reported data, the latest available information was used. For countries that did not reported data, estimates were modeled using data from countries with similar TB epidemiology.[20–24]

[b]The mean value of the estimate range given by the WHO is reported.

Table 4

Gap between the Estimated Number of MDRTB Cases and the Number Confirmed by National TB Programs: 2011[a]

Country	*Estimated cases of MDR-TB*	*Confirmed cases of MDR-TB*	*Gap between estimated and confirmed cases of MDR-TB*
Burundi	234	6	228
Kenya	3,913	166	3,747
Rwanda	327	76	251
Tanzania	747	68	679
Uganda	1,110	71	1,039
Total	**6,331**	**387**	**5,944**

[a]We provide the WHO estimated number of MDR cases and the number actually diagnosed and reported by national TB programs in 2011.[20–24]

Table 5

Relationship between Rifampicin Resistance and MDR-TB[a]

Country (Reference)	% of Rifampicin resistant isolates that are MDR-TB (number of MDR/number of rifampicin resistant isolates)
Burundi (Sanders *et al*)[4]	75 (15/20)
Kenya (Ogaro *et al*)[5]	90 (19/21)
Kenya (Ndung'u *et al*) [6]	75 (3/4)
Rwanda (Umubyeyi *et al*)[8]	97 (32/33)
Tanzania (Range *et al*)[9]	75 (12/16)
Tanzania (Urassa *et al*)[10]	100 (1/1)
Tanzania (Kibiki *et al*)[11]	100 (3/3)
Tanzania (Matee *et al*)[12]	100 (3/3)
Tanzania (Chonde *et al*)[13]	89 (16/18)
Uganda (Temple *et al*)[14]	96 (52/54)
Uganda (Asiimwe *et al*)[15]	100 (15/15)
Uganda (Jones-López *et al*)[16]	90 (18/20)
Uganda (Bazira *et al*)[17]	33 (2/6)
Uganda (Lukoye *et al*)[18]	80 (12/15)
Uganda (Albert *et al*)[19]	80 (20/25)
Overall for East Africa	**88 (223/254)**

[a]We included 15 published surveillance studies from East Africa with a well defined patient enrollment criteria reporting levels of Multidrug resistant tuberculosis (MDR-TB) and describing the correlation between Rifampicin Resistance and MDR-TB.

Table 6

Distribution of Genetic Mutations Conferring Resistance and Genotypes of MDR-TB of East Africa

Country of East Africa	# MDR-TB isolates	Rifampicin Mutations	Spoligotype	Reference (Year)
Burundi[a]				
Kenya	15	9/15 C526T 6/15 C531T	6/15 SIT 26 (CAS1) 2/15 SIT 1 (Beijing) 7/15 untyped	Githui *et al* (2004)[46]
Rwanda	13	7/13 S531L 2/13 S531L + T563A 2/13 S531L + T480I 1/13 S531L + T481A 1/13 A516V	N/A[b]	Umubyeyi *et al* (2007)[7]
Rwanda	3	N/A[b]	3/3 SIT 152 (T2)	Umubyeyi *et al* (2007)[47]
Rwanda	64	N/A[b]	34/64 SIT 52 (T2) 8/64 SIT 125 (T2) 1/64 SIT 853 (T2) 7/64 unclustered 14 isolates were not reported	Gafirita *et al* (2012)[48]
Tanzania	3	1/3 C531G 1/3 C531T 1/3 C526T	1/3 SIT 59 (LAM11-ZWE) 1/3 SIT 354 (EAI) 1/3 SIT 21 (CAS1-Kili)	Kibiki *et al* (2007)[11]
Uganda	15	N/A[b]	4/15 SIT 52 (T2) 3/15 SIT 128 (T2) 2/15 SIT 135 (T2) 1/15 UGA 7 (T2) 1/15 SIT 42 (LAM9) 1/15 UGA 18 (T2) 3/15 Others[c] (T2)	Asiimwe *et al* (2008)[15]
Uganda	13	9/13 S531L 1/13 H526D 3/13 wild type mutations[d]	N/A [b]	Albert *et al* (2010) [19]
Uganda	2	1/2 D516V+H526Y+H526D 1/2 S531L+530–533 wild type mutation	1/2 SIT 20 (Delhi/CAS) 1/2 SIT 135 (T2)	Bazira *et al* (2011)[17]

[a] No study published

[b] Not done

[c] Unique T2 isolates

[d] 1 isolate had both 513–517 and 516–519, 1 isolate had both 516–519 and 526–529, and 1 had 530–533 wild type mutations at specific regions in *rpoβ* gene.