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Patterns of anti-tuberculosis drug resistance among HIV-infected patients in Maputo, Mozambique, 2002–2003

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SUMMARY

SETTING: Two tuberculosis (TB) reference hospitals in Maputo, Mozambique.

OBJECTIVES: To assess the pattern of TB drug resistance and its risk factors in human immunodeficiency virus (HIV) patients.

DESIGN: Adult HIV-positive patients with TB diagnosed by culture of sputum or bronchial washing were enrolled during 2002–2003. Cultures of 111 patients were tested for rifampicin, isoniazid, streptomycin and ethambutol sensitivity. Chest X-ray, haemoglobin (Hb), total lymphocyte and CD4 counts were also performed.

RESULTS: Overall resistance to any drugs was found in 18% and multidrug-resistant TB (MDR-TB) in 9%. New cases of TB accounted for 62% of the studied group. Drug resistance in this subgroup was 13% compared with 26.3% in the previously treated subgroup, and MDR-TB was 5.8% vs. 15.8%. All patients presented Hb levels <9 g/dl and total lymphocyte counts <1200/μl. CD4 counts were significantly low in the drug resistance subgroup, with levels mostly <100/μl. Cavities on X-ray were seen only in drug-sensitive patients. No risk factors for drug resistance were detected.

CONCLUSIONS: Overall observed drug resistance was 18%, and MDR-TB 9%. Previously treated patients had high drug resistance (26.3%) and MDR-TB (15.8%).

KEY WORDS: tuberculosis; HIV; drug resistance; multidrug resistance; resistance pattern

DRUG-RESISTANT TUBERCULOSIS (TB) was a well-recognised problem even before the beginning of TB control programmes in the late 1970s and early 1980s. Drug resistance emerges through selection of mutant strains in treatment regimens that use inefficient drug combinations or in poor adherence to treatment. Deficient treatment supervision adds to these causes. The rate of drug resistance is therefore used to assess the effectiveness of national TB control programmes. According to the World Health Organization/International Union Against Tuberculosis and Lung Disease (IUATLD) Global Project on Anti-tuberculosis Drug Resistance Surveillance Report, approximately 50 million people are infected with drug-resistant TB strains.[1] The report refers to 13 countries where drug resistance varies from 6.3% to 24.8% and multidrug-resistant TB (MDR-TB, defined as resistance to at least isoniazid [H, INH] and rifampicin [R, RMP]) from 1% to 5.3%.[1] A 2003 WHO report presents data from 24 settings in 17 countries where the range of any resistance among new cases is 3.25–24.7% and for MDR-TB it is 0–5.3%.[2] In sub-Saharan Africa, two problems must be addressed regarding TB control: the high incidence of acquired immunedeficiency syndrome (AIDS) with high levels of human immunodeficiency virus (HIV) infection, and the increase in drug resistance, although it is still below that of some non-African countries.[3,4]

Mozambique has a population of 18 644 433. The TB prevalence rate is 265 per 100 000 population, with 48% of TB patients co-infected by HIV. The prevalence of HIV infection is 16%.[2] The National Tuberculosis Control Programme (NTCP) was launched in 1977, providing guidelines and standard drug regimens for the whole country. In 1984, the DOTS strategy was adopted for new TB cases, prescribing 2SRHZ/6TH.* In 2000, TH was replaced by EH due

* Z = pyrazinamide; E = ethambutol; S = streptomycin; T = thioacetazone. Numbers before the letters indicate the duration in months of the phase of treatment; numbers in subscript indicate the number of times the drug is taken each week.

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to the high level of adverse reactions observed mainly in HIV-infected patients.[4] In 2002, S was withdrawn, and the standard regimen adopted since then is 2RHZE/6EH for new cases, and 1SRHZE/2RHZE/5RH_3E_3 for retreatment cases. DOTS covers 100% of patients, but only 45% of the population has access to TB diagnosis. Daily EH is given indefinitely to patients who are persistently smear-positive after completing treatment with both regimens, due to the impossibility of providing nationwide cover for MDR-TB specific treatment.[5] From 2002 to 2003, the total number of TB cases increased by 15%, and MDR-TB by 3%.[5]

HIV-infected patients tend to show different clinical and radiological forms of TB, with low bacillary burden and frequent negative smear microscopy.[6] The present study assessed the pattern and extent of drug-resistant TB among HIV-infected patients in Maputo.

STUDIED POPULATION AND METHODS

Patient selection

From October 2002 to September 2003, a group of 111 HIV-infected patients with pulmonary TB was enrolled based on the following inclusion and exclusion criteria.

Inclusion criteria were: HIV-infected patients confirmed by two rapid and one enzyme-linked immunosorbent assay (ELISA) tests, age ⩾11 years, of either sex, with TB confirmed by two positive sputum smears or bronchial lavage samples, or smear-negative but presenting clinical and radiological alterations suggestive of TB.

Exclusion criteria were: patients with extra-pulmonary TB, diabetes or chronic renal failure, immunosuppressive therapy, pregnant women, >1 week of TB treatment or under antiretroviral therapy for AIDS.

Patients were part of a larger ongoing study on the prevalence of non-tuberculous mycobacteria in HIV patients recruited in two TB reference public hospitals in Maputo—the Hospital Central de Maputo (HCM), a university hospital to which difficult cases are referred, and Hospital Geral de Machava (HGM), where all chronic TB cases and those not eligible for ambulatory DOTS are hospitalised and treated. In both hospitals the only TB infection control procedure is to perform sputum smear examination as soon as possible (within 24 h), start anti-tuberculosis treatment and refer smear-positive patients as soon as possible for ambulatory DOTS.

Interviews were conducted just after enrolment, and patients were questioned about occupational, family, illness and past TB treatment history. A standardised protocol for clinical, laboratory and radiological evaluations was adopted. According to the Helsinki declaration, the ethics committees of the institutions approved the study protocol, and all patients provided written informed consent.

Sputum smear microscopy and culture

Sputum and bronchial lavage samples were processed by Ziehl-Neelsen stain, and then by fuchsin or auramine. Samples were sent immediately to the Laboratório Nacional de Referência de Tuberculose (LNRT), or kept refrigerated at 4°C and sent later.

Culture of sputum or bronchial lavage samples was performed in all cases. Löwenstein-Jensen and Stonebrink culture media were used simultaneously. *Mycobacterium tuberculosis* colonies usually develop in 21–27 days. Results were expressed in number of colonies observed per culture tube.

Susceptibility testing

Culture and drug sensitivity testing were performed at the LNRT following WHO/IUATLD guidelines.[7] The LNRT participates in an internationally quality assurance programme with the National Institute of Public Health, Norway.

Resistance to INH, SM, RMP and EMB was tested using cultures impregnated with these drugs. The criterion for resistance to a particular drug, defined by the LNRT, is growth of less than 20 colonies on medium containing the minimum inhibitory concentration of the drug. A resistance ratio (RR) is then provided by dividing the test strain MIC by the wild strain MIC. Drug resistance was defined in three categories: sensitive strain (RR < 4); doubtful (RR = 4); resistant strain (RR > 4). All positive cultures were tested against the following drug concentrations, in μg/ml: INH (0.025, 0.05, 0.1, 0.2 and 1); RMP (4.0, 8.0, 16.0 and 64); SM (2.0, 4.0, 8.0, 16.0 and 32); and EMB (1.0, 2.0, 4.0, 8.0 and 16.0).

Bronchial washing

All smear-negative patients were submitted to flexible fiberoptic bronchoscopy for bronchial lavage, after consent. Lidocaine was used for local anaesthesia. The sample was obtained after instillation of 5 ml saline in the most affected segmental or lobar bronchi.

HIV testing

A blood sample was collected for HIV testing after formal consent had been obtained and patients had been reassured about strict confidentiality of results. HIV-positive cases were then sent for counselling and specialised follow-up.

Two rapid immunochromatographic tests for HIV1 and HIV2 were performed: Unigold™ test (Trinity Biochem, Dublin, Ireland), with a sensitivity of 99.5% and specificity of 100%,[8] and Determine Abbott™ (Abbott Diagnostics, Abbott Park, IL, USA), with a sensitivity of 100% and specificity of 99.5%.[8] ELISA confirmed positive results of both tests.

Drug resistance definition

Current concepts of TB drug resistance were recently revised by the WHO.[1] Two categories were defined:

drug resistance among new cases (formerly 'primary drug resistance'), defined as the presence of resistant strains of *M. tuberculosis* in a newly diagnosed patient who has never received TB drugs, or has received them for less than 1 month; and drug resistance among previously treated cases (formerly 'acquired drug resistance'), defined as resistance found in a patient who has previously received at least 1 month of TB treatment.

Data analysis

Data were entered using Access™ (Microsoft Corp, Redmond, WA, USA) and analysed using Stata Intercooled™ 8.2 (Stata Corp, College Station, TX, USA). Data were split into two subgroups: patients with sensitive strains and those with resistant strains. Categorical variables were compared using the χ^2 test, and univariate analysis was performed to describe risk factors for resistance or sensitivity, expressing the results as odds ratios (OR) and 95% confidence intervals (CI). For all analyses a significance level of 0.05 was adopted.

RESULTS

A total of 111 HIV-infected patients were selected. Table 1 summarises the demographic information obtained. Overall, 32.4% of the 111 culture-positive patients were smear-negative. Similar distributions were observed in drug-sensitive and drug-resistant subgroups.

Table 2 summarises the resistance patterns among the 111 patients. Ninety-one (82%) strains showed sensitivity to all tested drugs, and 20 (18%) showed resistance to at least one drug. MDR-TB was seen in 10 cases (9%), and resistance to any drug was detected in nine new cases (13%). The most common kind of resistance among new cases was to SM (11.6%), followed by INH (8.7%), and RMP (5.8%). Resistance to only one drug was to SM (4.3%) and to INH (1.4%). Among previously treated cases, resistance to INH was the most common (26.3%), followed by RMP (15.8%) and to SM (10.5%). Resistance to only one drug was found only to INH in 5.5% of the cases.

Resistance to the drug combination SRHE was observed in only two new cases (2.9%). Resistance to EMB in isolated form was not found (Table 2).

Factors associated with resistance

No significant differences were found regarding most of the variables tested in the univariate analysis (Table 3). Nevertheless, low CD4 levels and Class III performance status were associated with drug resistance (Tables 4 and 5).

Clinical, laboratory and radiological alterations

All patients presented weight loss and fever during the period of disease; 82.9% presented cough, 66.7% chest pain, 59.5% dyspnoea and 38.7% diarrhoea (Table 4). Patients were classified into four clinical groups: Class 1, asymptomatic; Class II, symptomatic <50% of the day; Class III, symptomatic >50% of the day; Class IV, in bed most of the time. Class III patients were significantly more frequent in the drug-resistant subgroup than in the drug-sensitive subgroup ($P = 0.01$). Radiological alterations were similar in both subgroups, although cavities were seen only in patients with sensitive strains (two patients) (Table 4).

Table 1 Demographic characteristics of the 111 patients enrolled in the study

Variable	Median	IQR	*n* (%)
Age, years			
Whole group	33	26–42	—
Males	34	26–41	—
Females	32	24–42	—
Sex			
Masculine			67 (60)
Feminine			44 (40)
Race			
Black			101 (91)
Caucasian			9 (8)
Indian			1 (1)
Province			
Maputo			102 (92)
Gaza			4 (4)
Others			5 (5)

IQR = interquartile range.

Table 2 Patterns of resistance in the 111 studied patients

	Previously treated cases *n* (%)	New cases *n* (%)	Without information* *n* (%)	Total *n* (%)
Whole studied group	38 (100)	69 (100)	4 (100)	111 (100)
Sensitive to all drugs	28 (73.7)	60 (87.0)	3 (75.0)	91 (82.0)
Resistant to any drug	10 (26.3)	9 (13.0)	1 (25.0)	20 (18.0)
H	10 (26.3)	6 (8.7)	0 (0.0)	16 (14.4)
S	4 (10.5)	8 (11.6)	1 (25.0)	13 (11.7)
R	6 (15.8)	4 (5.8)	0 (0.0)	10 (9.0)
E	1 (2.6)	2 (2.9)	0 (0.0)	3 (2.7)
Resistant to only one drug	2 (5.3)	4 (5.8)	1 (25.0)	7 (6.3)
H	2 (5.3)	1 (1.4)	0 (0.0)	3 (2.7)
S	0 (0.0)	3 (4.3)	1 (25.0)	4 (3.6)
R	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
E	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Resistant to two drugs	5 (13.2)	1 (1.4)	0 (0.0)	6 (5.4)
HR	3 (7.9)	0 (0.0)	0 (0.0)	3 (2.7)
HS	2 (5.3)	1 (1.4)	0 (0.0)	3 (2.7)
Resistant to three drugs	3 (7.9)	2 (2.9)	0 (0.0)	5 (4.5)
HRS	2 (5.3)	2 (2.9)	0 (0.0)	4 (3.6)
HRE	1 (2.6)	0 (0.0)	0 (0.0)	1 (0.9)
Resistant to four drugs	0 (0.0)	2 (2.9)	0 (0.0)	2 (1.8)
HRSE	0 (0.0)	2 (2.9)	0 (0.0)	2 (1.8)
MDR-TB	6 (15.8)	4 (5.8)	0 (0.0)	10 (9.0)

* Lack of information regarding treatment status (new or previously treated cases).
H = isoniazid; R = rifampicin; S = streptomycin; E = ethambutol; MDR-TB = multidrug-resistant tuberculosis (to at least H+R).

Table 3 Univariate analysis results regarding variables supposed to be related to increased risk for TB drug resistance

Variable	Drug-resistant *n* (%)	Drug-sensitive *n* (%)	Total *n* (%)	OR	95%CI	*P*
Sex						
Male	11 (55)	56 (61.5)	67 (60.4)	1.0		
Female	9 (45)	35 (38.5)	44 (39.6)	1.3	0.5–3.5	0.59
Age, years						
<25	3 (16.7)	16 (18.6)	19 (18.3)	1.0		
25–34	8 (44.4)	33 (38.4)	41 (39.4)	1.3	0.3–5.6	0.73
35–44	2 (11.1)	20 (23.3)	22 (21.2)	0.5	0.1–3.7	0.52
⩾45	5 (27.8)	17 (19.8)	22 (21.2)	1.6	0.3–7.8	0.58
Previous treatment for TB						
No	9 (47.4)	60 (68.2)	69 (64.5)	1.0		
Yes	10 (52.6)	28 (31.8)	38 (35.5)	2.4	0.9–6.6	0.20
Contact with TB patient	19	91	110			
No	6 (31.6)	16 (17.6)	22 (20.0)	1.0		
Yes	5 (26.3)	21 (23.1)	26 (23.6)	0.4	0.2–2.5	0.51
Unknown	8 (42.1)	54 (59.3)	62 (56.4)	2.4	0.1–1.3	0.12
Past BCG vaccination	20	91	111			
No	2 (10.0)	7 (7.7)	9 (8.1)	1.0		
Yes	18 (90.0)	84 (92.3)	102 (91.9)	0.8	0.1–4	0.73
Mining work	11	55	66			
No	9 (81.8)	46 (83.6)	55 (83.3)	1.0		
Yes	2 (18.2)	9 (16.4)	11 (16.7)	1.1	0.2–6.2	0.90

TB = tuberculosis; OR = odds ratio; CI = confidence interval; BCG = bacille Calmette-Guérin.

Table 4 Distribution of clinical and radiological alterations in the 111 studied patients

Variable	Drug-resistant *n* (%)	Drug-sensitive *n* (%)	Total *n* (%)	OR	95%CI	*P*	*P**
Fever	20 (100)	91 (100)	111 (100)				
Weight loss	20 (100)	91 (100)	111 (100)				
Cough							
No	4 (20)	15 (16.5)	19 (17.1)				
Yes	16 (80)	76 (83.5)	92 (82.9)	0.79	0.2–2.7	0.71	
Chest pain							
No	10 (50)	26 (28.6)	36 (32.4)				
Yes	10 (50)	64 (70.3)	74 (66.7)	0.41	0.15–1.11	0.17	
Unknown	0 (0)	1 (1.1)	1 (0.9)				
External adenopathy	20	91	111				
No	13 (65.0)	56 (61.5)	69 (62.2)	1.0			
Yes	7 (35.0)	35 (38.5)	42 (37.8)	0.9	0.3–2.4	0.77	
Diarrhoea	20	91	111				
No	9 (45.0)	58 (63.7)	67 (60.4)	1.0			
Yes	11 (55.0)	32 (35.2)	43 (38.7)	2.2	0.8–6.0	0.25	
Unknown	0 (0.0)	1 (1.1)	1 (0.9)				
Dyspnoea	20	91	111				
No	5 (25.0)	38 (41.8)	43 (38.7)	1.0			
Yes	15 (75.0)	51 (56.0)	66 (59.5)	2.2	0.7–6.8	0.27	
Unknown	0 (0.0)	2 (2.2)	2 (1.8)				
Status performance	20	91	111				
Class I	8 (40.0)	53 (58.2)	61 (55.0)	1.0			
Class II	5 (25.0)	28 (30.8)	33 (29.7)	1.2	0.4–4.0	0.02	
Class III	7 (35.0)	8 (8.8)	15 (13.5)	5.8	1.5–22.2	0.02	0.01
Lacking information	0 (0.0)	2 (2.2)	2 (1.8)				
Radiological signs							
Interstitial	12 (60)	54 (59)	66 (59)	0.9	0.3–2.3	0.48	
Miliary	11 (55)	47 (52)	58 (52)	1.3	0.3–7	0.73	
Thoracic lymphadenopathy	9 (45)	40 (44)	49 (44)	1.0	0.4–2.8	0.93	
Bronchiectasis	5 (25)	25 (27)	30 (27)	0.9	0.29–2.7	0.82	
Cavity	0 (0)	2 (2)	2 (1.8)				
Bilateral	17 (89.5)	78 (88.6)	95 (88.8)	1.1	0.2–5.5	0.91	
Unilateral	2 (10.5)	10 (11.4)	12 (11.2)				

* χ^2 test for OR trend.
OR = odds ratio; CI = confidence interval.

Table 5 Laboratory parameters in the two subgroups of drug-resistant and drug-sensitive patients

	Drug-resistant			Drug-sensitive			
Variable	Median	Q1	Q3	Median	Q1	Q3	*P**
Haemoglobin g/dl	8.1	5.6	10.5	7.8	6.4	9.1	0.72
Leukocytes/μl	5100	2400	10 800	5500	4600	9400	0.20
Lymphocytes/μl	1065	756	2 008	1180	700	1800	0.96
CD4/μl	83	40	212	176	75	373	0.02†

* Mann-Whitney test.
† Significant.
Q = quarter.

Laboratory results showed no significant differences in median haemoglobin levels, leukocyte or lymphocyte count between drug-sensitive and drug-resistant patients (Table 5). Significant differences were found only in CD4 levels between subgroups ($P < 0.02$), with drug-resistant patients predominantly showing results <100/μl and none with CD4 >500/μl (Figure).

DISCUSSION

In Mozambique the incidence of TB and HIV infection has increased markedly in recent years, despite the efficiency of the NTCP, which is wholly DOTS-based. This could be explained by the social and economic difficulties during the civil war period, and the spread of HIV in recent decades.[4] Mac-Arthur et al. were the first to provide information on TB drug resistance among previously treated HIV-positive cases in the country, finding 24% resistance to any drug and 2.2% MDR-TB.[9]

The present study provides updated information using a selected group of HIV-positive TB patients in Maputo, all with a positive culture for *M. tuberculosis*; 82% had sensitive strains and 18% resistant strains.

The frequency of smear-negative and culture-positive patients was 32.4%, mainly in the drug-sensitive subgroup, indicating a considerable problem for most of the health centres in the country, where TB diagnosis is mainly based on sputum smear investigation. Diagnostic difficulties are increased in the case of HIV-infected patients with paucibacillary forms of TB. This frequency of false-negative smears seems to be variable. Githui et al. found 11% false-negative smears in HIV-infected patients and a similar frequency in HIV-negative TB patients.[10] In Zambia, 40% of HIV-infected patients with culture-positive TB had negative smears.[7] Mac-Arthur et al. found 49% false negatives, and in Ethiopia the frequency was 50%.[9,11] The prognosis for such patients is poor, and they are prone to present atypical forms of TB.

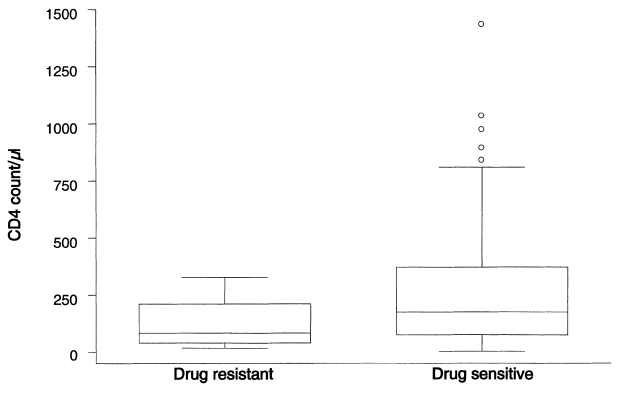

Figure Box plot of CD4 counts in both subgroups.

Resistance to any drug in new TB cases was 13% (9/69), with 11.6% for SM, 8.7% for INH and 5.8% for RMP. SM and INH are the drugs most commonly used in recent decades by the NTCP, which probably explains part of the resistance rate, similar to many other African countries.[1,12–15] MDR-TB among our patients was 5.8%, whereas Mac-Arthur et al. found an overall frequency of 3.5%.[9] High levels of drug resistance in new cases of TB could be explained by the rapid progression of TB infection to active disease, associated with a high risk of exposure to resistant strains due to NTCP failure.[16,17]

In the present study, resistant strains occurred mostly in previously treated cases (26.3% vs. 13% in new cases) and MDR-TB strains (15.8% vs. 5.8%). No resistance to EMB was found. Resistance in previously treated cases could be partially attributed to the deficient infection control measures for TB in the two hospitals studied, mainly in the HGM, where the mean period of hospitalisation is 2 months.

Drug resistance frequency in previously treated cases (26.3%) was rather similar to other African countries, i.e., 22% in the Republic of South Africa (8% MDR-TB);[1] 18.3% in Malawi[18] (0.5% MDR-TB); 22.8% in Botswana (0.5% MDR-TB).[16] We found a higher frequency of MDR-TB in previously treated cases (15.8%) than the 2.2% found by MacArthur et al.,[9] probably due to selection bias.

A significant association was found between Class III performance status, low CD4 levels and drug resistance. Other studies found that history of previous TB treatment, age, sex and mining work were risk factors for drug resistance.[15,16,19,20]

Class III performance status must be dependently associated with lower levels of CD4 lymphocytes seen in drug-resistant than drug-sensitive patients. That difference was statistically significant for counts $<100/\mu l$ ($P < 0.02$). HIV patients with TB have a reduced enrichment and activation of immune cells in the lung, reducing $CD4^+$ alveolitis as an effective immune response to acid-fast bacilli,[21] explaining the more severe TB cases, the need for retreatment and probably the high frequency of drug resistance in low CD4 level patients.

The median total lymphocyte count was <1200 in both subgroups. According to some authors, total lymphocyte numbers can predict disease progression.[22] An interesting finding is that none of the drug-resistant patients presented CD4 counts $>500/\mu l$.

No statistical association was found between haemoglobin levels and drug resistance status, which were low in both subgroups of patients (<9 g/dl). This may be explained by the high prevalence of malaria and chronic parasitic infestations.[23–25] A recent study proposed using an index built up by a combination of total lymphocyte count and haemoglobin level as a criteria for starting antiretroviral therapy in HIV-infected patients.[22] This index will need to be validated for populations where chronically low haemoglobin levels are regularly found.

Radiological alterations were similar in both subgroups, although cavities were seen more frequently in patients with elevated CD4 counts associated with drug sensitivity status.

CONCLUSIONS

Overall resistance and MDR-TB in HIV-infected patients were high in this study. MDR-TB was associated with CD4 levels $<100/\mu l$. Simple resistance to SM and INH is probably due to their extensive use in the NTCP in the last two decades.

Our results can not be generalised to the whole country, nor for all HIV patients with TB, due to a possible selection bias. We selected patients in reference hospitals to which most complicated cases are referred, and where patients may come into contact with MDR-TB-infected patients during diagnosis and treatment. Nevertheless, the data on resistance shown here represent a pattern of HIV-TB patients seeking treatment in hospitals in Mozambique, indicating a need to implement hospital-based TB infection control programmes and an MDR-TB treatment programme. There is also need for better epidemiological surveillance, strict enforcement of DOTS and coordination between the AIDS and TB control programmes.

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RÉSUMÉ

CONTEXTE : Deux hôpitaux de référence pour la tuberculose (TB) à Maputo, Mozambique.
OBJECTIFS : Evaluer le type de résistance aux médicaments antituberculeux ainsi que ses facteurs de risque chez les patients infectés par le virus de l'immunodéficience humaine (VIH).
SCHÉMA : Les patients adultes séropositifs pour le VIH et atteints d'une TB confirmée par la culture des expectorations ou des produits de lavage bronchique ont été enrôlés en 2002–2003. Les cultures provenant de 111 patients ont été testées pour leur sensibilités à la rifampicine, l'isoniazide, la streptomycine et l'éthambutol. On a pratiqué en outre un cliché thoracique, un dosage de l'hémoglobine, et un décompte des lymphocytes totaux et des CD4.
RÉSULTATS : On a observé un taux global de résistance à l'égard de n'importe quel médicament de 18% et un taux de TB multirésistante TB-MR de 9%. Les nouveaux cas de TB représentaient 62% du groupe étudié. Dans ce sous-groupe, la résistance aux médicaments est de 13% par comparaison avec 26,3% dans le sous-groupe traité préalablement, et respectivement de 5,8% contre 15,8% pour la TB-MR. Chez tous les patients, les niveaux d'Hb étaient inférieurs à 9 g/dl et le décompte de lymphocytes totaux inférieur à 1200/μl. Les décomptes de CD4 s'avéraient significativement abaissés dans le sous-groupe résistant aux médicaments, les niveaux étant la plupart du temps inférieurs à 100/μl. On n'a mis en évidence des cavités aux clichés thoraciques que chez les patients sensibles aux médicaments. On n'a pas pu déceler de facteurs de risque pour la résistance aux médicaments.
CONCLUSIONS : Une résistance globale à l'égard de n'importe quel médicament a été de 18% et la TB-MR de 9%. Le sous-groupe traité préalablement est celui où l'on observe la plus haute résistance aux médicaments (26,3%) et le plus haut taux de TB-MR (15,8%).

RESUMEN

MARCO DE REFERENCIA : Estudio realizado en dos hospitales de referencia para tuberculosis (TB) en Maputo, Mozambique.
OBJETIVOS : Evaluar las características de la TB farmacorresistente y sus factores de riesgo en pacientes infectados por el virus de la inmunodeficiencia humana (VIH).
MÉTODO : Durante 2002 y 2003 se incluyeron en el estudio adultos con serología VIH positiva y TB diagnosticada mediante cultivo del esputo o del lavado bronquial. Se estudió la sensibilidad a rifampicina, isoniacida, streptomicina y etambutol de los cultivos de 111 pacientes. También se analizaron la radiografía de tórax, la hemoglobina y el recuento total de linfocitos y de CD4.
RESULTADOS : Se observó una resistencia global a cualquier medicamento en el 18% de los pacientes y TB con multidrogorresistente (TB-MDR) en el 9%. Los casos nuevos de TB constituyeron el 62% del grupo estudiado. La resistencia a los medicamentos observada en este subgrupo fue del 13%, comparada con el 26,3% en el grupo de pacientes con tratamiento previo ; la tasa de TB-MDR fue del 5,8% y del 15,8%, respectivamente. Todos los pacientes presentaron una concentración de hemoglobina por debajo de 9 g/dl y un recuento total de linfocitos inferior a 1200/μl. El recuento de CD4 fue significativamente bajo en el subgrupo con farmacorresistencia, con valores generalmente inferiores a 100/μl. Sólo se observaron cavernas en la placa de tórax de pacientes con TB farmacosensible. No se detectaron factores de riesgo de farmacorresistencia.
CONCLUSIONES : La farmacorresistencia global observada fue del 18% y la TB-MDR del 9%. El subgrupo de pacientes con tratamiento antituberculoso previo tuvo un alto índice de farmacorresistencia (26,3%) y de TB-MDR (15,8%).