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Factors associated with an increased case-fatality rate in HIV-infected and non-infected South African gold miners with pulmonary tuberculosis

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SUMMARY

SETTING: A gold mining company in the Free State Province, South Africa.

AIM AND DESIGN: A retrospective cohort study to investigate factors associated with an increased case-fatality rate (CFR) at 6 months in human immunodeficiency virus (HIV) positive and negative tuberculosis (TB) patients.

RESULTS: Between April 1993 and March 1997, there were 2236 men with culture-confirmed pulmonary TB in whom HIV status and treatment outcome were known. The overall CFR within the first 6 months of therapy was low (3.6%). After adjusting for confounding factors, HIV infection (OR 15.0, 95%CI 7.4–30.6), self-presentation compared to detection by the active radiological screening programme (OR 5.6, 95%CI 2.6–12.2) and presence of silicosis (OR 3.0, 95%CI 1.4–6.3) were significantly associated with an increased CFR. Opportunistic infections accounted for 56.2% (36/64) of deaths in HIV-positive men. Cryptococcal disease accounted for 75% (27/36) of deaths from opportunistic infections.

CONCLUSION: HIV infection and silicosis are both powerful risk factors for TB and are associated with an increased risk of death. Strategies aimed at reducing these two risk factors within the workforce could reduce TB incidence and mortality. In settings with functional DOTS programmes and sufficient resources, expanding the DOTS programme to include active case detection should be explored as a means of reducing TB prevalence and mortality.

KEY WORDS: tuberculosis; mortality; HIV infection; silicosis; active case detection

IN MANY sub-Saharan African countries, human immunodeficiency virus (HIV) associated tuberculosis (TB) is reaching epidemic proportions,[1] and is associated with higher mortality rates than HIV-negative TB.[2–6]

The South African gold mining industry has a reported TB incidence in excess of 2000 per 100 000 population.[7,8] After trauma, TB is the single biggest cause of mortality amongst mine workers.[9] Among South African gold miners with TB, the prevalence of HIV infection has increased rapidly, to approximately 50% of all cases.[7] Gold miners are exposed to silica-containing dust, and silicosis has been shown to be a strong risk factor for TB.[10,11] Silicosis prevalence in South African miners is high[12,13] and increasing, probably as a result of changes in labour recruitment policies resulting in a more stable and therefore older workforce than was the case a few decades ago.

In order to improve survival of TB patients, factors associated with mortality need to be identified and appropriate interventions implemented. We investigated risk factors associated with an increased case-fatality rate (CFR) at 6 months for HIV-positive and -negative TB patients.

METHODS

Study population and site

During the study period from April 1993 to March 1997, miners working for a single company in the Free State Province, South Africa, were provided with free medical care, which included a TB control programme based at a single hospital. A radiological screening programme (RSP) for TB was in place. All miners had miniature chest radiographs (100 mm × 100 mm) taken annually; those suspected of having TB were investigated with a standard sized chest

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radiograph and sputum microscopy and culture. Data was captured prospectively onto a TB database.

A retrospective cohort of all men with culture-positive pulmonary TB and known HIV status between 1 April 1993 and 31 March 1997 was established. Men with an unknown treatment outcome and those transferred to another district were excluded. Age and duration of employment were obtained from the computerised payroll records of the company. Ethics approval was obtained from the University of the Witwatersrand and Anglogold Health Services Medical Research ethics committees.

Microbiology

All patients with suspected TB had three sputum specimens collected for microscopy and culture. Concentrated specimens were stained with auramine and examined with fluorescent microscopy. Ziehl-Neelsen staining was used to confirm all positive smears. Sputum was cultured on Löwenstein-Jensen slopes and incubated for up to 6 weeks. The local laboratory used a rapid DNA probe test (Gen-Probe Inc., San Diego, CA) for initial identification of *Mycobacterium tuberculosis*. Positive cultures were sent to a reference laboratory, the South African Institute of Medical Research (SAIMR), for further species identification and drug susceptibility testing.

Case definitions

The following definitions were used for method of detection, treatment category, site of disease, drug resistance and treatment outcome.

Method of detection

Self presentation: spontaneous presentation with symptoms; active: detection through the RSP.

Treatment category

A new case was defined as a person who had never previously been treated for TB; retreatment TB was a patient who had previously been treated for TB and then presented with active TB requiring re-treatment.

Site of disease

Patients who were sputum culture positive were classified as having either pulmonary TB (PTB) alone or in combination with extra-pulmonary TB (PTB + EPTB).

Drug resistance

Single resistance: resistance to a single primary TB drug, i.e., isoniazid (H), rifampicin (R), streptomycin (S) or ethambutol (E); any resistance: resistance to any of the primary TB drugs; MDR: resistance to at least H and R.

Treatment outcome

The following case definitions were used to define outcome for initially smear-positive men. Cure: completion of treatment with documented smear conversion from positive to negative and/or negative smears within a month of completing treatment; treatment completion: completion of treatment without bacteriological confirmation of cure; and failure: smear or culture positive at end of treatment.

HIV testing and CD4 lymphocyte count

HIV testing with pre- and post-test counselling was offered to all patients presenting with suspected TB, with an uptake of more than 90%. In accordance with World Health Organization recommendations, HIV infection was diagnosed if both the screening (Enzymun-Test® Anti-HIV 1 + 2 + subtype O, Boehringer Mannheim Immunodiagnostics, Mannheim, Germany) and confirmatory ELISA (IM®$_x$ system HIV-1/HIV-2 III Plus, Abbott Diagnostics, Abbott Park, IL) were positive.

CD4 lymphocyte counts were requested at the discretion of the attending physician; those taken within the first 2 months of TB diagnosis were used in the analysis. CD4 lymphocyte estimation was performed using the manual Coulter Kit® before November 1996, after which the Coulter® STKS system was used (Coulter Corporation, Miami, FL, USA).

Treatment regimens

Prior to 1995, new TB cases were treated with RH and pyrazinamide (Z) for 5 months. Retreatment cases were treated with RHZS for 6 months. New treatment regimens were phased in from 1995, in line with national TB guidelines. New cases of TB were treated with RHZE for 2 months, followed by RH for 4 months. Retreatment TB was treated with RHZSE for 2 months, RHEZ for the third month and RHE for 5 months. Individualised treatment regimens were used for MDR TB. All TB therapy was dispensed 5 days per week and directly observed by nursing staff at the primary health care clinic.

Cause of death

The most likely cause of death was determined by reviewing clinical records and results of limited autopsies of the heart and lungs, which were mandated by law for purposes of compensation. Cause of death was classified as TB, pneumonia, HIV-associated opportunistic infections, and other. The autopsy cause of death was used when the autopsy findings and clinical cause of death were compatible, or where autopsy revealed pathology sufficiently extensive as to be the cause of death not diagnosed clinically. For the small proportion of cases without autopsy data, the clinical cause of death was used.

Radiological disease

A zone score was used to assess the extent of TB disease on the chest radiograph at the time of diagnosis. Each lung was divided into zones by dividing the dis-

tance between the apex of the lung and the ipsilateral diaphragm by three, and recording the total number of zones with disease for each patient. The radiological pattern of TB was classified as 1) typical, if infiltrates or fibrocavitation occurred predominantly in the upper lobes or apical segment of the lower lobes, or 2) atypical, if the changes, including cavitation, occurred predominantly in the lower lobes, excluding the apical segments or if there was lobar consolidation, isolated thoracic lymphadenopathy, or a normal chest radiograph. The presence or absence of silicosis was also noted for each chest radiograph (International Labour Organisation category 1/1 or greater). Two readers scored the chest radiographs in a blinded fashion. Where results were discordant a result was obtained by consensus.

Statistical methods

STATA 6.0 (STATA Corporation, College Station, TX) and Epi-Info 6.02 (CDC, Atlanta, GA) software were used for analysis. Associations between categorical variables were investigated using χ^2 or Fisher's exact tests as appropriate. Differences between groups were expressed as odds ratios (OR) with 95% confidence intervals (95%CI). Student's *t*-test was used to test for differences in means of continuous variables between groups. A Mantel Haenszel test and multiple logistic regression were used to investigate for confounding between variables. Likelihood ratio tests were used to test for overall significance for inclusion of each variable in the logistic regression model.

RESULTS

Between April 1993 and March 1997, 2578 patients with culture confirmed pulmonary TB had a known HIV status; 167 men with unknown treatment outcomes and 175 who were transferred to another district before completion of TB treatment were excluded from further analysis. The remaining 2236 (86.7%) patients were analysed with respect to the CFR at 6 months. The overall CFR was 3.6% (81/2236), and increased significantly from 1.6% (17/1037) for the period 1993–1994 to 5.3% (64/1199) for the period 1995–1996 ($P < 0.00001$).

Patient characteristics

Differences in base-line characteristics between HIV-positive and HIV-negative men are shown in Table 1. There were 608 (27.2%) HIV-positive and 1628 (72.8%) HIV-negative men. Chest radiographs at diagnosis were available for 1466 (90%) HIV-negative and 548 (90.1%) HIV-positive men. HIV-positive men were significantly younger, were more likely to self present and to have new rather than retreatment TB. The extent of radiographic TB disease, assessed by a zone score, was not significantly different between HIV-positive and HIV-negative men. Significantly more HIV-positive men had died within the first 6 months of TB treatment compared to HIV-negative men (10.5% vs 1.0%, $P < 0.0001$). Treatment outcomes among men who were initially smear-positive and who survived to the end of treatment differed significantly by HIV status, in that there was a higher proportion of treatment cures among the HIV-positive group ($P < 0.00001$). This difference was mainly due to confounding by time period, as both the proportion of HIV-positive men ($P < 0.0001$) and documentation of cure ($P < 0.0001$) increased after 1995. After adjusting for year of entry into the study there was no significant association between HIV status and treatment outcome ($P = 0.97$).

Table 1 Differences in base-line characteristics between HIV-positive and HIV-negative patients

	HIV-negative *n* (%)	HIV-positive *n* (%)	*P* value
Total	1628 (100)	608 (100)	
Mean age	42.8	40.5	<0.00001*
How detected			
RSP	973 (59.8)	252 (41.4)	<0.00001
Self presentation	655 (40.2)	356 (58.6)	
Sputum status			
Negative	364 (22.4)	141 (23.2)	0.7
Positive	1263 (77.6)	466 (76.8)	
Treatment category			
New	1209 (74.3)	489 (80.4)	<0.001
Retreatment	419 (25.7)	119 (19.6)	
Vital status (6 months)			
Alive	1611 (99.0)	544 (89.5)	<0.00001
Dead	17 (1.0)	64 (10.5)	
Treatment outcomes†			
Cured	902 (56.2)	364 (69.5)	<0.00001
Completed	671 (41.8)	155 (29.6)	
Failure	32 (2.0)	5 (1.0)	
Zone score			
⩽3	790 (53.9)	293 (53.5)	0.9
>3	676 (46.1)	255 (46.5)	
Silicosis			
Absent	1281 (87.4)	509 (92.9)	<0.0001
Present	185 (12.6)	39 (7.1)	

* Student test for differences between continuous variables.
† Treatment outcomes for smear positive men who survived to completion of treatment.
RSP = radiological screening programme.

Risk factors for increased CFR

Unadjusted and adjusted odds ratios for associations between HIV status, method of detection, sputum status, age group, treatment category, extent of disease and presence of silicosis and the CFR at 6 months are shown in Table 2. HIV positivity, smear positivity, self-presentation, extent of disease >3 zones and presence of silicosis were all significantly associated with a higher CFR in the univariate analysis. Active case detection of TB by the RSP compared to self-presentation was associated with a significantly lower CFR in both HIV-negative and HIV-positive men (Figure). After multivariate analysis,

Table 2 Associations between risk factors and case fatality rate at 6 months; unadjusted and adjusted odds ratios (OR) and 95% confidence intervals (CI)

		Unadjusted		Adjusted	
	Deaths/total	OR	95%CI	OR	95%CI
HIV status					
Negative	17/1628	1		1	
Positive	64/608	11.15	6.3–20.1	15.0	7.4–30.6
How detected					
RSP	12/1225	1		1	
Self presentation	69/1011	7.4	3.9–14.6	5.6	2.6–12.2
Sputum status					
Positive	72/1729	1		1	
Negative	9/505	0.4	0.2–0.9	0.9	0.4–2.0
Treatment category					
New	55/1698	1		1	
Retreatment	26/538	1.5	0.9–2.5	1.5	0.8–2.8
Age group (years)					
0–29	6/147	1.4	0.5–3.7	1.1	0.4–3.0
30–39	23/780	1		1	
40–49	36/885	1.4	0.8–2.5	1.2	0.6–1.9
50+	12/409	1.0	0.5–2.1	1.0	0.4–2.3
Extent of disease					
⩽3 zones	32/1083	1		1	
>3 zones	47/931	1.8	1.1–2.8	1.1	0.6–1.9
Silicosis					
Absent	64/1790	1		1	
Present	15/224	1.9	1.0–3.6	3.0	1.4–6.3
Drug resistance					
F/S	59/1758	1		1	
S/R	5/131	1.1	0.4–3.1	0.9	0.3–3.0
MDR	1/17	1.8	0.0–13.4	1.2	0.1–13.8
Any	8/173	1.4	0.6–3.1	1.2	0.5–3.0

RSP = radiological screening programme. All variables were included in the multivariate analysis; F/S = fully susceptible; S/R = single resistance; MDR = multidrug resistance; Any = resistance to any TB drug.

HIV infection, self-presentation compared to detection by the RSP and the presence of silicosis were significantly associated with an increased CFR. Smear status and extent of disease were no longer significantly associated with mortality after controlling for confounding by method of detection (Mantel Haenszel test OR 0.58, 95%CI 0.28–1.18 and OR 1.2, 95%CI 0.76–1.92, respectively). The presence of sin-

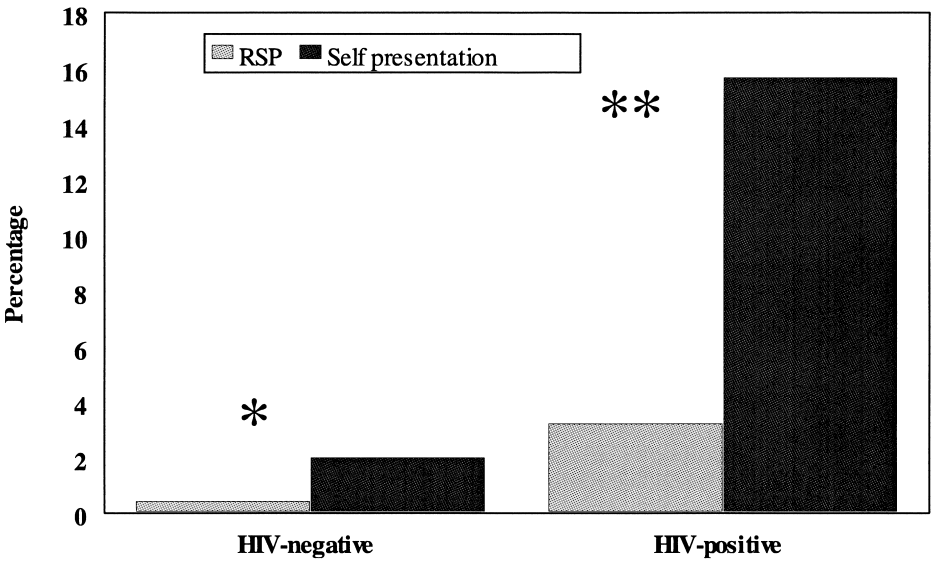

Figure Case-fatality rate in HIV-negative and HIV-positive men stratified by method of detection. RSP = detection by the active radiological screening programme. *$P < 0.001$, ** $P < 0.00001$.

gle, MDR or resistance to any primary TB drug was not associated with an increased CFR compared to fully susceptible TB. Standard treatment regimens were used for 94.1% (2105/2236) of all patients. Ethambutol containing regimens were associated with a significantly higher CFR (6.2%, 59/950 vs 1.2%, 14/1155). This difference was mainly due to confounding by time period, as the proportion of HIV-positive men, self-presentation and use of ethambutol-containing regimens increased after 1995. After adjusting for year of entry into the study, HIV status and method of detection, there was no significant association between treatment regimen and outcome (Mantel Haenszel test OR 2.3, 95%CI 0.82–6.42).

Risk factors for a higher CFR at 6 months in HIV-negative and HIV-positive men were further investigated separately. Associations between method of detection, sputum status, treatment category, extent of disease and presence of silicosis and CFR were investigated for HIV-negative men (data not shown). Self-presentation compared to detection by the RSP (adjusted OR 8.0, 95%CI 1.8–36.5) and presence of silicosis compared to absence of silicosis (adjusted OR 3.5, 95%CI 1.1–11.0) were the only two factors significantly associated with increased CFR in HIV-negative men.

In addition to the above factors, time period, CD4 group, site of disease and radiological pattern were analysed for associations with increased CFR in HIV-positive men (Table 3).

Self-presentation compared to detection by the RSP (adjusted OR 4.3, 95%CI 1.9–9.6), PTB + EPTB compared to PTB alone (adjusted OR 3.1, 95%CI 1.7–5.6) and presence of silicosis compared to absence of silicosis (OR 2.8, 95%CI 1.17–6.8), were all significantly predictive of a higher CFR. Smear-negative compared to smear-positive disease was associated with a significantly lower CFR (adjusted OR 0.32, 95%CI 0.13–0.81). Although a CD4 lymphocyte count $<200 \times 10^6$/L compared to CD4 lymphocyte count $\geqslant 200 \times 10^6$/L was associated with a significantly higher CFR (OR 6.21, 95%CI 3.12–12.48), CD4 counts were not used in the multivariate analysis as they were not obtained uniformly or randomly.

Cause of death

Clinical records were available on all of the 81 men who died within the first 6 months of TB treatment; the results of limited autopsies were available for 69 (85.2%). The cause of death was significantly different between HIV-negative and HIV-positive men (Table 4). A significantly higher proportion of deaths in the HIV-negative men were due to TB than in the HIV-positive group (64.7% and 21.9%, respectively, $P < 0.01$). This reflects the high risk of death from other causes in HIV-positive men rather than a high 6-month CFR in HIV-negative men. Deaths from TB occurred within the first 2 months of treatment in 90.9% and 85.7% of HIV-negative and HIV-positive men, respectively. In HIV-positive men, death from opportunistic infections accounted for 56.2% (36/64) of deaths and occurred after the first 2 months of treatment in 88.9% of the men (32/36). The majority of deaths from opportunistic infections occurred in HIV-positive men with a CD4 lymphocyte count of $<200 \times 10^6$/L (31/36, 86.1%).

Table 3 Associations between risk factors and case fatality rate at 6 months in HIV-positive men; unadjusted and adjusted odds ratios (OR) and 95% confidence intervals (CI)

	Deaths	Unadjusted		Adjusted	
	n	OR	95%CI	OR	95%CI
How detected					
RSP	8/252	1		1	
Self presentation	56/356	5.7	2.5–13.3	4.3	1.9–9.6
Sputum status					
Positive	58/466	1		1	
Negative	6/141	0.3	0.1–0.8	0.3	0.1–0.8
Time period					
1993–1994	10/176	1		1	
1995–1996	54/432	2.4	1.1–5.1	1.7	0.8–3.7
Treatment category					
New	46/489	1		1	
Retreatment	18/119	1.7	0.9–3.2	1.5	0.8–2.9
Age group (years)					
0–29	5/62	0.9	0.3–2.7	0.9	0.3–2.6
30–39	21/239	1		1	
40–49	30/220	1.6	0.9–3.1	1.2	0.6–2.3
50+	7/83	1.0	0.4–2.5	0.5	0.2–1.4
Extent of disease					
⩽3 zones	27/293	1		1	
>3 zones	37/255	1.7	0.95–2.9	0.97	0.5–1.7
Site of disease					
PTB alone	25/355	1		1	
PTB + EPTB	39/193	3.3	1.9–6.0	3.1	1.7–5.6
Radiological pattern					
Typical	45/450	1		1	
Atypical	19/98	2.2	1.2–4.1	1.4	0.7–2.8
Silicosis					
Absent	54/509	1		1	
Present	10/39	2.9	1.2–6.7	2.8	1.2–6.8
CD4 group*					
⩾500	5/67	3.7	0.97–13.4		
200–499	11/109	5.1	1.8–15.0		
<200	41/107	28.2	11.5–72.3		

* CD4 lymphocyte count $\times 10^6$/L. CD4 group was excluded from the multivariate analysis as they were not obtained uniformly or randomly.
PTB = pulmonary TB; PTB + EPTB = presence of extra-pulmonary TB; RSP = radiological screening programme.

Table 4 Cause of death in HIV-negative and HIV-positive men

Cause of death	HIV-positive *n* (%)	HIV-negative *n* (%)	*P* value
Number of deaths	64 (100)	17 (100)	
TB	14 (21.9)	11 (64.7)	<0.01
Pneumonia	10 (15.6)	2 (11.8)	>0.05
Opportunistic infections*	36 (56.2)	0 (0)	<0.001
Other	4 (6.3)	4 (23.5)	>0.05

* Cryptococcal disease (meningitis/pneumonitis) 27 (75%); *Pneumocystis carinii* pneumonia 3 (8.3%); lymphocytic interstitial pneumonitis 1 (2.8%); unconfirmed 5 (13.9%).

Table 5 All cause- and disease-specific case-fatality rate (TB and opportunistic infections) stratified by method of detection in HIV-positive and HIV-negative men

	HIV-negative				HIV-positive			
	Passive (n = 655) n dead	RSP (n = 973) n dead	OR	95%CI	Passive (n = 356) n dead	RSP (n = 252) n dead	OR	95%CI
All causes	13	4	4.9	1.5–20.7	56	8	5.7	2.5–13.3
TB	10	1	15.1	2.1–655	11	3	2.6	0.7–14.9
Opportunistic infections	—	—		—	33	3	8.5	2.6–43.6

RSP = radiological screening programme; OR = odds ratio; CI = confidence interval.

In HIV-negative men self-presentation was associated with a significantly higher CFR from TB (OR 15.1, 95%CI 2.1–655), while in HIV-positive men self-presentation was associated with a higher CFR from opportunistic infections (OR 8.5, 95%CI 2.6–43.6) but not TB (OR 2.6, 95% CI 0.7–14.9) (Table 5). Miners with silicosis had a significantly higher CFR from TB (5/39) compared to those without silicosis (9/509, unadjusted OR 8.2, 95%CI 2.2–29.0).

DISCUSSION

This study demonstrated a low overall CFR (3.6%) within the first 6 months of tuberculosis treatment in a high incidence setting. HIV infection, self-presentation compared to detection by the RSP and presence of silicosis were all significantly associated with a higher CFR.

The overall CFR more than tripled, from 1.6% in the first half of the study period to 5.3% in the second half. This increase in CFR corresponded with the advancing HIV epidemic. Despite the high TB incidence, the CFR rates of 1.0% and 10% in HIV-negative and HIV-positive men, respectively, were similar to those in other published data for gold miners,[8] but were low in comparison to the general population from South Africa[14,15] and other sub-Saharan African countries.[3,15,16] It has been suggested that the increasing TB mortality in the general population may be due in part to the overburdening of health care services as a result of the impact of the HIV epidemic on TB case rates.[14] Factors that may have contributed to a lower CFR in gold miners would include a healthy worker effect, ready access to good health care, high treatment completion rates,[15,17,18] and active case detection.[19]

Active case detection has been widely held to be of limited value, including in high prevalence settings, because of the cost and fears that active case detection may compromise the implementation of the DOTS strategy. However, it has recently been advocated that in high prevalence settings the implementation of active case detection as an extension of the DOTS strategy may be a cost-effective intervention that may yield enormous benefits in averting TB cases and deaths.[19] Mass miniature radiography, symptom and sputum screening are possible methods of active case detection. The presence of a large-scale routine RSP for TB in this study is unique. The prevalence of TB detected by the RSP has remained high but relatively constant over time, despite the rising incidence of TB associated with the increasing HIV prevalence.[7] Men who were detected by the RSP had a significantly lower CFR (1%) compared to those who self presented (6.8%). However, it is likely that selection bias accounted for a large part of the observed difference in CFR, i.e., men who self presented were more likely to have advanced HIV disease or silicosis, and therefore accelerated progression of TB, thereby reducing the likelihood of detection by the annual RSP and increasing the risk of death.

In settings with functional DOTS programmes and sufficient resources, expanding the DOTS programme to include active case detection, particularly for high-risk groups, should be explored as a means of reducing TB prevalence and mortality. High-risk groups that may be suitable for active screening programmes would include prisoners,[20,21] immigrants from high prevalence countries,[22,23] silica exposed workers and other occupational groups. The use of active screening programmes in general populations with a high prevalence of TB should await studies that confirm that it is both feasible and cost-effective in this setting.

HIV infection, and particularly the degree of immunosuppression in HIV-positive individuals with pulmonary TB, has been reported as a major determinant of mortality.[6,8] In this study, TB was confirmed as an early cause of mortality, i.e., within the first 2 months of treatment in HIV-positive men. By contrast, most deaths from opportunistic infections occurred after the first 2 months of treatment. Cryptococcal disease accounted for the majority of deaths from opportunistic infections. This was similar to that reported in another group of South African gold miners,[8] but contrasts with those from other sub-Saharan African countries where bacterial infections[3] or other opportunistic infections[24] tend to be the cause of death later on in the course of TB treatment. The difference in death from bacterial infections may be due to the quality of sanitation and health care available for miners compared to the general popula-

tion in most sub-Saharan African countries. Chemoprophylaxis with trimethoprim-sulfamethoxazole (TMP-SMX) has been shown to prevent *Pneumocystis carinii* pneumonia, bacterial infections and cerebral toxoplasmosis.[25] A significant reduction in morbidity and mortality in West African HIV-positive TB patients given TMP-SMX chemoprophylaxis has been reported.[26] Chemoprophylaxis with TMP-SMX might have provided benefit to 13 (20.3%) of 64 HIV-positive men who died of bacterial pneumonia (10) or pnemocystosis (3). This contrasts with results of an autopsy study reported from West Africa, in which eight (57%) of 14 adult HIV-positive TB patients died of causes that were potentially preventable with TMP-SMX.[24] In our setting, therefore, TMP-SMX chemoprophylaxis for HIV-positive TB patients may be less effective in reducing mortality.

Another major determinant of a higher CFR in both HIV-negative and HIV-positive men in this study was the presence of silicosis. A possible limitation of the study is that the diagnosis of silicosis in the presence of TB is difficult due to similarities in radiographic presentation. However, a recent comparative radiological and autopsy study of silicosis in the current study population showed no significant differences in sensitivity and specificity in the radiological diagnosis of silicosis because of TB scarring.[13] Silicosis is a strong risk factor for TB and has a combined effect with HIV infection which is multiplicative.[27] It has previously been reported that men with silicosis who had an occurrence of TB had a higher risk of death compared to those with silicosis who had not had TB.[28] However, a significantly increased mortality rate in both HIV-negative and positive TB patients with silicosis compared to non-silicotic TB patients has not previously been reported. These results have important implications for silica exposed workers, particularly in high TB incidence settings. The presence of silicosis may accelerate the progression of TB similarly to HIV infection. This may explain why men with silicosis were more likely to self-present than be detected by the RSP (data not shown) and have a higher CFR. Due to the high prevalence of silicosis and HIV infection in this workforce and their combined effect on TB incidence and mortality, improvement in the dust control programmes should be a high priority.

In summary, HIV infection and silicosis are both powerful risk factors for TB and are associated with an increased risk of death. Strategies aimed at reducing these two risk factors within the workforce could reduce TB incidence and mortality. High rates of successful treatment completion and cure under a DOTS programme would contribute to a lower TB mortality. In settings with functional DOTS programmes and sufficient resources, expanding the DOTS programme to include active case detection should be explored as a means of reducing TB prevalence and mortality.

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RÉSUMÉ

CADRE : Une compagnie de mines d'or dans la Province de Free State en Afrique du Sud.
OBJECTIF ET SCHÉMA : Investiguer, dans une étude rétrospective de cohorte, les facteurs associés à une augmentation du taux de létalité (CFR) à 6 mois chez les patients tuberculeux séropositifs ou séronégatifs pour le VIH.
RÉSULTATS : Entre avril 1993 et mars 1997, il y a eu 2236 hommes atteints d'une TB pulmonaire confirmée par la culture et chez qui le statut du VIH et le résultat du traitement étaient connus. Le CFR global au cours des 6 premiers mois du traitement fut bas (3,6%). Après ajustement pour les facteurs confondants, l'infection VIH (OR 15,0 ; IC 95% 7,7–30,6), le fait de se présenter spontanément plutôt que dans le cas d'une détection par un programme de dépistage radiologique actif (OR 5,6 ; IC 95% 2,6–12,2) et la présence de silicose (OR 3,0 ; IC 95% 1,4–6,3) sont associés de manière significative à un accroissement du CFR. Les infections opportunistes sont responsables de 56,2% (36/64) des décès chez les hommes séropositifs pour le VIH. La cryptococcose rend compte de 75% (27/36) des décès par infections opportunistes.
CONCLUSION : L'infection par le VIH et la silicose sont tous deux de puissants facteurs de risque pour la TB et associés à un accroissement du risque de décès. Des stratégies visant à réduire ces deux facteurs de risque au sein de la main d'œuvre pourraient réduire l'incidence de la TB et la mortalité. Dans des cadres dotés de programmes fonctionnels du DOTS et de ressources suffisantes, l'extension du programme DOTS pour y inclure une détection active des cas devrait être explorée comme moyen de réduction de la prévalence et de la mortalité de la TB.

RESUMEN

MARCO DE REFERENCIA : Una compañía minera de oro en la Provincia Free State, Sud-África.
OBJETIVO Y MÉTODO : Investigar los factores asociados con una tasa aumentada de letalidad (CFR) a los 6 meses en pacientes TB, VIH positivos y negativos, en un estudio retrospectivo de cohortes.
RESULTADOS : Entre abril de 1993 y marzo de 1997 habían 2236 varones con TB pulmonar con cultivo positivo en quienes se conocía el estatus del VIH y el resultado del tratamiento. La CFR total en los 6 primeros meses fue baja (3,6%). Después de ajustar los factores confundentes, la infección por VIH (OR 15,0, IC95% 7,4–30,6), la consulta espontánea comparada con la detección por programas de catastro radiológico (OR 5,6, IC95% 2,6–12,2) y la presencia de silicosis (OR 3,0, IC95% 1,4–6,3) estaban asociadas significativamente con un aumento de la CFR. Las infecciones oportunistas constituyeron el 56,2% (36/64) de las muertes en los hombres VIH positivos. La enfermedad por cryptococus representó el 75% (27/36) de las muertes por infecciones oportunistas.
CONCLUSIÓN : La infección por el VIH y la silicosis son poderosos factores de riesgo para la TB y están asociadas con un riesgo aumentado de muerte. Las estrategias orientadas a reducir estos dos factores de riesgo en los trabajadores podrían disminuir la incidencia y la mortalidad de la TB. En contextos con programas funcionales de DOTS y suficientes recursos, la expansión de los programas de DOTS para incluir la detección activa de casos podría ser explorada como medio para reducir la prevalencia y la mortalidad de la TB.