Original Article

Mycobacterium tuberculosis and nontuberculous mycobacterial isolates among patients with recent HIV infection in Mozambique*,**

Doença pulmonar por *Mycobacterium tuberculosis* e micobactérias não-tuberculosas entre pacientes recém-diagnosticados como HIV positivos em Moçambique, África

Elizabete Abrantes Nunes[1], Eduardo Mello De Capitani[2], Elizabete Coelho[3], Alessandra Costa Panunto[4], Orvalho Augusto Joaquim[5], Marcelo de Carvalho Ramos[6]

Abstract

Objective: Mycobacteriosis is frequently diagnosed among HIV-infected patients. In Mozambique, where few patients are under antiretroviral therapy and the prevalence of tuberculosis is high, there is need for better characterization of mycobacteria at the species level, as well as for the identification of patterns of resistance to antituberculous drugs. **Methods:** We studied a sample of 503 HIV-infected individuals suspected of having pulmonary tuberculosis. Of those 503, 320 tested positive for mycobacteria through sputum smear microscopy or culture of bronchoalveolar lavage fluid. **Results:** Acid-fast bacilli were observed in the sputum of 73% of the individuals presenting positive cultures. Of 277 isolates tested, only 3 were nontuberculous mycobacteria: 2 were identified as *Mycobacterium avium* and one was identified as *M. simiae*. Strains initially characterized as *M. tuberculosis* complex through polymerase chain reaction restriction analysis (PRA) of the hsp65 gene were later confirmed as such through PRA of the gyrB gene. Among the M. tuberculosis isolates, resistance patterns were as follows: to isoniazid, 14%; to rifampin, 6%; and multidrug resistance, 5%. Previously treated cases showed significantly higher rates of resistance to first-line antituberculous drugs. The most common radiological pattern was interstitial infiltrate (in 67%), followed by mediastinal lymph node enlargement (in 30%), bronchiectasis (in 28%), miliary nodules (in 18%) and cavitation (in 12%). Patients infected with nontuberculous mycobacteria presented clinical profiles indistinguishable from those of other patients. The median CD4 lymphocyte count in this group was 134 cells/mm^3. **Conclusions:** There is a strong association between tuberculosis and AIDS in Mozambique, as expected in a country with a high prevalence of tuberculosis. Although drug resistance rates are high, the isoniazid-rifampin regimen continues to be the appropriate choice for initial therapy.

Keywords: Tuberculosis; Mycobacteria, atypical; HIV; Acquired immunodeficiency syndrome; Drug Resistance, Multiple; Mozambique.

Resumo

Objetivo: A micobacteriose é frequentemente diagnosticada entre pacientes infectados pelo HIV. Em Moçambique, onde apenas um pequeno número de pacientes encontra-se sob tratamento anti-retroviral, e a tuberculose tem alta prevalência, existe a necessidade de melhor caracterização destes agentes bacterianos, em nível de espécie, bem como de se caracterizar os padrões de resistência às drogas antituberculosas. **Métodos:** Em uma coorte de 503 indivíduos HIV positivos suspeitos de tuberculose pulmonar, 320 apresentaram positividade para baciloscopia ou cultura no escarro e no lavado brônquico. **Resultados:** Bacilos álcool-ácido resistentes foram detectados no escarro em 73% dos casos com cultura positiva. De 277 isolados em cultura, apenas 3 mostraram-se tratar de micobactérias não-tuberculosas: 2 *Mycobacterium avium* e uma *M. simiae*. Todos os isolados de *M. tuberculosis* inicialmente caracterizados através de reação em cadeia de polimerase (RCP) do gene hsp65 foram posteriormente caracterizados como tal através de RCP do gene gyrB. Resistência à isoniazida foi encontrada em 14% dos casos; à rifampicina em 6%; e multirresistência em 5%. Pacientes previamente tratados para tuberculose mostraram tendência a taxas maiores de resistência às drogas de primeira linha. O padrão radiológico mais freqüente encontrado foi o infiltrado intersticial (67%), seguido da presença de linfonodos mediastinais (30%), bronquiectasias (28%), padrão miliar (18%) e cavidades

---

* Study carried out as a joint venture of the State University at Campinas School of Medical Sciences, Campinas, Brazil, and the Eduardo Mondlane University School of Medicine, Maputo, Mozambique.

1. Assistant Professor Eduardo Mondlane University School of Medicine, Maputo, Mozambique.
2. Head of the Department of Pulmonology. State University at Campinas School of Medical Sciences, Campinas, Brazil.
3. Microbiologist in the Molecular Biology Laboratory. Maputo Central Hospital, Maputo, Mozambique.
4. Biologist in the Laboratory of Mycobacterial Study. State University at Campinas School of Medical Sciences, Campinas, Brazil.
5. Statistician for the Department of Community Health. Eduardo Mondlane University School of Medicine, Maputo, Mozambique.
6. Tenured Associate Professor of Infectious Diseases. State University at Campinas School of Medical Sciences, Campinas, Brazil.
Correspondence to: Eduardo Mello De Capitani. Caixa Postal 7042, CEP 13076-970, Campinas, SP, Brasil.
Tel 55 19 3521-7595. E-mail: capitani@fcm.unicamp.br

Financial support: This study received financial support from the *Fundação de Amparo à Pesquisa do Estado de São Paulo* (FAPESP, Foundation for the Support of Research in the State of São Paulo; Grant no. 2002/00165-5).
Submitted: 17 December 2007. Accepted, after review: 30 January 2008.

**A versão completa em português deste artigo está disponível em www.jornaldepneumologia.com.br

(12%). Os pacientes infectados por micobactérias não-tuberculosas não apresentaram manifestações clínicas distintas das apresentadas pelos outros pacientes. A mediana de linfócitos CD4 entre todos os pacientes foi de 134 células/mm^3. **Conclusões:** Tuberculose e AIDS em Moçambique estão fortemente associadas, como é de se esperar em países com alta prevalência de tuberculose. Embora as taxas de resistência a drogas sejam altas, o esquema isoniazida-rifampicina continua sendo a escolha apropriada para o início do tratamento.

Descritores: Tuberculose; Micobactérias atípicas; HIV; Síndrome de imunodeficiência adquirida; Resistência a múltiplos medicamentos; Moçambique.

Introduction

Infection with HIV is a condition associated with a high risk of mycobacterial disease, primarily attributable to *Mycobacterium tuberculosis* and nontuberculous mycobacteria (NTM). Approximately 50% of all HIV-infected individuals develop mycobacterial infections at some stage of their lives.[1] Tuberculosis (TB) can occur at the earliest stages of HIV-infection, when cellular immunity is still preserved. However, infections caused by *M. tuberculosis* in combination with NTM, especially with *M. avium* complex (MAC), can remain latent until a time when the immune system has been severely impaired. Most data related to the epidemiology of infection caused by MAC preceded the era of highly active antiretroviral therapy. According to one group of authors,[2] due to the introduction of prophylactic treatment for *Pneumocystis jirovecii* pneumonia, as well as to the longer survival rates resulting from the introduction of zidovudine therapy, there has been a reduction in the incidence of MAC infection among AIDS patients. In 1992, those authors found the incidence of such infection to be 19% in a cohort of 1,006 patients with three AIDS-defining events. The aspect most closely related to the development of MAC infections in those patients was the low number of CD4 cells in the peripheral blood.[2] The incidence of MAC infection among AIDS patients has been shown to range from 10.5% to 21.6% in some United States cities, compared with 2.4% and 2.6% in Trinidad and Kenya, respectively.[3] In Southeast England, 356 of 803 mycobacterial strains isolated from 727 patients infected with HIV were MAC.[4] Among 240 HIV-infected patients presenting positive cultures for mycobacteria in Argentina, 82.9% of the isolates were *M. tuberculosis* and 12% were MAC.[5] The prevalence and characteristics of these infections have been well described for the HIV-infected populations in developed countries. However, such data is rarely available for developing countries. As reported, the rate of MAC infection is lower in developing countries than in developed ones. This has been attributed to prior exposure and acquired immunity. However, it might also be that some centers from developing countries are ill equipped to correctly identify such infections. In Mozambique, TB is the most frequently diagnosed mycobacterial disease, with a prevalence of 250/100,000 inhabitants and a mortality rate of 124/100,000. The prevalence of TB among HIV-infected patients is 47%.[6] Due to limited economic resources, NTM identification is not routinely performed in Mozambique. Therefore, one could question whether in some HIV patients with negative smear microscopy for acid-fast bacilli (AFB) and under TB treatment, as well as in those being treated for multidrug resistant TB (MDR-TB), as determined using the routinely performed sensitivity test, the disease is actually caused by NTM. This study provides insight into the problem in a selected population of HIV-infected patient in the city of Maputo.

Methods

The study was carried out in two large general hospitals located in Maputo: the *Hospital Central de Maputo* and the *Hospital Geral de Machava*. The first is the reference for TB in the southern region of the country, and the second is the national reference for TB cases. Most TB/HIV co-infected patients requiring hospitalization are admitted to one of those two facilities. The study was conducted from October of 2002 through August of 2004.

All patients over 11 years of age admitted with suspicion of pulmonary TB and for whom the HIV status was known were evaluated. The diagnosis of TB was made on the basis of complaints, clinical findings, and chest X-ray findings, as well as of the results of smear microscopy for AFB and culture. Patients were categorized clinically into four classes: asymptomatic (Class I); symptomatic less than 50% of the day (Class II); symptomatic more

than 50% of the day (Class III); in bed most of the time (Class IV). Patients were questioned regarding previous treatment for TB, which was also checked in patient records. Strict patient confidentiality of test results was guaranteed, and all participating patients (or their parents/guardians) gave written informed consent. The ethics committees of the involved Institutions approved the study protocol.

A sample of peripheral blood was drawn from each enrolled patient in order to determine the levels of albumin, lactate dehydrogenase, and hemoglobin, as well as to perform a complete blood count and CD4 lymphocyte count.

Chest X-rays were taken at admission. Findings were categorized into the following patterns: interstitial, alveolar consolidation, nodules, cavitations, bronchiectasis, and mediastinal lymph node enlargement.

Smear microscopy for AFB, culture, and drug sensitivity tests

Sputum samples and bronchoalveolar lavage fluid were processed by Ziehl-Neelsen, fuchsin, or auramine staining. In all cases, Löwenstein-Jensen and Stonebrink culture media were used simultaneously for sputum or bronchoalveolar lavage fluid cultures. Tests of drug sensitivity to isoniazid, streptomycin, ethambutol, and rifampin were conducted according to the guidelines established by the World Health Organization and the International Union against Tuberculosis and Lung Disease. We defined MDR as resistance to rifampin and isoniazid. All tests were carried out at the National Reference Laboratory of Tuberculosis, located in Maputo. The Laboratory participates in an international quality assurance program sponsored by the *Istituto Supeirore di Sanità di Roma*, in Rome, Italy.

Polymerase chain reaction restriction analysis of the hsp65 gene was used for species level identification of isolates.[7] Strains of the *M. tuberculosis* complex were further identified with amplification and restriction of gyrB gene products.[8] These tests were performed at the State University at Campinas Bacterial Pathogenesis Laboratory, located in Campinas, Brazil.

Patients presenting negative smear microscopy for AFB were submitted to flexible fiberoptic bronchoscopy. The bronchoalveolar lavage fluid was obtained after instillation of 5-mL aliquots of saline into the most affected segmental or lobar bronchi.

HIV testing

A blood sample was collected for HIV testing. Rapid immunochromatographic assays were used for the detection of HIV-1 (UnigoldT test; Trinity Biochem, Dublin, Ireland) and HIV-2 (Determine AbbottT; Abbott Diagnostics, Park, IL, USA). Results

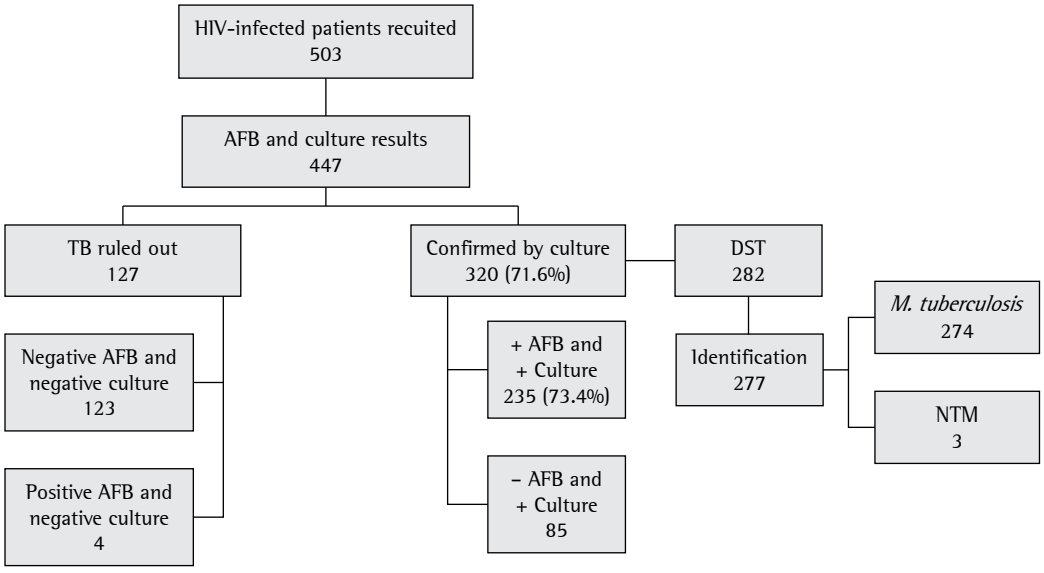

Figure 1 - Patients involved in the study according to the test results. AFB: acid-fast bacilli; TB: tuberculosis; DST: drug sensitivity tests; and NTM: nontuberculous mycobacteria.

were further confirmed by rapid enzyme-linked immunosorbent assay.

CD4 counts

To determine CD4 lymphocyte counts, we used flow cytometry (Epics-XL-MCL; Beckman Coulter, Fullerton, CA, USA) in accordance with the manufacturer recommendations.

Statistical analysis

Data were analyzed using the Stata Intercooled program, version 8.2 (Stata Corp., College Station, TX, USA). Univariate analysis was used to describe demographic variables and variables related to drug resistance, using the chi-square test to determine statistical significance. For hematological parameters, the Mann-Whitney test was performed.

Results

A total of 503 HIV-infected patients were recruited (Figure 1). Among those 503, smear microscopy for AFB and culture had been performed in sputum or bronchoalveolar lavage fluid specimens for 447. Positive mycobacterial culture results were obtained in 320 patients. Of those 320, 235 (73.4%) also presented a positive smear microscopy for AFB. All data presented here are related to the group of patients in which mycobacterial infection was confirmed through culture (n = 320). Drug sensitivity tests were performed in 258 isolates. Identification of mycobacteria to the species level was achieved in 277 isolates. A substantial number of isolates could not be identified (n = 43) or were not submitted to drug sensitivity tests (n = 62), most due to preservation problems during transport. Only 3 isolates were characterized as NTM. Table 1 shows the demographic characteristics of patients presenting mycobacterial infections, as confirmed through smear microscopy or culture. Most patients, regardless of gender, were in the economically productive age bracket. The predominance of black patients reflects the demographic profile of the country.

Weight loss, fever, and cough were the most frequent clinical findings observed, and 50.6% of patients were categorized as Class I. The most common radiologic pattern was interstitial (in 66.8%), followed by mediastinal lymph node enlargement (in 30%), and bronchiectasis (in 27.5%). Miliary nodules were seen in 17.8% of cases, and cavitation was seen in 12.1%. These data can be seen in Table 2. All three individuals infected with NTM presented clinical manifestations rather similar to those of the cases of *M. tuberculosis* infection. The median CD4 lymphocyte count was 151 cells/mm^3, and the median total lymphocyte count was 1140.5 cells/mm^3. Cavities seen on chest X-rays were associated with CD4 lymphocyte counts > 200 cells/mm^3 (Figure 2).

Table 1 - Demographic characteristics of 320 HIV-infected patients with pulmonary tuberculosis, Mozambique, 2006.

Age (years), median	33
Female	30
Male	34
Gender, n	
Female	196
Male	124
Race, n	
Black	292
Caucasian	27
Other	1
Place of birth, n	
Maputo Province	262
Gaza Province	31
Tete Province	14
Other	13
Residence, n	
Maputo Province	306
Other	14

Mycobacteria identification

Out of the 277 cultures in which mycobacteria were identified to the species level, 274 (99%) tested positive for *M. tuberculosis*, 2 (0.7%) tested positive for *M. avium*, and 1 (0.4%) tested positive for *M. simiae*. In the *M. tuberculosis* complex group, the gyrB polymerase chain reaction restriction analysis patterns confirmed *M. tuberculosis* in all isolates.

Table 3 summarizes the drug resistance data. Sensitivity tests to antituberculous drugs were performed in 258 *M. tuberculosis* isolates and in 3 NTM isolates. New TB cases accounted for 179 (69%) of the patients, and 74 (29%) of the patients reported having previously been treated for

Table 2 - Distribution of clinical and radiological findings in 320 patients presenting positive cultures for mycobacteria.

Variables	n	%
Signs and symptoms		
Weight loss	320	100.0
Fever	317	99.0
Cough	274	86.0
Diaphoresis	219	68.0
Thoracic pain	208	65.0
Diarrhea	124	39.0
Dyspnea	142	44.0
Lymph node enlargement	127	40.0
Hemoptysis	15	5.0
Clinical Status Performance		
Class I	162	51.0
Class II	103	32.0
Class II	42	13.0
Class IV	1	0.3
No information	12	4.0
Chest X-ray findings		
Interstitial pattern	214	67.0
Miliary pattern	57	18.0
Lymph node enlargement	96	30.0
Bronchiectasis	88	28.0
Cavities	39	12.0
Bilateral findings	250	78.0

Class I: asymptomatic; Class II: symptomatic less than 50% of the day; Class III: symptomatic more than 50% of the day; and Class IV: in bed most of the time.

TB. In the remaining 5 cases (2%), this information could not be obtained. Resistance to at least one of the drugs tested was seen in 44 cases (17%). There were 13 isolates (5%) that presented MDR, which was significantly more frequent ($p < 0.03$) in the previously treated individuals (9%) than in those classified as new cases (3%). Resistance to at least one drug was found in 23 (12.9%) of the 179 new cases. The most common drug resistance was to isoniazid (in 11%), followed resistance to streptomycin (in 7%) and resistance to rifampin (in 4%). Resistance to isoniazid alone was seen in 6%, and resistance to streptomycin alone was seen in 2%. Resistance to ethambutol alone was not observed. Resistance to at least one drug was seen in 19 (26%) of the 74 previously treated cases. In that group, the most common resistance was to isoniazid (in 23%), followed by resistance to rifampin (in 11%) and resistance to streptomycin (in 9%). Again, resistance to ethambutol alone was not observed.

Resistance to the isoniazid-rifampin combination was higher among the previously treated cases than among the new cases. Overall, resistance to any single drug or combination of drugs occurred most frequently among the previously treated cases. As expected, the NTM isolated showed resistance to most of the drugs tested. Resistance to all of the drugs tested was found for *M. simiae*. Of the 2 *M. avium* isolates, one was sensitive only to rifampin, and the other was sensitive only to streptomycin.

Discussion

In Mozambique, AIDS and TB are firmly established. Comorbidities such as malarial infection, sickle cell anemia, malnutrition, and intestinal parasites contribute to the high mortality observed among such patients. In Mozambique, where data regarding TB and AIDS is incomplete, TB is ranked among the 10 leading preventable causes of deaths reported in Maputo.[10] Although a nationwide TB treatment program has been run by paramedical staff since 1985, the results have been disappointing.[11] The present study shows that TB/HIV co-infected patients in the Maputo area have low levels of hemoglobin and albumin, probably reflecting the above mentioned conditions, making the treatment of such patients even more difficult. Most of the affected individuals are in the economically productive age bracket, which implies a heavy socioeconomic burden. The clinical presentation of TB in the studied population was the classic triad of fever, sweats, and cough. Shortness of breath in combination with interstitial alterations seen on chest X-rays was a common finding, making *P. jirovecii* pneumonia one of the major differential diagnoses, especially among those with elevated serum lactate dehydrogenase, which was found in most of the patients evaluated. In a large case series study and review of the literature,[12] the chest X-rays of TB/HIV co-infected patients were analyzed. The predominant findings were infiltrates, followed by interstitial infiltrate and lymphadenopathy. Low CD4 lymphocyte counts were associated with hilar/mediastinal lymphadenopathy and inversely associated with pleural effusion and cavitary disease. Our results corroborate those findings; NTM were isolated from sputum samples in only 3 cases. According

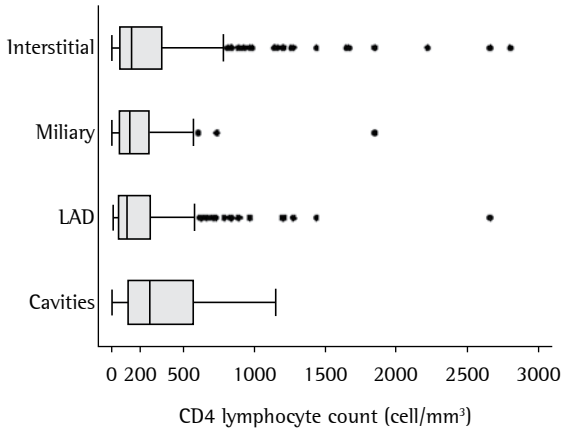

Figure 2 - Box plot showing the distribution of the radiographic alterations according to the CD4 lymphocyte counts. LAD: lymphadenopathy.

to other reports from developing countries, where the prevalence of TB is quite high, NTM isolation is rare. In one case, the probable causative agent was *M. simiae*. There have been few reports of *M. simiae* infection in HIV-infected patients.[13-15] Although its association with human disease is not frequent, pulmonary infection with *M. simiae* has been reported in monkey trainers and in other individuals having close contact to these animals,[16] as well as in patients with pre-existing pulmonary disease, such as cavitary TB, carcinoma and chronic obstructive pulmonary disease.[13] Transmission is thought to be airborne and fecal-oral since it has been detected in healthy human feces.[16] The isolate found in this study was resistant to all common antituberculous drugs, as were *M. simiae* described in other case reports.

As expected, resistance of *M. tuberculosis* to at least one antituberculous drug was significantly lower among new cases of TB than among the previously treated cases. This pattern of resistance to at least one anti tuberculous drug in previously treated cases is similar to that observed in other African countries.[17-19] This high resistance rate among new cases might have been the result of concurrent situations: TB/HIV co-infection, which makes patients more susceptible when exposed to an environment in which there is continuous transmission of resistant mycobacteria[20]; the use of certain antituberculous drugs for the treatment of other diseases; and decreased absorption of the antituberculous drugs due to concurrent diarrhea caused by parasitic diseases and intestinal bacterial infections, resulting in lower serum concentrations of the drug. The high resistance rates observed among the previously treated cases is of great concern, since it implies that conditions are conducive to the acquisition of additional resistance, leading to MDR-TB. Resistance to isoniazid was more common than was

Table 3 - Distribution of *M. tuberculosis* strains isolated from 279 patients according to resistance patterns to isoniazid, rifampin, ethambutol, and streptomycin, together with the history of previous tuberculosis treatment.

Sensitivity/Resistance	Previously treated (n = 74)	New cases (n = 179)	No data (n = 5)	Total (n = 258)	p*
	n (%)	n (%)	n	n	
Sensitive to all drugs tested	55 (75)	156 (87)	3	214	0.02
Single-drug resistance	10 (13)	15 (9)	1	26	0.29
INH	8 (10)	10 (6)	-	18	
SM	1 (1)	4 (2)	1	6	
RIF	1 (1)	1	-	2	
EMB	-	-	-	-	
Simultaneous resistance	9 (8)	8 (2)	1	18	0.19
INH+RIF	3 (5)	1	-	4	
INH+SM	2 (3)	3 (2)	-	5	
INH+RIF+SM	3 (5)	2 (1)	1	6	0.01
INH+RIF+ EMB	1	-	-	1	
INH+RIF+SM+EMB	-	2 (2)	-	2	0.64
MDR-TB	7 (11)	5 (3)	1	14	0.03

INH: isoniazid; SM: streptomycin; RIF: rifampin; EMB: ethambutol; MDR: multidrug resistance (resistance to at least INH and RIF). *Pearson's chi-square test.

resistance to any of the other drugs tested and, at 14.9%, was considerably higher than 5.9% worldwide rate reported by the World Health Organization.[6] According to that report, a higher than 10% rate of resistance to isoniazid and rifampicin can predict the development of MDR-TB. This finding increases concerns regarding the prophylactic use of isoniazid in HIV-infected individuals in Mozambique. The results of the drug sensitivity testing carried out in the present study indicates the need for strict enforcement of the directly observed therapy, short-course strategy, better epidemiological surveillance of TB cases, and coordination between AIDS and TB control programs.

References

1. Nightingale SD, Byrd LT, Southern PM, Jockusch JD, Cal SX, Wynne BA. Incidence of Mycobacterium avium-intracellulare complex bacteremia in human immunodeficiency virus-positive patients. J Infect Dis. 1992;165(6):1082-5.
2. Chaisson RE, Moore RD, Richman DD, Keruly J, Creagh T. Incidence and natural history of Mycobacterium avium-complex infections in patients with advanced human immunodeficiency virus disease treated with zidovudine. The Zidovudine Epidemiology Study Group. Am Rev Respir Dis. 1992;146(2):285-9.
3. Fordham von Reyn C, Arbeit RD, Tosteson AN, Ristola MA, Barber TW, Waddell R, et al. The international epidemiology of disseminated Mycobacterium avium complex infection in AIDS. International MAC Study Group. AIDS. 1996;10(9):1025-32.
4. Yates MD, Pozniak A, Grange JM. Isolation of mycobacteria from patients seropositive for the human immunodeficiency virus (HIV) in south east England: 1984-92. Thorax. 1993;48(10):990-5.
5. Di Lonardo M, Isola NC, Ambroggi M, Rybko A, Poggi S. Mycobacteria in HIV-infected patients in Buenos Aires. Tuber Lung Dis. 1995;76(3):185-9.
6. Aziz MA. Anti-tuberculosis drug resistance in the world: third global report : the WHO/IUATLD Global Project on Anti-tuberculosis Drug Resistance Surveillance, 1999-2002. Geneva: World Health Organization, 2004.
7. Telenti A, Marchesi F, Balz M, Bally F, Böttger EC, Bodmer T. Rapid identification of mycobacteria to the species level by polymerase chain reaction and restriction enzyme analysis. J Clin Microbiol. 1993;31(2):175-8.
8. Niemann S, Harmsen D, Rüsch-Gerdes S, Richter E. Differentiation of clinical Mycobacterium tuberculosis complex isolates by gyrB DNA sequence polymorphism analysis. J Clin Microbiol. 2000;38(9):3231-4.
9. Mac-Arthur A, Gloyd S, Perdigão P, Noya A, Sacarlal J, Kreiss J. Characteristics of drug resistance and HIV among tuberculosis patients in Mozambique. Int J Tuberc Lung Dis. 2001;5(10):894-902.
10. Dgedge M, Novoa A, Macassa G, Sacarlal J, Black J, Michaud C, et al. The burden of disease in Maputo City, Mozambique: registered and autopsied deaths in 1994. Bull World Health Organ. 2001;79(6):546-52.
11. Salomao MA. The National Tuberculosis Control Programme in Mozambique, 1985-1990. Bull Int Union Tuberc Lung Dis. 1991;66(4):175-8.
12. Perlman DC, el-Sadr WM, Nelson ET, Matts JP, Telzak EE, Salomon N, et al. Variation of chest radiographic patterns in pulmonary tuberculosis by degree of human immunodeficiency virus-related immunosuppression. The Terry Beirn Community Programs for Clinical Research on AIDS (CPCRA). The AIDS Clinical Trials Group (ACTG). Clin Infect Dis. 1997;25(2):242-6.
13. Vandercam B, Gala JL, Gerain J, Degraux J, Bourlond A, Colebunders B, et al. About two cases of Mycobacterium simiae infection in AIDS: review of the pathogenicity. Acta Clin Belg. 1998;53(3):206-12.
14. Al-Abdely HM, Revankar SG, Graybill R. Disseminated Mycobacterium simiae infection in patients with AIDS. J Infect. 2000;41(2):143-7.
15. Huminer D, Dux S, Samra Z, Kaufman L, Lavy A, Block CS, et al. Mycobacterium simiae infection in Israeli patients with AIDS. Clin Infect Dis. 1993;17(3):508-9.
16. Sampaio JL, Artiles N, Pereira RM, Souza JR, Leite JP. Mycobacterium simiae infection in a patient with acquired immunodeficiency syndrome. Braz J Infect Dis. 2001;5(6):352-5.
17. Tudó G, González J, Obama R, Rodríguez JM, Franco JR, Espasa M, et al. Study of resistance to anti-tuberculosis drugs in five districts of Equatorial Guinea: rates, risk factors, genotyping of gene mutations and molecular epidemiology. Int J Tuberc Lung Dis. 2004;8(1):15-22.
18. Bretzel G, Aziz M, Wendl-Richter U, Adatu F, Aisu T, van Wijnen A, et al. Anti-tuberculosis drug resistance surveillance in Uganda 1996-1997. Int J Tuberc Lung Dis. 1999;3(9):810-5.
19. Dosso M, Bonard D, Msellati P, Bamba A, Doulhourou C, Vincent V, et al. Primary resistance to antituberculosis drugs: a national survey conducted in Côte d'Ivoire in 1995-1996. Ivoirian Study Group on Tuberculosis Resistance. Int J Tuberc Lung Dis. 1999;3(9):805-9.
20. Kritski A, Dalcolmo M, del Bianco R, del Melo FF, Pinto WP, Schechther M, et al. Association of tuberculosis and HIV infection in Brazil [Article in Portuguese]. Bol Oficina Sanit Panam. 1995;118(6):542-54.