

# Impact of human immunodeficiency virus infection on the outcome of treatment and survival of tuberculosis patients in Mwanza, Tanzania

J. van den Broek,\* S. Mfinanga,<sup>†</sup> C. Moshiro,<sup>‡</sup> R. O'Brien,<sup>§</sup> A. Mugomela,<sup>¶</sup> M. Lefi\*\*

\*Royal Tropical Institute, Amsterdam, The Netherlands, <sup>†</sup>National Institute of Medical Research, Muhimbili Research Station and Central Tuberculosis Laboratory, Dar es Salaam, <sup>‡</sup>Department of Epidemiology and Biostatistics, University of Dar es Salaam, Dar es Salaam, Tanzania, <sup>§</sup>Division of TB Elimination, CDC, Atlanta, Georgia, USA, <sup>¶</sup>Bugando Medical Centre, Mwanza, \*\*National Tuberculosis and Leprosy Programme, Mwanza, Tanzania

## SUMMARY

**SETTING:** Little is known about the outcome of tuberculosis (TB) treatment and subsequent survival of human immunodeficiency virus (HIV) infected patients treated under routine programme conditions in a developing country. We followed a cohort of HIV-positive and HIV-negative tuberculosis patients during therapy and assessed their vital and tuberculosis status 3 years after completion of treatment in Mwanza, Tanzania.

**METHODS:** Newly diagnosed and relapse tuberculosis cases consecutively registered over a 6-month period were enrolled into an epidemiological study of TB/HIV. Treatment outcome was based on information in tuberculosis treatment registers. Patients surviving treatment were assessed 3 years later by personal interview. Cause of death was determined by verbal autopsy.

**RESULTS:** Of 561 patients enrolled into the study, 505 patients alive at completion of treatment were eligible for assessment at 3 years. Except for mortality, HIV infection was not statistically associated with differing

treatment outcomes. At time of follow-up, the overall mortality was 19% and was associated with HIV infection (hazard ratio [hr] 3.7, 95% confidence interval [CI] 2.6–5.2) and age 35 years and over (hr 1.5, 95% CI 1.02–2.1), but not with type of tuberculosis, gender, or initial drug resistance. By life table analysis, probability of survival at 4 years was 35% for HIV-positive patients compared to 90% for HIV-negative patients. Although no relapse cases were diagnosed, verbal autopsy suggested equivalent low rates of relapse in both groups.

**CONCLUSION:** These results demonstrate the effectiveness of the current approach to the treatment of tuberculosis patients regardless of HIV status. However, HIV-related mortality remains high both during and following completion of treatment, and further studies are needed to determine if this mortality might be reduced by simple interventions which are feasible in developing countries.

**KEYWORDS:** tuberculosis; HIV; outcome of treatment; survival; Tanzania

IN TANZANIA, as in other sub-Saharan African countries, human immunodeficiency virus (HIV) infection has led to significant increases in tuberculosis cases.<sup>1-4</sup> HIV infection is also associated with unusual clinical presentations of tuberculosis, increases in extra-pulmonary and acid-fast bacilli (AFB) smear-negative pulmonary disease, and atypical findings on chest radiography, all making the diagnosis of HIV-associated tuberculosis problematic.<sup>5,6</sup> Treatment outcome, especially when non-rifampicin-containing regimens are used, is poorer among HIV-infected patients.<sup>7,8</sup> HIV-positive tuberculosis patients are also at increased risk of relapse following treatment with regimens without rifampicin,<sup>9,10</sup> and possibly also following treatment with rifampicin-containing short-course regimens.<sup>11,12</sup>

These reports, and others,<sup>13,14</sup> all indicate that HIV-infected patients experience significantly greater

mortality, especially during the initial period of tuberculosis treatment. However, there is little published information on outcome of treatment and longer term survival of HIV-infected patients under programme conditions. This information would be useful for assessing the cost-effectiveness of short-course chemotherapy for HIV-infected tuberculosis patients in sub-Saharan Africa.

The present study reports on the outcome of treatment and long-term survival of a cohort of HIV-positive and HIV-negative tuberculosis patients registered in 1991 in the Mwanza region of northern Tanzania. In 1991, 1909 new and relapsed tuberculosis cases were registered in the region, for a case notification rate of 95 per 100 000 population. Between 1984 and 1995, registered tuberculosis cases in the region increased by on average 10% per year.

Correspondence to: J van den Broek, Royal Tropical Institute, Wibautstraat 137j, 1097 DN Amsterdam, The Netherlands. Article submitted 7 February 1997. Final version accepted 26 February 1998.

[A version in French of this article is available from the IUATLD Secretariat in Paris]

## MATERIALS AND METHODS

All newly diagnosed and relapse tuberculosis patients registered between 1 April and 31 September, 1991, in the Mwanza region were enrolled as part of a systematic country-wide survey of HIV seroprevalence in TB cases. The survey design provided for HIV testing of a representative sample of approximately one-sixth of all new and relapse cases registered in the country between January 1991 and December 1993, with linkage to demographic, clinical and bacteriological data for these cases. All newly registered new and relapse cases, both pulmonary and extra-pulmonary, aged 15 years and older, were eligible for the study. Detailed information about study procedures has been published.<sup>3,4</sup>

All patients were diagnosed and treated following the guidelines of the Tanzania National Tuberculosis and Leprosy Programme (NTLP). New AFB smear-positive pulmonary patients, as well as seriously ill smear-negative and extra-pulmonary patients, received an 8-month short-course regimen with daily supervised rifampicin (R), isoniazid (H), pyrazinamide (Z) and streptomycin (S) for 2 months, followed by 6 months of daily self-administered isoniazid and thioacetazone (T) in combination form (2SHRZ/6TH). Relapsed smear-positive patients and failure cases were treated with an 8-month retreatment regimen which included ethambutol (E) (2SHRZE/1HRZE/5H<sub>3</sub>R<sub>3</sub>E<sub>3</sub>), and all other patients received a 12-month regimen without rifampicin (2STH/10TH). Patients experiencing skin reactions and those suspected of HIV infection received ethambutol in place of thioacetazone.

The outcome of treatment was determined by review of the District Tuberculosis Treatment registers, with the outcomes (cured, treatment completed, treatment failure, died, transferred and lost) based on standard definitions.<sup>15</sup> For this study, transferred and lost patients were grouped together as 'uncertain outcome.'

During October and November 1995, all patients who did not die during treatment were reassessed by District Tuberculosis and Leprosy Coordinators (DTLC). The DTLCs, who were trained in diagnosis and treatment of tuberculosis and leprosy, interviewed study patients at their homes when possible. For patients no longer living at the last known address, relatives and neighbours were questioned to determine the patients' current status. For patients who had been transferred from the Mwanza region during treatment or who subsequently moved from the region, the DTLC attempted to obtain follow-up information from the DTLC where the patient was believed to be living. Verbal consent to participate in the follow-up study was obtained from patients or relatives.

The DTLCs attempted to establish the current status of every patient as either alive and free of tuberculosis, having developed recurrent tuberculosis (relapse), or

having died. For patients with suspected recurrent tuberculosis, including those with chronic cough for more than 3 weeks, a sputum specimen was taken for AFB smear and mycobacterial culture. Relapse cases were diagnosed according to NTLP guidelines. For all patients who died after completing treatment, attempts were made to establish the cause of death from relatives or neighbours, based on the technique of verbal autopsy.<sup>16</sup>

Statistical analysis was done by  $\chi^2$  test, Fisher's exact test, logistic regression, log rank test and Cox regression. A Kaplan-Meier survival curve based on the results of Cox regression was plotted, using Stata® (Stata Corporation, Texas, USA) and Excel (Microsoft® Corporation, USA) computer packages. In the survival analysis all new and relapsed AFB smear- and/or culture-positive cases were grouped together as 'bacteriologically positive' and all other types as 'bacteriologically negative' cases of tuberculosis.

## RESULTS

Of 594 patients enrolled during the initial epidemiological study, 561 patients who met the case definition, were at least 15 years of age, and whose HIV status was known, were included in this study. Of these, 447 were new and 35 relapsed bacteriologically positive pulmonary tuberculosis, 54 new bacteriologically negative pulmonary and 24 new extra-pulmonary tuberculosis patients. Overall 146 (26%) patients were HIV-positive, and the HIV status was not significantly different between the types of tuberculosis ( $P = 0.352$ ).

Of 83 HIV-positive tuberculosis patients with isolates of *Mycobacterium tuberculosis* and drug susceptibility results, 11 (13%) had strains resistant to H, R, T, and/or S, while out of 251 HIV-negative patients 22 (9%) had resistant strains; the difference was not statistically significant ( $P = 0.278$ ). Single drug resistance was found for 26 patients, while two had strains resistant to two drugs, three to three drugs, and two to four drugs.

### Outcome of treatment

At the end of treatment, 428 were cured or had completed their treatment as prescribed, 56 had died during treatment, seven were treatment failures and 70 had either absconded or been transferred out. There were no statistically significant differences in treatment outcome between the types of tuberculosis (Table 1,  $P = 0.465$ ).

HIV-positive tuberculosis patients had significantly higher rates of death and uncertain outcome ( $P < 0.001$ ). Controlling for age, sex, and HIV status in a logistic regression analysis, mortality was somewhat higher in patients with drug resistance, although the difference did not achieve statistical sig-

**Table 1** Outcome of treatment by type of tuberculosis and by HIV status

	Cured/ TC (%)	Died (%)	Failure (%)	Uncertain outcome* (%)	Total (100%)
New AFB + PTB	341 (76)	46 (10)	6 (1)	54 (12)	447
Relapse	30 (86)		1 (3)	4 (12)	35
New AFB - PTB	41 (75)	7 (13)		7 (13)	55
Extra PTB	16 (67)	3 (13)		5 (21)	24
HIV+	86 (59)	24 (16)	4 (3)	32 (22)	146
HIV-	342 (82)	32 (8)	3 (1)	38 (9)	415
Total	428 (76)	56 (10)	7 (1)	70 (12)	561

\*Uncertain outcome: lost to follow-up and transferred out.  
TC = treatment completed; AFB = acid-fast bacilli; PTB = pulmonary tuberculosis.  
 $\chi^2$  (bacteriologically positive/negative) = 2.56, *df* = 3, *P* = 0.465.  
 $\chi^2$  (HIV status) = 33.68; *df* = 3, *P* < 0.001.

nificance (odds ratio = 2.0, 95% confidence interval [CI] 0.7–5.9).

### Survival

For the 505 patients who had not died during treatment, a total of 465 home visits were made. Among these patients, 427 were found or reported to be still alive, an additional 51 had died and for 27 information on their status could not be obtained (Table 2). Thus, the total number of deaths in this cohort was 107 (19%), of whom 10% died during treatment and 9% during the 3 years thereafter. Among the HIV-negative patients, 8% (32/415) died during treatment and an additional 6% (24/415) during the following 3 years. Among the 146 HIV-positive patients, 16% (24/146) died during treatment and an additional 18% (27/146) during the follow-up period. Mortality was significantly greater among the HIV-positive patients (*P* < 0.0001), but did not differ by bacteriological status (*P* = 0.465). For those patients with uncertain treatment outcome, vital status at follow-up was established for 71% of the HIV-negative and for 53% of HIV-positive patients.

In a multivariate analysis with Cox regression, controlling for bacteriological status, age group, sex

**Table 2** Survival status of HIV-negative and HIV-positive tuberculosis patients who were alive on completing treatment

Outcome of treatment	HIV status	Alive (%)	Died (%)	Unknown (%)	Total (100%)
Cured/TC	HIV -	319 (93)	22 (6)	1 (0.3)	342
	HIV +	62 (72)	24 (28)	0	86
Uncertain outcome	HIV -	26 (68)	1 (3)	11 (29)	38
	HIV +	15 (47)	2 (6)	15 (47)	32
Failure	HIV -	2 (67)	1 (33)		3
	HIV +	3 (75)	1 (25)	0	4

and HIV infection, mortality was strongly associated with HIV infection (hazard ratio = 3.7, 95% CI 2.6–5.2) and age 35 years and over (hazard ratio = 1.5, 95% CI 1.02–2.1) (Table 3). The log rank test confirmed an association of higher mortality in the older age groups, although this was statistically significant only for HIV-negative patients (*P* = 0.0012) compared with HIV-positive patients (*P* = 0.1878). Controlling for age, sex and HIV infection, the mortality of patients with drug resistance (21%, 7/33) was not significantly different from that of those with susceptible organisms (16%, 49/301) (hazard ratio = 1.3, 95% CI 0.7–2.6).

Kaplan Meier survival curves for HIV-positive and HIV-negative tuberculosis patients for the age groups 15–34 years and 35 years and over are plotted in the Figure. The probability of survival for HIV-positive patients at the end of treatment (12 months) was 0.73 (95% CI 0.63–0.81) for those aged below 35, and 0.64 (95% CI 0.45–0.78) for those aged 35 and over. The probability of survival of HIV-positive patients at 56 months (at follow-up) was 0.39 (95% CI 0.21–0.58) for those below 35 years, and 0.29 (95% CI 0.09–0.53) for those aged 35 and over. The median survival times for HIV-positive patients were 19 months and 22 months for those below 35 and for those 35 years and over, respectively.

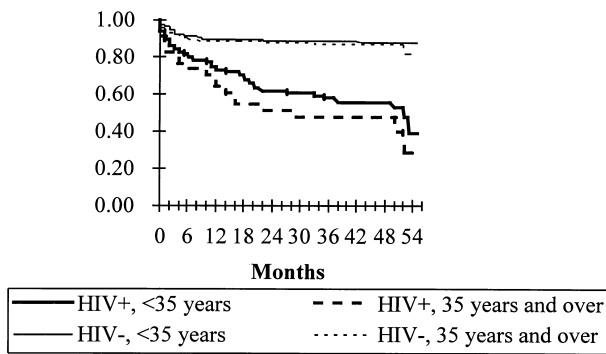
Extrapolation by simple logistic regression of the life tables in the Kaplan Meier analysis showed that the life expectancy of HIV-positive patients was 6.5 years for those below 35 years and 4.7 years for those 35 years of age and over. On the other hand, HIV-negative tuberculosis patients were estimated to have a life expectancy of 29.7 and 23.5 years, respectively, for patients aged under 35 and those aged 35 years and over.

### Cause of death

The cause of death, using the verbal autopsy technique, could be established for 88% (45/51) of the

**Table 3** Hazard ratios and 95% confidence intervals for mortality of tuberculosis patients during and after treatment over an observation period of 56 months

Variable	Hazard ratio	95% confidence interval
Type of tuberculosis		
Bacteriologically positive	1	
Bacteriologically negative	1.1	0.7–1.8
Sex		
Male	1	
Female	0.7	0.5–1.1
Age group		
15–34 years	1	
≥35 years	1.5	1.02–2.1
HIV infection		
Negative	1	
Positive	3.7	2.6–5.2



**Figure** Kaplan Meier survival curve for HIV+ and HIV- tuberculosis patients per age group.

cases who died after completing treatment. Out of all causes of death, 14 were directly associated with tuberculosis (five among HIV-positive patients and nine among HIV-negative patients), 20 were attributable to HIV and acquired immune-deficiency syndrome (AIDS) related symptoms, such as emaciation and severe diarrhoea (80% HIV-positive), one following severe side effects of thioacetazone (HIV-positive), and 10 due to other causes (20% HIV positive). Among HIV-negative tuberculosis patients, four deaths were attributed to HIV and AIDS.

## DISCUSSION

These findings confirm the efficacy of treatment regimens for HIV-positive and HIV-negative tuberculosis patients and the effectiveness of the National Tuberculosis and Leprosy Programme in Tanzania. However, they also show that HIV-infected patients experience high mortality, both during and following treatment, so that 4 years after the initial diagnosis of tuberculosis, approximately two-thirds of HIV-positive patients had died. The hazard ratio for mortality for HIV-positive patients was 3.7 times higher than for HIV-negative patients. As expected, mortality was also higher in the older age groups, but this was only statistically significant in HIV-negative patients. HIV infection was less prevalent in these older age groups, as was shown in an earlier report,<sup>4</sup> suggesting that HIV infection was a stronger determinant for mortality than age.

Mortality was highest immediately after start of treatment; it was higher among HIV-positive patients, and remained higher throughout the observation period. The high initial mortality suggests that a proportion of tuberculosis patients report in advanced stages of tuberculosis disease and/or HIV infection. During the last 6 months of the study period the mortality (and censoring) increased again; this is probably explained by recall bias of the respondents regarding the dates of death of their relatives.

The median survival in our study is consistent with a report from Zambia,<sup>14</sup> but was better than those

reported in other studies among AIDS patients with tuberculosis in Uganda,<sup>17</sup> suggesting that tuberculosis is a feature of the advanced stages of HIV infection and AIDS in those studies. The patients in our study had longer median survival times than AIDS patients in a rural Ugandan cohort,<sup>18</sup> where they ranged from over 4.5 years to 1.1 year, in Zaire,<sup>19</sup> where there was a median survival of 5.8 months, and in Tanzania,<sup>20</sup> which had a median survival of less than 3 months. In these studies the major causes of death were severe wasting, diarrhoea and Kaposi's sarcoma, and the reports did not provide information on the occurrence of tuberculosis, except in Tanzania where 19% of the patients had the disease. One other report from Mexico suggests that HIV-positive tuberculosis patients have a longer survival than AIDS patients without mycobacterial infection.<sup>21</sup>

The longer median survival for our patients suggests that tuberculosis responds very well to treatment. However, longer survival could also be explained by high initial mortality in tuberculosis patients undetected or not notified by the regular health services, leading to a selection bias of the patients with less advanced disease. We could not substantiate this assumption, although we are aware that in other regions in Tanzania mortality among HIV-positive tuberculosis patients is reportedly much higher than in the Mwanza region.<sup>22</sup> Data from the United States indicates that HIV-infected tuberculosis patients, matched for stage of HIV infection, have a poorer survival than HIV-infected patients without tuberculosis.<sup>23</sup> Furthermore, it has been suggested that immune activation in tuberculosis may accelerate the course of HIV infection, providing an explanation for the results of observational studies.<sup>24</sup> Comparison of all these data would be more valid if the clinical and immunological stages of HIV infection, such as CD<sub>4</sub> counts or beta-2 microglobulin levels, were known.

History taking, together with physical and bacteriological examination of suspected relapse cases during the follow-up did not reveal recurrence of tuberculosis in our cohort. The probability of relapse of tuberculosis in Mwanza, and in the whole of Tanzania, is believed to be small (i.e., less than 10%), and we may have missed relapse patients, especially among those patients not visited. Moreover, based on verbal autopsy, as many as 4% of the HIV-positive patients and 2% of the HIV-negative patients may have died from recurrent tuberculosis. Nonetheless, the probability of tuberculosis relapse appears to be low, and equivalent among HIV-positive and HIV-negative patients.

We considered the verbal autopsy technique sufficiently sensitive for our purpose of establishing death, because of the limited possibilities of likely causes of death. Of all deaths among HIV-positive patients, 59% were related to AIDS or related conditions, including diarrhoea and wasting syndrome. We rea-



lise that tuberculosis and wasting syndromes are frequently associated in Africa,<sup>3</sup> and verbal autopsies do not allow any distinction to be made between these conditions. Among HIV-negative patients four died under suspected AIDS-related conditions, which could have been a result of incident HIV infection after the diagnosis of HIV-negative tuberculosis. Out of 27 deaths related to HIV infection, one was attributed to thioacetazone toxicity, a problem which was not widely recognised when this study was done.

## CONCLUSION

The prognosis of tuberculosis in HIV-infected persons is poor. Deaths occurring during and after treatment in the observation period of 56 months were statistically significantly higher in HIV-positive than in HIV-negative tuberculosis and in older age groups, regardless of type of tuberculosis, sex and presence of resistant strains. The response to treatment was good and similar in HIV-positive and HIV-negative tuberculosis patients. No relapses were diagnosed during the period of follow-up, indicating that chemotherapy was equally effective for HIV-positive and HIV-negative tuberculosis patients. This underlines the necessity to treat tuberculosis properly, under direct observation with rifampicin-containing regimens, regardless of HIV status and initial resistance pattern. The results of this study also confirm the effectiveness of the National Tuberculosis and Leprosy Programme in Tanzania.

## Acknowledgements

We thank the Principle Secretary, Ministry of Health and the Director General of the National Institute for Medical Research for permission to publish the results of this study. We are grateful to Mr Peter Msalenge, Mr George Masubo, Mr Marko Lubango, Mr Martin Degeh, Mr Constantine Innocent, Mr Dodoma, Mr James Zayumba and Mr Chaim Kisondele (the District Tuberculosis and Leprosy Coordinators) of the Mwanza region, who took the extra responsibility for the intake of tuberculosis patients, collection of blood and sputum specimens, and examination of patients and relatives at their homes. Likewise, we thank all the laboratory technicians for testing the extra sputum specimens.

The study was supported by the World Health Organisation Global Tuberculosis Programme.

## References

- van Cleeff M R A, Chum H J. The proportion of tuberculosis cases in Tanzania attributable to human immunodeficiency virus. *Int J Epidemiol* 1995; 24: 637–642.
- Narain J P, Raviglione M C, Kochi A. HIV-associated tuberculosis in developing countries: epidemiology and strategies for prevention. *Tubercle Lung Dis* 1992; 73: 311–321.
- Chum H J, O'Brien R J, Chonde T M, et al. An epidemiological study of tuberculosis and HIV infection in Tanzania, 1991–1993. *AIDS* 1996; 10: 299–309.
- van den Broek J, Borgdorff M W, Pakker N G, et al. HIV-1 infection as a risk factor for the development of tuberculosis: a case-control study in Tanzania. *Int J Epidemiol* 1993; 22: 1159–1165.
- Lucas S B, De Cock K M, Hounnou A, et al. Contribution of tuberculosis to slim disease in Africa. *BMJ* 1994; 308: 1531–1533.
- Jones B E, Young S M M, Antoniskis D, et al. Relationship of the manifestations of tuberculosis to CD4 cell counts in patients with human immunodeficiency virus infection. *Am Rev Respir Dis* 1993; 148: 1292–1297.
- Githui W, Nunn P, Juma E, et al. Cohort study of HIV-positive and HIV-negative tuberculosis, Nairobi, Kenya: comparison of bacteriological results. *Tubercle Lung Dis* 1992; 73: 203–209.
- Okwera A, Whalen C, Byekwaso F, et al. Randomized trial of thiacetazone and rifampicin-containing regimen for pulmonary tuberculosis. *Lancet* 1994; 344: 1323–1328.
- Hawken M, Nunn P, Gathua S, et al. Increased recurrence of tuberculosis in HIV-1 infected patients in Kenya. *Lancet* 1993; 342: 332–337.
- Small P M, Schechter G F, Goodman P C, et al. Treatment of tuberculosis in patients with advanced human immunodeficiency virus infection. *N Engl J Med* 1991; 324: 289–294.
- Perriens J H, Colebunders R L, Karahunga C, et al. Increased mortality and tuberculosis treatment failure rate among human immunodeficiency virus (HIV) seropositive compared with HIV seronegative pulmonary tuberculosis treated with 'standard' chemotherapy in Kinshasa, Zaire. *Am Rev Respir Dis* 1991; 144: 750–755.
- Elliott A M, Halwiindi B, Hayes R J, et al. The impact of human immunodeficiency virus on response to treatment and recurrence rate in patients treated for tuberculosis: two year follow-up of a cohort in Lusaka, Zambia. *Trans Roy Soc Trop Med Hyg* 1995; 98: 9–21.
- Richter C, Koelemay M J W, Swai A B M, et al. Predictive markers of survival in HIV-seropositive and in HIV-seronegative Tanzanian patients with extrapulmonary tuberculosis. In: *Extra-pulmonary tuberculosis and HIV infection in Tanzania*. Dordrecht; ICG Printing, 1996.
- Elliott A M, Halwiindi B, Hayes R J, et al. The impact of human immunodeficiency virus on mortality of patients treated for tuberculosis in a cohort study in Zambia. *Trans Roy Soc Trop Med Hyg* 1995; 89: 78–82.
- World Health Organization. *Treatment of tuberculosis: guidelines for National Programmes*. 2nd ed. WHO/TB/97.220. Geneva; WHO 1997.
- McLarty D. Policy implications of adult morbidity and mortality. A preliminary report. University of Dar es Salaam, Tanzania. December 1993.
- Migliori G B, Borghesi A, Adriko C, et al. Tuberculosis and HIV infection association in a rural district of northern Uganda: epidemiological and clinical considerations. *Tubercle Lung Dis* 1992; 73: 285–290.
- Morgan D, Malamba S, Okpongo M, et al. HIV disease progression and median survival in a rural Ugandan cohort. Xle International Conference on AIDS. Vancouver, July 1996. Abstract Tu.B. 310.
- Salinari R K, Chiabrera F, Ceravolo C. Preliminary survival analysis of AIDS data from Goma, Zaire. *Tropical Doctor* 1990; 20: 169–170.
- Mbaga K J, Pallangyo M, Bakari M, Aris E A. Survival time of patients with Acquired immune deficiency syndrome: experience with 274 patients in Dar es Salaam. *E African Med J* 1990; 67: 95–96.
- Molina-Gamboa J D, Ponce-de-Leon S, Sifuentes-Osorino J, et al. Mycobacterial infection in Mexican AIDS patients. *J Acquir Immune Defic Syndr Hum Retrovirol* 1996; 11: 53–58.
- National Tuberculosis and Leprosy Programme of Tanzania. *Annual Reports 1990–1995*. Dar-es Salaam, Tanzania.
- Whalen C, Horsburgh, C R, Hom D, et al. Accelerated course of human immunodeficiency virus infection after tuberculosis. *Am J Respir Crit Care Med* 1995; 151: 129–135.
- Wallis R S, Vjecha M, Amir-Tahmassebi M, et al. Influence of tuberculosis on human immunodeficiency virus (HIV-1): enhanced cytokine expression and elevated beta-2-microglobulin in HIV-1 associated tuberculosis. *J Infect Dis* 1993; 167: 43–48.

**CADRE :** Les résultats du traitement de la tuberculose et la survie consécutive chez les patients infectés par le VIH, traités dans les conditions de routine du programme dans un pays en développement, ne sont guère connues. Nous avons suivi une cohorte de patients tuberculeux VIH(+) et VIH(-) au cours du traitement et apprécié leur état en matière de survie et de tuberculose trois ans après la fin du traitement à Mwanza, Tanzanie.

**MÉTHODES :** Nous avons enrôlé dans une étude épidémiologique de la tuberculose et du VIH les cas nouvellement diagnostiqués et les rechutes de tuberculose enregistrés consécutivement au cours d'une période de six mois. Le résultat du traitement repose sur l'information provenant du registre de traitement de la tuberculose. Les patients survivant après traitement ont été examinés trois ans après lors d'une interview personnelle. La cause de mort a été déterminée par «autopsie verbale.»

**RÉSULTATS :** L'enrôlement a concerné 561 patients dont 505 en vie à la fin du traitement ont pu être évalués à zans. Sauf en ce qui concerne la mortalité, l'infection par le VIH n'est pas statistiquement associée à une différence

dans les résultats du traitement. Au moment du suivi, la mortalité générale est de 19% et est associée avec infection VIH (ratio de risque [rr]: 3,7, l'intervalle de confiance [IC] à 95% : 2,6-5,2) et avec un âge égal ou supérieur à 35 ans (rr : 1,5%, IC à 95% : 1,02-2,1), mais non avec le type de tuberculose, le sexe ou la résistance initiale aux médicaments. La probabilité de survie à 4 ans, calculée par analyse des tables de survie, atteint 35% pour les patients VIH(+) par comparaison avec 90% pour les patients VIH(-). Bien qu'on n'ait pas diagnostiqué de cas de rechute, «l'autopsie verbale» suggère des taux bas et équivalents de rechute dans les deux groupes.

**CONCLUSION :** Ces résultats démontrent l'efficacité de l'approche actuelle du traitement des patients tuberculeux quel que soit leur statut VIH. Toutefois, la mortalité en relation avec le VIH reste élevée à la fois pendant et après la fin du traitement, et des études ultérieures s'imposent pour déterminer si cette mortalité pourrait être réduite par des interventions simples et accessibles dans les pays en développement.

**MARCO DE REFERENCIA :** Se sabe poco sobre el resultado del tratamiento de la tuberculosis y la posterior supervida en los pacientes infectados por VIH, en condiciones de programa en un país en desarrollo. Hemos seguido una cohorte de pacientes tuberculosos VIH positivos y VIH negativos durante el tratamiento y evaluado su estado y la evolución de la tuberculosis 3 años después de haber cumplido el tratamiento, en Mwanza, Tanzania.

**MÉTODOS :** Los casos nuevos y las recaídas de tuberculosis registrados consecutivamente durante un período de 6 meses fueron incorporados a un estudio epidemiológico de TB/VIH. Los resultados de tratamiento de la tuberculosis se obtuvieron de las informaciones de los registros. Los pacientes sobrevivientes fueron evaluados 3 años más tarde a través de entrevistas personales. Las causas de muerte se determinaron por informe verbal de la necropsia.

**RESULTADOS :** Se incorporaron al estudio 561 pacientes, de los cuales 505 estaban vivos después del tratamiento y fueron evaluados a los 3 años. Con excepción de la mortalidad, la infección por VIH no estuvo asociada estadísticamente con los diferentes resultados del trata-

miento. En el momento del seguimiento, la mortalidad total fue del 19% y estaba asociada con la infección por VIH (coeficiente de riesgo instantáneo : 3, 7 ; intervalo de confianza de 95% [IC] 2,6-5,2) y con la edad superior a los 35 años (coeficiente de riesgo instantáneo : 1, 5; IC 1,02-2,1), pero no con el tipo de tuberculosis, sexo o resistencia inicial a las drogas. De acuerdo con el análisis de tablas de vida, la probabilidad de supervivencia a los 4 años fue de 35% para los pacientes VIH positivos y de 90% para los VIH negativos. Aunque no se diagnosticaron casos de recaídas, las 'necropsias verbales' sugirieron índices de recaídas bajos y equivalentes en ambos grupos.

**CONCLUSIÓN :** Estos resultados demuestran la eficacia de los tratamientos de la tuberculosis independientemente de la asociación con VIH. Sin embargo, la mortalidad relacionada con la infección por VIH es alta durante y después del tratamiento, por lo que son necesarios estudios ulteriores para determinar si esta mortalidad puede ser reducida por intervenciones simples y factibles en los países en desarrollo.