INT J TUBERC LUNG DIS 17(8):1036–1042

http://dx.doi.org/10.5588/ijtld.12.0842

Multidrug- and isoniazid-resistant tuberculosis in three high HIV burden African regions

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SUMMARY

SETTING: Despite major progress in the surveillance of drug-resistant tuberculosis (TB), data are lacking for many low-resource countries. World Health Organization estimates of multidrug-resistant TB (MDR-TB) rates in Africa are low, and based on very limited data from the African continent.

OBJECTIVE: To measure MDR-TB prevalence in sub-Saharan African regions with a high prevalence of human immunodeficiency virus (HIV).

METHOD: We conducted three anti-tuberculosis drug resistance surveys in sub-Saharan African regions with high HIV-TB coinfection prevalence: Homa Bay (Kenya), Chiradzulu (Malawi) and West Nile region (Uganda).

RESULTS: The prevalence of MDR-TB in new patients was found to be low in the three regions: 1.4% (95%CI 0.2–2.6) in Homa Bay, 2.0% (95%CI 0.4–3.6) in Chiradzulu and 0.6% (95%CI 0.0–1.5) in the West Nile region. We found no significant association between MDR-TB and HIV infection. Nonetheless, ⩾10% of the new cases surveyed were resistant to isoniazid (INH).

CONCLUSION: The relatively high rate of resistance to INH highlights the need for rapid detection of INH resistance in addition to rifampicin (RMP) resistance, to allow rapid modification of treatment to avoid the acquisition of RMP resistance. Drug resistance should be monitored periodically.

KEY WORDS: tuberculosis; survey; resistance; isoniazid

IN 2010, there were an estimated 8.8 million incident cases of tuberculosis (TB) globally.[1] Of these, 2.3 million occurred in the Africa Region, where a high number of TB cases are attributable to the human immunodeficiency virus (HIV) epidemic.[1] Strains of *Mycobacterium tuberculosis* resistant to anti-tuberculosis drugs have been reported worldwide.[2] These forms of TB do not respond to the standard 6-month treatment with first-line anti-tuberculosis drugs and require longer treatment with drugs that are less potent and more toxic. Multidrug-resistant TB (MDR-TB) is caused by bacteria resistant to at least isoniazid (INH, H) and rifampicin (RMP, R), the most effective anti-tuberculosis drugs. Surveillance data on drug-resistant TB (DR-TB) reveal that worldwide 3.4% (95% confidence interval [CI] 1.9–5.0) and 19.8% (95%CI 14.4–25.1) of new and previously treated TB cases, respectively, are MDR-TB.[3]

According to the World Health Organization (WHO), the estimated proportion of MDR-TB cases in Africa is 1.9% (95%CI 0.6–3.3) in new cases and 9.4% (95%CI 3.0–15.8) in previously treated cases.[3] These estimates are based on limited data from the African continent, where most of the countries lack figures on DR-TB. This is particularly true for Malawi, Uganda and Kenya.

We aimed to estimate the prevalence and predictors of DR-TB among new TB cases in three high HIV burden regions of eastern Africa: Chiradzulu (Malawi), Homa Bay (Kenya) and the West Nile Region (Uganda), where Médecins Sans Frontières (MSF) provides support for TB and HIV care. The available data on drug resistance at national level in these countries are based on estimations using mathematical models or old national surveys.[2,4,5]

STUDY POPULATION AND METHODS

Design and study population

Three cross-sectional surveys were designed using the same protocol adapted from the guidelines of the WHO and the International Union Against Tuberculosis and Lung Disease for the surveillance of drug resistance in TB.[6] All newly diagnosed smear-positive TB patients aged ⩾14 years were eligible for the study.

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Article submitted 2 November 2012. Final version accepted 4 March 2013.

[A version in French of this article is available from the Editorial Office in Paris and from the Union website www.theunion.org]

In Kenya, the survey was conducted in the district hospital of Homa Bay, the referral TB centre for three districts with a population of >600 000. HIV prevalence in this area was estimated to be 21% in the adult population (15–49 age-group) in 2006.[7] In Malawi, the survey was conducted in the District Hospital of Chiradzulu, which covers a population of 252 000, with an estimated HIV prevalence of 25% in the adult population.[8] In Uganda, the survey took place in the Arua Regional Referral Hospital of the West Nile Administrative Region, to which smear-positive patients from the nine districts of the region, covering a population of around two million, were referred. HIV prevalence in this area was estimated to be 2.3% in the 15–49 age-group.[9]

Patient information

Clinical and epidemiological information was collected from each of the patients enrolled. Data included age, sex, region of residence, duration of illness, TB contact history in the last 2 years, history of anti-tuberculosis treatment (number of previous anti-tuberculosis treatment courses and outcomes) and HIV status. Patients were considered as new cases if they had never received treatment for TB or had taken anti-tuberculosis drugs for <1 month in the past, or as previously treated cases if they had received ⩾1 month of anti-tuberculosis drugs in the past. Previously treated cases included treatment failures, TB relapses and returns after default using standard TB case definitions.[5] Free access to voluntary counselling and testing for HIV was available at each site.

Procedures

Two early-morning sputum samples were systematically collected from each eligible patient to reduce the risk of specimen loss in case of contamination. Specimens were shipped every 2 weeks to the mycobacteriology laboratory of the Institute of Tropical Medicine in Antwerp, Belgium, for *M. tuberculosis* culture and drug susceptibility testing (DST). After the addition of 1% cetylpyridinium chloride (CPC) transportation medium, one of the samples was stored at room temperature until shipment; the other sample without CPC was stored at 4–8°C until shipment. The samples were shipped by air as per the United Nations Model Regulations on the transport of dangerous goods.[10]

All samples were decontaminated using the Petroff method. The sediments obtained from the samples with CPC were inoculated on Löwenstein-Jensen (LJ) solid medium. The samples without CPC were inoculated on liquid medium with the BACTEC™ MGIT™ 960 system (BD, Franklin Lakes, NJ, USA). MGIT-positive cultures were confirmed positive for acid-fast bacilli (AFB) using blood agar and microscopy. If the culture was positive for AFB and was contaminated with other bacteria or fungi, the suspension was again decontaminated to isolate the mycobacteria. When isolation was not possible, the culture was considered contaminated. Identification was performed with LJ enriched with *p*-nitrobenzoic acid, which is known to inhibit growth of *M. tuberculosis* complex. A case was defined as *M. tuberculosis* culture-positive if at least one of the two culture results was positive for *M. tuberculosis*. Other cases were reported as culture-negative, contaminated or positive for non-tuberculous mycobacteria.

DST for first-line drugs was performed using the MGIT 960 SIRE method for any positive culture. DST was performed as per the manufacturer's guidelines at the following concentrations: streptomycin 1.0 μg/ml, INH 0.1 μg/ml, RMP 1.0 μg/ml, ethambutol (E) 5.0 μg/ml. DST for pyrazinamide (Z, PZA) and second-line drugs were performed on MDR-TB strains. Ofloxacin (OFX), ethionamide (ETH), kanamycin (KM) and capreomycin were tested on TH11 agar medium using the proportion method, para-aminosalicylic acid (PAS) on LJ and PZA on MGIT 960. The following standard concentrations were used: OFX 2 μg/ml, ETH 10 μg/ml, KM 6 μg/ml, CM 10 μg/ml, PAS 0.5 μg/ml and PZA 100 μg/ml.

Sample size and statistical analyses

The sample size was calculated for each survey based on the expected prevalence of RMP resistance among new patients with TB for the three settings (5%), a maximal acceptable absolute error of 2.5% and a CI of 95%. Sample sizes were increased by 20% to account for expected losses (i.e., contamination, non-growing cultures, missing DST results). Consecutive previously treated cases were also enrolled during the intake period for new cases.

Data were entered using EpiData 3.1 software (EpiData Association, Odense, Denmark), and cleaned and analysed using Stata for Windows 10.1 (StataCorp, College Station, TX, USA). MDR-TB prevalence and INH resistance were calculated with 95%CI for all new cases and for the group of HIV-infected new cases. Prevalence ratios (PRs) and 95%CI were calculated to measure the degree of association between independent variables and MDR-TB and any resistance to INH through generalised linear models for the binomial family. All variables with $P < 0.20$ in univariate analysis were included in a multivariable analysis. We used an alpha error of 5% for all statistical tests.

Ethical approval

The study was approved by the National Health Sciences Research Committee of Malawi, Lilongwe, Malawi; the AIDS Research Committee of the Uganda National Council for Science and Technology, Kampala, Uganda; the Kenyan Medical Research Institute Scientific Ethical Committee, Nairobi, Kenya; and

the Comité Consultatif de Protection des Personnes dans la Recherche Médicale, Saint Germain en Laye, France. Written informed consent to participate in the survey was provided by the patients or by the parents/care givers in the case of minors.

RESULTS

Patient characteristics

Patients were recruited between September 2007 and September 2010 in the West Nile region, December 2007 and October 2009 in Homa Bay and April 2008 and November 2009 in Chiradzulu (Figure). Of the 1479 pulmonary TB patients screened for eligibility, 219 (14.8%) met at least one exclusion criterion and 38 refused to participate, and a final 1222 patients were included in the study—1108 new and 114 previously treated cases. The baseline patient characteristics are shown in Table 1: 8.6% of the patients were previously treated cases in Homa Bay, 9.4% in Chiradzulu and 10.0% in West Nile; HIV prevalence among smear-positive TB patients was 71.8% (95%CI 67.2–76.3) in Homa Bay, 72.0% (95%CI 67.5–76.5) in Chiradzulu and 28.2% (95%CI 23.6–32.8) in West Nile, and between 60% and 80% of previously treated cases were TB relapses in the three sites. Relapsed TB cases were HIV-infected in respectively 90.5% (19/21), 93.6% (29/31) and 44.0% (11/25) of the cases in Homa Bay, Chiradzulu and West Nile.

Bacteriological results

A total of 2342 sputum samples from the 1222 patients were sent to the laboratory in Antwerp. The final culture result was reported as contaminated in respectively 19/429 (4.4%), 24/392 (6.1%) and 28/401 (7.0%) patients in Homa Bay, Chiradzulu and West Nile. *M. tuberculosis* culture-positive results were reported for 390/429 (90.9%) patients in Homa Bay, 325/392 (82.9%) in Chiradzulu and 361/401 (90.0%) in West Nile. All positive cultures underwent DST.

Patterns of drug resistance among new cases are presented by site in Table 2. MDR-TB prevalence among new cases was 1.4% (95%CI 0.2–2.6) in Homa Bay, 2.0% (95%CI 0.4–3.6) in Chiradzulu and 0.6% (95%CI 0.0–1.5) in West Nile. Of the 13 MDR-TB strains, two were also resistant to PZA and one to KM, while 11 were susceptible to second-line drugs and PZA. MDR-TB prevalence and any INH drug resistance in new HIV-infected cases are shown in Table 3.

DST results for previously treated cases are shown in Table 4. Three of the MDR-TB isolates presented additional resistance to PZA and one was also resistant to ETH. Any INH resistance occurred in respectively 2 (5.9%), 4 (17.4%) and 12 (33.3%) previously treated cases in Homa Bay, Chiradzulu and West Nile. Overall, any INH resistance occurred in 21.7% (13/60) of relapses and 15.2% (5/33) of other previously treated cases ($P = 0.447$).

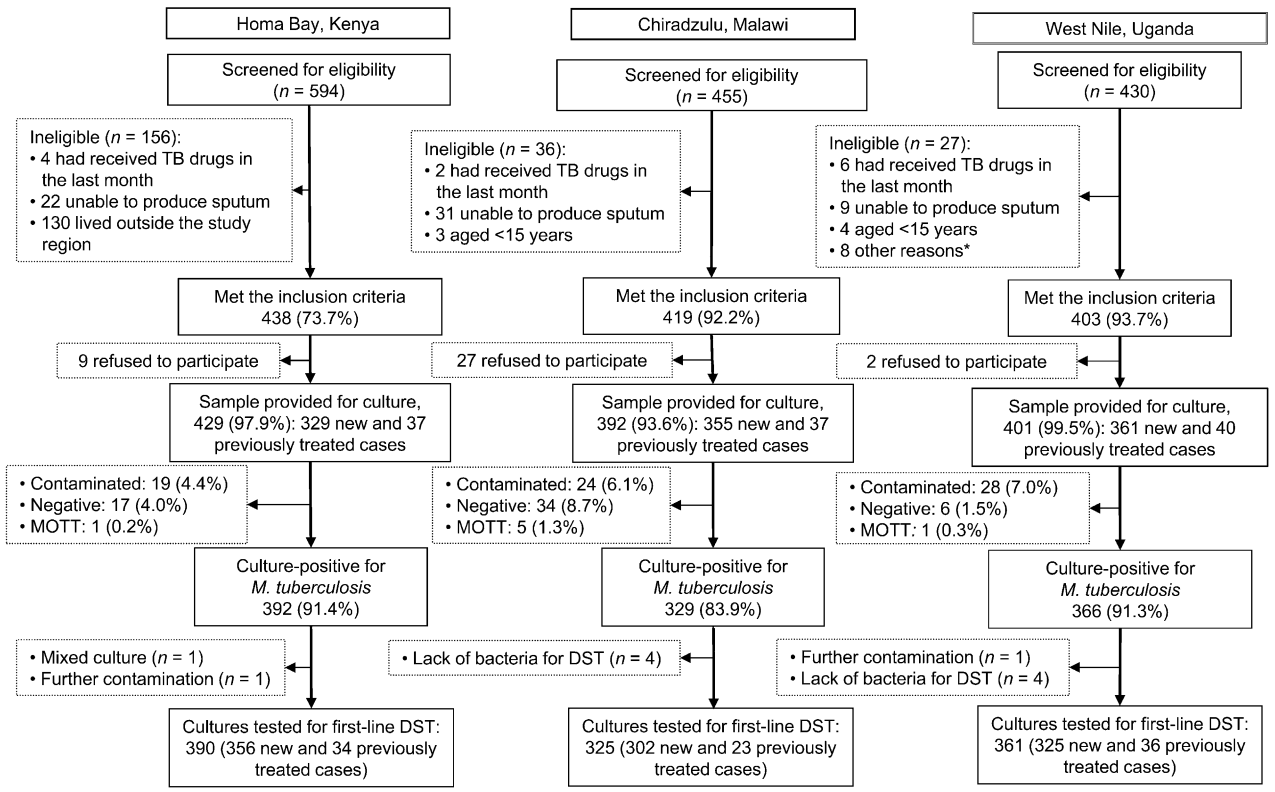

Figure Flow chart of the study inclusion process by study site. *Language barrier ($n = 3$), unknown reason ($n = 5$). TB = tuberculosis; MOTT = mycobacteria other than tuberculosis; DST = drug susceptibility testing.

Table 1 Baseline characteristics of included patients by study site

	Homa Bay, Kenya		Chiraduzulu, Malawi		West Nile, Uganda	
	New cases *n* (%)	Previously treated cases *n* (%)	New cases *n* (%)	Previously treated cases *n* (%)	New cases *n* (%)	Previously treated cases *n* (%)
Sex	(*n* = 392)	(*n* = 37)	(*n* = 355)	(*n* = 37)	(*n* = 361)	(*n* = 40)
Male	199 (50.8)	20 (54.1)	174 (49.0)	22 (59.5)	253 (70.1)	34 (85.0)
Female	193 (49.2)	17 (45.9)	181 (51.0)	15 (40.5)	108 (29.9)	6 (15.0)
Age group, years	(*n* = 389)	(*n* = 37)	(*n* = 352)	(*n* = 37)	(*n* = 361)	(*n* = 40)
15–29	199 (51.2)	16 (43.2)	117 (33.2)	4 (10.8)	136 (37.7)	14 (35.0)
30–44	129 (33.2)	16 (43.2)	164 (46.6)	27 (73.0)	172 (47.6)	18 (45.0)
⩾44	61 (15.7)	5 (13.5)	71 (20.2)	6 (16.2)	53 (14.7)	8 (20.0)
HIV status	(*n* = 344)	(*n* = 35)	(*n* = 338)	(*n* = 37)	(*n* = 329)	(*n* = 40)
Negative	103 (29.9)	4 (11.4)	102 (30.2)	3 (8.1)	240 (72.9)	25 (62.5)
Positive	241 (70.1)	31 (88.6)	236 (69.8)	34 (91.9)	89 (27.1)	15 (37.5)
Duration of cough for the current episode, months	(*n* = 388)	(*n* = 37)	(*n* = 355)	(*n* = 37)	(*n* = 361)	(*n* = 40)
<1	135 (34.8)	12 (32.4)	44 (12.4)	3 (8.1)	34 (9.4)	8 (20.0)
1–6	230 (59.3)	22 (59.5)	294 (82.8)	30 (81.1)	269 (74.5)	26 (65.0)
7–12	15 (3.9)	0	10 (2.8)	3 (8.1)	37 (10.2)	3 (7.5)
>12	8 (2.1)	3 (8.1)	7 (2.0)	1 (2.7)	21 (5.8)	3 (7.5)
Contact with TB patient in the last 2 years	(*n* = 387)	(*n* = 35)	(*n* = 355)	(*n* = 37)	(*n* = 360)	(*n* = 40)
No	308 (79.6)	23 (65.7)	275 (77.5)	22 (59.5)	268 (74.4)	30 (75.0)
Yes	79 (20.4)	12 (34.3)	80 (22.5)	15 (40.5)	92 (25.6)	10 (25.0)
Type of previously treated patient	NA	(*n* = 35)	NA	(*n* = 36)	NA	(*n* = 41)
Failure		1 (2.9)		3 (8.3)		4 (9.8)
Relapse		21 (60.0)		31 (86.1)		25 (61.0)
Return after default		13 (37.1)		2 (5.6)		10 (24.4)
Unknown		0		0		2 (4.8)
Site of previous treatment		(*n* = 32)		(*n* = 35)		(*n* = 40)
MSF programme		26 (81.2)		18 (51.4)		25 (62.5)
In the district, but not in MSF programme		3 (9.4)		7 (20.0)		7 (17.5)
Outside the district		3 (9.4)		10 (28.6)		8 (20.0)

HIV = human immunodeficiency virus; TB = tuberculosis; NA = not applicable; MSF = Médecins Sans Frontières.

Table 2 Prevalence of resistance to FLDs among new TB cases

	Homa Bay, Kenya (*n* = 356) *n* (%)	Chiradzulu, Malawi (*n* = 302) *n* (%)	West Nile, Uganda (*n* = 325) *n* (%)
Susceptible to all FLDs	296 (83.1)	243 (80.5)	232 (71.4)
Any resistance to FLDs	60 (16.9)	59 (19.5)	93 (28.6)
H	36 (10.1)	33 (10.9)	53 (16.3)
R	6 (1.7)	8 (2.6)	5 (1.5)
S	25 (7.0)	27 (8.9)	49 (15.1)
E	23 (6.5)	18 (6.0)	31 (9.5)
Monoresistance	42 (11.8)	41 (13.6)	60 (18.5)
H	19 (5.3)	17 (5.6)	24 (7.4)
R	1 (0.3)	2 (0.7)	1 (0.3)
S	12 (3.4)	13 (4.3)	20 (6.2)
E	10 (2.8)	9 (3.0)	15 (4.6)
MDR-TB	5 (1.4)	6 (2.0)	2 (0.6)
HR	0	1 (0.3)	0
HRE	0	2 (0.7)	0
HRS	0	1 (0.3)	0
HRSE	5 (1.4)	2 (0.7)	2 (0.6)
Other FLD resistance patterns			
Total	13 (3.7)	12 (4.2)	31 (9.5)
HE	5 (1.4)	1 (0.3)	4 (1.2)
HS	5 (1.4)	7 (2.3)	15 (4.6)
HSE	2 (0.6)	2 (0.7)	8 (2.5)
RS	0	0	2 (0.6)
SE	1 (0.3)	2 (0.7)	2 (0.6)

FLD = first-line drugs; TB = tuberculosis; H = isoniazid; R = rifampicin; S = streptomycin; E = ethambutol; MDR-TB = multidrug-resistant TB.

Association between multidrug-resistant tuberculosis, any isoniazid resistance and baseline patient characteristics

Of the 18 MDR-TB patients detected in the three surveys, 13 were male, 11 were HIV-infected and 9 had had contact with a TB patient in the last 2 years. No statistically significant differences in MDR-TB prevalence were observed between non-HIV- and HIV-infected patients (PR 2.07, 95%CI 0.66–6.45). Baseline patient characteristics associated with any INH resistance are shown in Table 5. After multivariate analysis, TB relapse remained significantly associated with any INH resistance.

DISCUSSION

MDR-TB prevalence was low in the three African regions where the surveys were conducted. No recent nationwide data on anti-tuberculosis drug resistance are available for these three countries for comparison. Official figures for Uganda are based on a subnational survey performed in 1996–1997 that showed an MDR-TB prevalence of 0.5% (95%CI 0.1–1.9).[5] In a recent study performed in Kampala, 1.1% of 473 new cases were MDR-TB.[11] The last published information on drug resistance for Kenya dates from

Table 3 Multidrug and isoniazid resistance among new TB and HIV co-infected patients

	Homa Bay, Kenya (*n* = 221)		Chiradzulu, Malawi (*n* = 203)		West Nile, Uganda (*n* = 78)	
	n (%)	95%CI	*n* (%)	95%CI	*n* (%)	95%CI
MDR-TB	2 (0.9)	0.0–2.1	4 (2.0)	0.0–3.9	1 (1.3)	0.0–3.8
Any INH resistance	19 (8.6)	4.9–12.3	26 (12.8)	8.2–17.4	15 (19.2)	10.5–28.0

TB = tuberculosis; HIV = human immunodeficiency virus; CI = confidence interval; MDR-TB = multidrug-resistant TB; INH = isoniazid.

Table 4 Prevalence of resistance to FLDs among previously treated TB cases

	Homa Bay, Kenya (*n* = 34) *n* (%)	Chiradzulu, Malawi (*n* = 23) *n* (%)	West Nile, Uganda (*n* = 36) *n* (%)
Susceptible to all FLDs	32 (94.1)	17 (73.9)	22 (61.1)
Any resistance to FLDs	2 (5.9)	6 (26.1)	14 (38.9)
H	2 (5.9)	4 (17.4)	12 (33.3)
R	0	3 (13.0)	4 (11.1)
E	0	2 (8.7)	1 (2.8)
S	0	4 (17.4)	5 (13.9)
Monoresistance	2 (5.9)	3 (12.9)	9 (25.0)
H	2 (5.9)	1 (4.3)	8 (22.2)
R	0	1 (4.3)	0
E	0	0	0
S	0	1 (4.3)	1 (2.8)
MDR-TB	0	2 (8.7)	3 (8.4)
HR	0	0	1 (2.8)
HRS	0	0	1 (2.8)
HRSE	0	2 (8.7)	1 (2.8)
Other FLD resistance patterns			
Total	0	1 (4.3)	2 (5.6)
HS	0	1 (4.3)	1 (2.8)
RS	0	0	1 (2.8)

FLD = first-line drugs; TB = tuberculosis; H = isoniazid; R = rifampicin; E = ethambutol; S = streptomycin; MDR-TB = multidrug-resistant TB.

1995, with no MDR-TB among the 445 new cases tested.[6] No national data are available for Malawi, but data from the Karongo District (Northern Malawi) from 1997–1998 report 1.1% MDR-TB among new cases.[12] Compared to other countries in the same region, the results are similar to reports from the United Republic of Tanzania in 2007 (MDR-TB 1.1%, 95%CI 0.4–2.8) and Ethiopia in 2005 (1.6%, 95%CI 0.9–2.7), but are lower than the MDR-TB prevalence among new cases reported in Rwanda in 2005 (3.9%, 95%CI 2.6–5.7) and in Mozambique in 2006 (3.5%, 95%CI 2.5–4.7).[13,14] Despite the limited number of previously treated cases, the proportion of MDR-TB was higher among previously treated cases than among new cases, as expected. No extensively drug-resistant TB cases were detected at any of the sites.

We found no significant association between MDR-TB or INH resistance and HIV infection. Although poorly documented in population-based studies, the association between HIV infection and DR-TB remains controversial in sub-Saharan Africa.[11,15–17] An independent association was reported in the last national drug resistance survey in Swaziland, a

Table 5 Factors associated with isoniazid resistance

		Univariate analysis			Multivariate analysis		
	n/*N* (%)	PR	95%CI	*P* value	Adjusted PR	95%CI	*P* value
Sex							
Male	93/618 (15.1)	Reference			Reference		
Female	47/458 (10.3)	0.68	0.49–0.95	0.023	0.76	0.54–1.06	0.106
Age, years							
⩾45	19/167 (11.4)	Reference			—		
30–44	64/463 (13.8)	1.21	0.75–1.96	0.427	—		
15–29	57/442 (14.8)	1.13	0.70–1.85	0.615	—		
Site							
Chiradzulu, Malawi	37/288 (12.8)	Reference			Reference		
Homa Bay, Kenya	38/351 (10.8)	0.86	0.56–1.31	0.476	1.17	0.76–1.80	0.475
West Nile, Uganda	65/296 (22.0)	1.58	1.09–2.3	0.017	1.78	1.18–2.69	0.006
TB contact							
No	99/809 (12.2)	Reference			—		
Yes	41/260 (15.8)	1.29	0.92–1.80	0.139	—		
HIV status							
Negative	60/424 (14.1)	Reference			Reference		
Positive	69/564 (12.2)	0.86	0.62–1.19	0.376	1.03	0.83–1.28	0.800
TB patient type							
New case	122/983 (12.4)	Reference			Reference		
Relapse	13/60 (21.7)	1.74	1.05–2.90	0.032	1.71	1.03–2.81	0.035
Other previously treated case	5/33 (15.2)	1.22	0.54–2.78	0.635	1.15	0.51–2.60	0.733

PR = prevalence ratio; CI = confidence interval; TB = tuberculosis; HIV = human immunodeficiency virus.

country with very high HIV and DR-TB prevalence.[6] The prevalence of HIV infection in the West Nile region was lower than in the other sites; this difference might affect the incidence of TB in the regions, but is less likely to affect DR-TB prevalence.

Given the low MDR-TB prevalence among new cases, there is no reason to modify the WHO-recommended DOTS-based treatment strategy. In these three MSF-supported programmes, the Xpert® MTB/RIF assay (Cepheid, Sunnyvale, CA, USA) was recently introduced for the detection of *M. tuberculosis*, as recommended by the WHO for high HIV burden regions. This will allow rapid identification of potential MDR-TB.[18] However, the positive predictive value of the Xpert MTB/RIF assay for detecting RMP resistance in populations with a low risk of MDR-TB is relatively low. In regions with low MDR-TB prevalence, any case of RMP resistance should therefore be further confirmed using DST.[18]

On the other hand, in these three regions, ⩾10% of the new cases were resistant to INH, with a significantly higher prevalence in the West Nile region than in the other two sites. We have no explanation for this difference; it is very unlikely to be due to the misuse of INH preventive therapy (IPT), which has not been systematically proposed for paediatric contacts and had not been introduced for HIV-infected individuals in any of the studied sites at the time of the surveys. The prevalence of INH resistance is higher than that reported by former Kenyan (7.3%) and Ugandan national surveys (6.7%), and was similar (16%) to previous reports in another district of Malawi (Karonga) in 1997–1998.[5,6,15] Using the standard 6-month treatment regimen, one in 10 new cases would receive RMP monotherapy during the continuation phase, with the potential risk of acquiring RMP resistance. These patients would benefit from rapid DST for INH resistance to initiate effective treatment and prevent the additional acquisition of RMP resistance.[19] Unfortunately, rapid testing of INH resistance is not available at regional- or district-level health facilities in resource-limited countries. Furthermore, the optimal regimen for the treatment of INH-resistant strains has not yet been determined, and the WHO-recommended 9-month RZE regimen was associated with poor outcomes in a recent large retrospective study in Georgia.[20,21] Since 2010, the WHO has recommended using HRE in the continuation phase of treatment among new cases in populations with known or suspected high levels of INH resistance.[22] Nonetheless, it remains unclear if these recommendations would also apply to settings with 10% primary INH resistance.

If the results of the surveys reflect the overall patterns of resistance of *M. tuberculosis* strains circulating in the three regions, IPT may be ineffective in about 10% of HIV-positive patients and more than 20% of relapsed TB cases. Nevertheless, the majority of HIV-infected persons in these regions would still benefit.

The study had some limitations. Due to the low proportion of previously treated cases among newly diagnosed TB patients in the three sites, the sample size was not sufficiently powered to measure MDR-TB prevalence in previously treated cases, and as a result of the low number of MDR-TB cases detected, the statistical power was not enough to identify factors associated with a high risk of MDR-TB. In the absence of recent resistance data in the three countries, sample size estimation was based on an overestimation of the prevalence of RMP resistance in new cases (5%), which resulted in a reduction of precision compared to estimates (2.5%).

In conclusion, this survey reports low MDR-TB prevalence among new cases in three high HIV burden regions of Eastern Africa. The relatively high rate of INH resistance highlights the need for rapid detection of INH resistance in addition to RMP resistance, which could be used at peripheral levels to allow rapid modification of the treatment regimen and avert the acquisition of RMP resistance. As the laboratory capacity is inadequate for the introduction of a drug resistance surveillance system, drug resistance should be monitored using periodic surveys, ideally at country level.

Acknowledgement

This study was funded by Médecins Sans Frontières, Paris, France.
Conflict of interest: none declared.

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RÉSUMÉ

CADRE : Bien que des progrès importants aient été réalisés dans la surveillance de la résistance aux antituberculeux, des données manquent toujours dans de nombreux pays à faibles ressources. Selon les estimations de l'Organisation Mondiale de Santé la prévalence de la tuberculose multirésistante (TB-MDR) en Afrique est faible, mais elles ne sont basées que sur quelques données du continent africain.

OBJECTIF : Mesurer la prévalence de la TB-MDR dans trois régions africaines subsahariennes avec une prévalence élevée du virus de l'immunodeficience humaine (VIH).

MÉTHODE : Nous avons mené trois enquêtes de résistance aux antituberculeux dans des régions d'Homa Bay (Kenya), de Chriradzulu (Malawi) et du West Nile (Ouganda) qui ont une prévalence élevée de TB-VIH.

RÉSULTATS : La prévalence de la TB-MDR chez les nouveaux cas de TB est faible dans ces trois régions : 1,4% (95%IC 0,2–2,6) à Homa Bay, 2,0% (95%IC 0,4–3,6) à Chiradzulu et 0,6% (95%IC 0–1,5) dans la région du West Nile. Nous n'avons pas trouvé d'association significative entre la TB-MDR et l'infection due au VIH. Par contre, ⩾10% des nouveaux cas de TB enquêtés étaient résistants à l'isoniazide (INH).

CONCLUSION : La prévalence relativement élevée de la résistance à l'INH confirment les besoins d'une détection rapide de la résistance à l'INH en complément de la résistance à la rifampicine (RMP), afin de pouvoir adapter le traitement et réduire les risques d'amplification de la résistance à la RMP. Un monitoring régulier de la résistance aux antituberculeux est nécessaire.

RESUMEN

MARCO DE REFERENCIA: A pesar del reciente progreso en la vigilancia de la tuberculosis (TB) drogorresistente, seguimos sin conocer los niveles de resistencia en gran parte de los países en vías de desarrollo. La Organización Mundial de la Salud (OMS) estima que los niveles de TB multidrogorresistente (TB-MDR) en el continente africano son bajos, sin embargo estas estimaciones se basan en escasos datos de unos pocos países.

OBJETIVOS: Medir la prevalencia de TB-MDR en regiones del África sub-sahariana con altas tasas de co-infección con el virus de inmunodeficiencia humana (VIH).

METODO: Llevamos a cabo tres estudios transversales en tres regiones del África sub-sahariana con alta prevalencia de co-infección VIH-TB: Homa Bay (Kenia), Chiradzulu (Malawi) y la región de West Nile (Uganda).

RESULTADOS: La prevalencia de TB-MDR fue baja en las tres regiones estudiadas: 1,4% (IC95% 0,2–2,6) en Homa Bay, 2,0% (IC95% 0,4–3,6) en Chiradzulu y 0,6% (IC95% 0,0–1,5) en la región de West Nile. Sin embargo, ⩾10% de los pacientes nuevos eran resistentes a la isoniacida (INH). No se encontró asociación entre la infección por el VIH y la TB-MDR.

CONCLUSION: La relativamente alta prevalencia de resistencia a la INH subraya la necesidad de detectar rápidamente resistencia a INH, en combinación con la resistencia a la rifampicina (RMP), para poder adaptar el tratamiento lo antes posible y disminuir el riesgo de adquisición de resistencia a la RMP. Los niveles de resistencia en estos países deberían medirse de manera sistemática.