

Comparison of AIDS Progression and Survival in Persons with Pulmonary versus Extrapulmonary Tuberculosis in Los Angeles

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ABSTRACT

The objective of this research was to compare the demographics, acquired immune deficiency syndrome (AIDS) progression, and survival in persons with AIDS with pulmonary tuberculosis (PTB) versus extrapulmonary tuberculosis (EPTB), because there are limited population-based data on this topic. A population-based longitudinal study with 3 years of follow-up was performed. Data were collected every 6 months from medical records of persons with AIDS and TB treated at private and public medical facilities throughout Los Angeles County (LAC). Participants included a population-based sample of 216 persons with AIDS and PTB and 166 persons with AIDS and EPTB (including 113 persons with both PTB and EPTB), with an AIDS diagnosis reported in 1993. Compared to persons with AIDS with PTB, persons with AIDS and EPTB were 2.2 times more likely to be Latino than white (95% confidence intervals [CIs]: 1.2, 4.0) and 1.7 times more likely to be foreign-born (95% CIs: 1.1, 2.5). Compared to persons with AIDS with PTB, persons with AIDS and EPTB had similar antiretroviral and PCP prophylaxis use; lower CD4 counts at time of AIDS diagnosis ($p = 0.0004$); no differences in CD4 counts over the total follow-up period ($p = 0.4$); higher rates of total opportunistic infections (OIs) (incidence density ratio [IDR] = 2.0; 95% CIs: 1.6, 2.4); and comparable survival curves ($p = 0.07$). Persons with AIDS and EPTB had a more complicated medical course with lower CD4 counts at time of AIDS diagnosis and more OIs over the follow-up period than persons with AIDS and PTB, however the survival profiles for the two groups were comparable.

INTRODUCTION

THE DIFFERENCES BETWEEN the impact of pulmonary tuberculosis (PTB) and extrapulmonary tuberculosis (EPTB) on acquired immune deficiency syndrome (AIDS) progression and survival are not well understood.¹ Two

clinic-based studies that did not distinguish by tuberculosis (TB) type in detail showed disease acceleration and reduced survival in a group of human immunodeficiency virus (HIV)-infected persons with TB² and a separate group of persons with AIDS,³ while another showed minimal influence of TB on HIV disease progression

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and mortality.⁴ Although EPTB is considered a more severe form of disease than PTB in clinical staging systems,⁵ there is limited population-based research with sufficient sample sizes and follow-up data that compares the progression of AIDS in persons with PTB and EPTB. This study compares the demographics, immunologic outcomes, rates of opportunistic infection, and survival for a population-based sample of persons with AIDS with PTB and EPTB using follow-up data over a 3-year period.

MATERIALS AND METHODS

The study group in this investigation included all persons reported with AIDS (1993 AIDS case definition) in Los Angeles County (LAC) in 1993 and who were first diagnosed with TB of any type from 1991 through 1993. The LAC AIDS registry was matched with the LAC TB registry to ensure that TB data were complete for persons reported with AIDS during the study period. Persons diagnosed with TB and AIDS were further subdivided into two groups: (1) persons who were reported with AIDS in 1993 who had one or more episodes of PTB between 1991 and 1993 and (2) persons who were reported with AIDS in 1993 who had at least one episode of EPTB between 1991 and 1993 with or without any episodes of PTB. Persons with a previously active TB infection diagnosed before 1991 were excluded.

Medical records were reviewed every 6 months beginning in January 1994 for 3 years or until death for all persons with AIDS and TB of any type. All follow-ups ended in October 1996. Trained medical record abstractors extracted data on demographics; CD4 counts; use of anti-retroviral (ARV) medications and *Pneumocystis carinii* pneumonia (PCP) prophylaxis; the development of opportunistic infections, and death.

A control group was constructed of persons reported with AIDS in 1993 with no history of TB of any type from 1991 to 1996. Medical record reviews were not conducted for the control group after an AIDS diagnosis except to confirm the date of death. The control group was further divided into clinical and immunologic AIDS cases for purposes of comparison.

The goal of the analysis was to compare the

demographic, clinical, and mortality characteristics of persons with AIDS and EPTB to persons with AIDS and PTB. For the EPTB, PTB, and non-TB/AIDS control group, univariate analyses of demographic and HIV-risk characteristics are presented. Odds ratios (OR) and 95% confidence intervals (CIs) were calculated to compare the demographics of persons with EPTB to the PTB group and the combined TB groups to the non-TB/AIDS control group.

The mean, median, and frequency distribution of CD4 counts are presented at the time of an AIDS diagnosis and at 6 months, 1, 2, and 3 years of follow-up for the coinfecting persons. Because of the nonnormal distribution of CD4 counts, the nonparametric Wilcoxon rank-sum test was used to compare the CD4 counts at AIDS diagnosis of the two TB groups to each other and the combined TB groups to the non-TB/AIDS group. A mixed linear model was used to assess differences in the decline of CD4 counts over time for the two TB groups while accounting for differing lengths of follow-up, dissimilar intervals between follow-up, and missing data on CD4 counts.

The number of opportunistic infections (OI) per 100 person-months for the two TB groups are presented and only the first occurrence of an OI is included in the rate calculation, because subsequent events are likely to be recurrences of latent infections.⁶ Person-time for the OI rates was calculated based on the time from the date of the first TB diagnosis to the date of first OI occurrence or to death or to the date last seen in a medical setting. Incidence density ratios (IDRs) and 95% CIs were calculated to compare the OI rates in the two TB groups.

Kaplan-Meier survival curves were constructed to evaluate the probability of survival for the four study groups from time of AIDS diagnosis. A Cox proportional hazards model was also fitted to evaluate the predictive value of numerous factors on survival for the PTB/AIDS and EPTB/AIDS groups combined, while controlling for confounding. Analyses were conducted with and without the 14 multidrug-resistant (MDR) TB cases. The results in the two groups were almost identical so the combined results are presented. All analyses were conducted using SAS Version 6.10 (SAS Institute, Cary, NC).

RESULTS

Of the 6,287 AIDS cases reported in LAC in 1993, 6.1% (*n* = 415) had either PB or EPTB diagnosed from 1991 to 1993. Follow-up was completed for 382 (92%) persons, and of these, 216 or 56% had PTB only, and 166 or 43% had EPTB with or without pulmonary involvement. Table 1 shows the demographic characteristics

of the EPTB/AIDS, PTB/AIDS, and non-TB/AIDS groups. When compared to persons with AIDS with PTB, persons with AIDS who were diagnosed with EPTB were 2.2 times (95% CIs: 1.2, 4.0) more likely to be Latino than white; 1.7 times more likely to be foreign-born (95% CIs: 1.1, 2.5); and were slightly younger. When comparing persons with AIDS with TB of any type to persons reported with AIDS

TABLE 1. DEMOGRAPHIC CHARACTERISTICS OF PERSONS WITH AIDS WITH PTB , EPTB AND NON-TB AIDS CASES

| | AIDS/EPTB (n = 166) | | AIDS/PTB (n = 216) | | OR ^a | 95% CI | Non-TB/AIDS (n = 5160) | | OR ^b | 95% CI | |
|---------------------------------|------------------------|----|-----------------------|----|-----------------|------------|---------------------------|----|-----------------|------------|-------|
| | N | % | N | % | | | N | % | | | |
| Race/Ethnicity | | | | | | | | | | | |
| White | 20 | 12 | 41 | 19 | referent | | 2,554 | 50 | referent | | |
| Black | 48 | 29 | 79 | 37 | 1.2 | (0.7, 2.4) | 1,022 | 20 | 5.2 | (3.9, 6.9) | |
| Latino | 93 | 56 | 87 | 40 | 2.2 | (1.2, 4.0) | 1,464 | 28 | 5.1 | (3.9, 6.8) | |
| Other | 5 | 3 | 7 | 3 | 1.5 | (0.4, 5.2) | 107 | 2 | 4.7 | (2.6, 8.5) | |
| Unknown | 0 | 0 | 2 | 1 | — — | | 13 | 0 | — — | | |
| Gender | | | | | | | | | | | |
| Male | 157 | 95 | 204 | 94 | 1.0 | (0.4, 2.5) | 4,781 | 93 | 1.4 | (0.9, 2.1) | |
| Female | 9 | 5 | 12 | 6 | | | 379 | 7 | | | |
| Country of Birth | | | | | | | | | | | |
| Foreign-born | 81 | 49 | 76 | 35 | 1.7 | (1.1, 2.5) | 1,121 | 22 | 2.4 | (1.9, 2.9) | |
| USA | 81 | 49 | 127 | 59 | | | 3,522 | 68 | | | |
| Unknown | 4 | 2 | 13 | 6 | | | 517 | 10 | | | |
| Mode of HIV Exposure | | | | | | | | | | | |
| MSM ^c | 80 | 48 | 97 | 45 | referent | | 3,823 | 74 | referent | | |
| IDU ^d | 25 | 15 | 42 | 19 | 0.7 | (0.4, 1.3) | 420 | 8 | 3.4 | (2.6, 4.6) | |
| MSM & IDU | 33 | 20 | 32 | 15 | 1.3 | (0.7, 2.2) | 334 | 7 | 4.2 | (3.2, 5.6) | |
| NIR ^e | 20 | 12 | 40 | 19 | 0.6 | (0.3, 1.1) | 245 | 5 | 5.3 | (4.0, 7.1) | |
| Other | 8 | 5 | 5 | 2 | 1.9 | (0.6, 6.1) | 338 | 7 | 0.8 | (0.5, 1.5) | |
| Facility Type of AIDS Diagnosis | | | | | | | | | | | |
| Public/ federal | 120 | 72 | 161 | 75 | 0.9 | (0.6, 1.5) | 2,000 | 39 | 4.5 | (3.6, 5.6) | |
| Private | 44 | 27 | 54 | 25 | | | 3,132 | 61 | | | |
| Unknown | 2 | 1 | 1 | 0 | | | 28 | 1 | | | |
| Age at AIDS Diagnosis | | | | | | | | | | | |
| | | | | | | T | P | | T | P | |
| <20 | 1 | 1 | 3 | 1 | | | 19 | <1 | | | |
| 20-29 | 42 | 25 | 49 | 23 | | | 896 | 17 | | | |
| 30-39 | 77 | 46 | 83 | 38 | | | 2,278 | 44 | | | |
| 40-49 | 33 | 20 | 50 | 23 | | | 1,338 | 26 | | | |
| 50-59 | 11 | 7 | 23 | 11 | | | 468 | 9 | | | |
| 60+ | 2 | 1 | 8 | 4 | | | 161 | 3 | | | |
| Mean | | 35 | | 38 | | 2.3 | 0.02 | | 38 | -2.8 | 0.005 |

^aOdds ratios comparing the AIDS/EPTB group to AIDS/PTB group.

^bOdds ratios comparing TB groups combined to non-TB/AIDS group.

^cMSM: men who have sex with men.

^dIDU: injection drug user.

^eNIR: no identified risk.

AIDS, acquired immunodeficiency syndrome; TB, tuberculosis; EPTB, extrapulmonary tuberculosis; PTB, pulmonary tuberculosis; HIV, human immunodeficiency virus.

without TB, persons with TB were more likely to be African American, Latino, or a race other than white, foreign-born, an injection drug user (IDU), or a man who has sex with men who is also an IDU or has no identified HIV risk; and received an AIDS diagnosis at a public medical facility (see Table 1).

The results from the mixed effects model show a significantly lower CD4 count at time of AIDS diagnosis for the EPTB group compared to the PTB group while the results from the Wilcoxon rank sum test shows no difference. Other results from the Wilcoxon rank sum test show that the mean CD4 count was lower for the EPTB group compared to the PTB group at 6-months ($p = 0.009$) and 1-year ($p = 0.0006$) follow-up points with no differences seen at 2 and 3 years of follow-up. The decline in CD4 counts over the whole follow-up period was also not significantly different for the two TB groups ($p = 0.4$) (see Table 2).

Among persons with AIDS and PTB, 39% had been taking antiretroviral medications at some time and 42% had been on PCP prophylaxis, proportions that were not statistically different from persons with AIDS and EPTB (39% and 46%, respectively). Of the 179 episodes of EPTB in the 166 persons with AIDS and EPTB, 56 (31%) were in the lymph nodes and 27 (15%) were in the blood, and the remaining were at other sites.

Among persons with AIDS and EPTB with or without pulmonary involvement, the most common opportunistic infections that occurred during the follow-up period were PCP, candidiasis of the esophagus, *Mycobacterium avium*, toxoplasmosis, herpes simplex, and wasting (Table 3). As shown in the incidence density ratios (IDRs), OIs that were statistically more common in persons with AIDS with EPTB compared to persons with PTB only, included cryptosporidiosis, HIV encephalopathy, herpes simplex, *Mycobacterium avium* (specified and unspecified), and toxoplasmosis. The rate for total OIs was also higher in the EPTB group compared to the PTB group with an IDR = 2.0 (95% CIs: 1.6, 2.4). Among all persons with AIDS and TB and a history of any antiretroviral use, there was a tendency towards slightly lower OI rates.

The median survival from time of AIDS diagnosis was 30 months for the EPTB group, 43

months for the PTB group, 22 months for the non-TB clinical AIDS group, and 54 months for the non-TB immunologic AIDS group. The Kaplan-Meier survival curves are shown in Figure 1 for all four groups. As shown in Figure 1, the EPTB group had a more rapid progression to death than the PTB group and the non-TB immunologic AIDS control group, while the non-TB clinical group had the worst survival pattern. The survival curve for the EPTB group was not significantly different from the survival curve for the PTB group ($p = 0.07$). The survival pattern for the non-TB clinical AIDS group was significantly worse compared to the PTB group ($p = 0.0001$), the EPTB group ($p = 0.0002$), and both TB groups combined ($p = 0.0001$). The survival pattern for the non-TB immunologic group was statistically better compared to the EPTB group ($p = 0.0001$) and both groups combined ($p = 0.0001$) (see Fig. 1).

As shown in the proportional hazards regression model in Table 4, persons with TB and AIDS who were 40 years of age or older and had CD4 counts less than 200 cells per microliter at time of AIDS diagnosis and had no history of ARV use, had a higher hazard of death than persons without those characteristics. Age at AIDS diagnosis was no longer as strong a predictor of survival, however, when included with other variables in the multivariate model, with CD4 counts at AIDS diagnosis and antiretroviral use emerging as the strongest predictors of survival among these co-infected persons.

DISCUSSION

Among this population of persons with AIDS in LAC, EPTB was significantly more common among Latinos, but not among African Americans when compared to whites, a pattern that is different than what was found nationally where EPTB was elevated among African Americans with AIDS, and less so among Latinos with AIDS.⁷ The finding of more TB of any type among nonwhite persons with AIDS in LAC compared to white persons is consistent with national data, however.^{8,9} The finding of more TB of any type among foreign-born persons and IDUs with AIDS is also consistent with data on HIV risk patterns in

TABLE 2. CD4 LYMPHOCYTE COUNTS AT AIDS DIAGNOSIS AND FOLLOW-UP FOR PERSONS WITH AIDS WITH PTB, EPTB AND NON-TB AIDS

| | <i>AIDS/EPTB</i> (n = 166) | | <i>AIDS/PTB</i> (n = 216) | | <i>Clinical Non-TB/AIDS</i> (n = 2,656) | | <i>Immunologic Non-TB/AIDS</i> (n = 2,504) | | |
|--|-------------------------------|------------|------------------------------|--------------------|--|-----|---|--------|-----------|
| | N | % | N | % | N | % | N | % | |
| CD4 counts within 6 months of AIDS diagnosis (cells/ per microliter) | | | | | | | | | |
| ≤50 | 44 | 27 | 45 | 21 | 738 | 28 | 489 | 20 | |
| 51–≤100 | 35 | 21 | 27 | 13 | 356 | 13 | 427 | 17 | |
| 101–≤200 | 36 | 22 | 38 | 18 | 544 | 20 | 1,309 | 52 | |
| 201–≤300 | 11 | 7 | 12 | 6 | 113 | 4 | 180 | 7 | |
| 301+ | 10 | 6 | 28 | 13 | 55 | 2 | 89 | 4 | |
| Missing infor | 30 | 18 | 66 | 31 | 850 | 32 | 10 | <1 | |
| Mean | 121 | | 181 | | 99 | | 132 | | |
| Median | 79 | | 110 | | 73 | | 132 | | |
| Range | 0–697 | | 2–1,120 | | 0–1,780 | | 0–921 | | |
| | $Z^{a,b} = -1.9$ | | $p = 0.06$ | | $Z^{a,c} = 4.1$ $p = 0.0001$ | | $Z^{a,d} = -2.8$ $p = 0.006$ | | |
| | <i>AIDS/EPTB</i> | | | <i>AIDS/PTB</i> | | | | | |
| CD4 counts at follow-up | N | Mean | Med | N | Mean | Med | Z^a | p | |
| 6 month | 122 | 122 | 76 | 150 | 184 | 115 | -2.6 | 0.009 | |
| 1 year | 74 | 79 | 41 | 89 | 169 | 110 | -3.5 | 0.0006 | |
| 2 year | 42 | 102 | 48 | 60 | 154 | 85 | -1.5 | 0.1 | |
| 3 year | 21 | 134 | 86 | 30 | 158 | 79 | -0.12 | 0.9 | |
| Mixed effects model parameter ^b | | | | Parameter estimate | | | Standard error | T | p value |
| CD4 at AIDS diagnosis | | TB type | | | | | | | |
| | | EPTB (ref) | | 2.98 | | | 0.077 | 3.8 | 0.0004 |
| | | PTB | | 3.35 | | | 0.105 | | |
| Change in CD4 Count per month of follow-up ^c | | EPTB (ref) | | -0.032 | | | 0.005 | 0.8 | 0.42 |
| | | PTB | | -0.024 | | | 0.007 | | |

^aWilcoxon Rank-Sum Test statistic used for nonparametric data.

^bComparing PTB group to EPTB group.

^cComparing PTB/EPTB group combined to clinical non-TB AIDS group.

^dComparing PTB/EPTB group combined to immunologic non-TB AIDS group.

^eCD4 counts were fourth square root-transformed.

AIDS, acquired immune deficiency syndrome; PTB, pulmonary tuberculosis; EPTB, extrapulmonary tuberculosis; TB, tuberculosis.

persons with AIDS and TB in the United States.⁸

Results from the mixed effects model showed a significantly lower CD4 count at AIDS diagnosis for the EPTB compared to the PTB group, which was not found using the Wilcoxon rank sum test. The mixed effects model is likely to be more reliable, however, because the method accounts for missing data, differing lengths of follow-up, and varied intervals between follow-ups.

The CD4 count at the time of AIDS diagnosis for the non-TB clinical AIDS group was significantly lower than that for the two TB/AIDS groups. This is consistent with data on HIV-infected persons seen at an urban clinic in which TB, candidiasis and herpes zoster occurred at median CD4 counts greater than 100 cells per microliter compared to all other IOs which occurred at median CD4 counts less than 50 cells per microliter.¹⁰

The lack of a difference in CD4 counts over

TABLE 3. RATES OF OPPORTUNISTIC INFECTION DURING FOLLOW-UP PERIOD FOR PERSONS WITH AIDS WITH PTB AND EPTB

| Opportunistic infection | AIDS/EPTB ^a (n = 166) | | AIDS/PTB ^b (n = 216) | | IDR ^d | 95% CI |
|--|-------------------------------------|-------------------|------------------------------------|-------------------|------------------|-----------|
| | N | Rate ^c | N | Rate ^c | | |
| Candidiasis, lung | 10 | 0.38 | 5 | 0.14 | 2.7 | 0.9, 7.9 |
| Candidiasis, esophagus | 18 | 0.72 | 15 | 0.41 | 1.8 | 0.9, 3.5 |
| Cervical cancer | 0 | — | 0 | — | — | — |
| Coccidiomycosis | 1 | 0.04 | 0 | — | — | — |
| Cryptococcosis | 14 | 0.54 | 8 | 0.22 | 2.5 | 1.0, 5.9 |
| Cryptosporidiosis ^e | 10 | 0.38 | 2 | 0.05 | 7.6 | 1.7, 34.7 |
| Cytomegalovirus | 11 | 0.42 | 13 | 0.36 | 1.2 | 0.5, 2.6 |
| CMV retinitis | 7 | 0.26 | 11 | 0.30 | 0.9 | 0.3, 2.2 |
| HIV encephalopathy ^e | 11 | 0.41 | 3 | 0.08 | 5.1 | 1.4, 18.4 |
| Herpes simplex ^e | 15 | 0.60 | 4 | 0.11 | 5.5 | 1.8, 16.4 |
| Histoplasmosis | 4 | 0.15 | 1 | 0.03 | 5.0 | 0.6, 44.7 |
| Isoporiasis | 1 | 0.04 | 1 | 0.03 | 1.3 | 0.1, 21.3 |
| Kaposi's sarcoma | 14 | 0.54 | 13 | 0.35 | 1.5 | 0.7, 3.3 |
| Burkitt's lymphoma | 0 | — | 1 | 0.03 | — | — |
| Lymphoma, IB | 2 | 0.07 | 0 | — | — | — |
| Lymphoma, brain primary | 0 | — | 0 | — | — | — |
| <i>Mycobacterium avium</i> ^e | 17 | 0.66 | 9 | 0.24 | 2.8 | 1.2, 6.2 |
| <i>Mycobacterium</i> , unspecified ^e | 10 | 0.39 | 4 | 0.11 | 3.6 | 1.1, 11.3 |
| <i>Pneumocystis carinii</i> pneumonia | 37 | 1.60 | 34 | 1.05 | 1.5 | 1.0, 2.4 |
| Recurrent pneumonia | 1 | 0.04 | 8 | 0.22 | 0.2 | 0.0, 1.5 |
| Multifocal leukoencephalopathy | 1 | 0.04 | 0 | — | — | — |
| <i>Salmonella</i> septicemia | 0 | — | 0 | — | — | — |
| Toxoplasmosis ^e | 16 | 0.63 | 8 | 0.22 | 2.9 | 1.2, 6.7 |
| Wasting | 15 | 0.57 | 10 | 0.27 | 2.1 | 1.0, 4.7 |
| All opportunistic infections ^e | 215 | 0.93 | 150 | 4.01 | 2.0 | 1.6, 2.4 |

^aPersons with AIDS with EPTB with or without pulmonary involvement.

^bPersons with AIDS with PTB.

^cRate per 100 person-months.

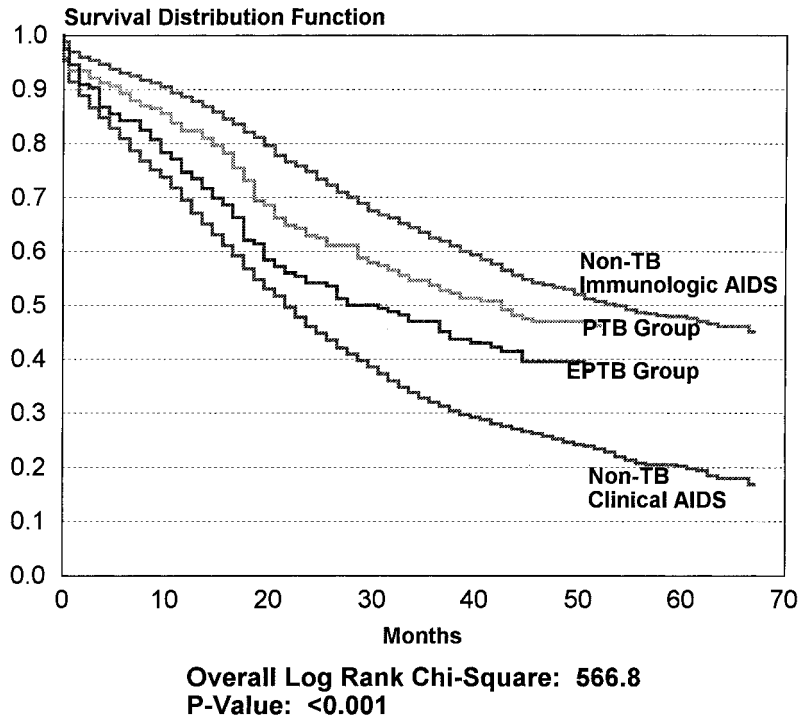
^dIncidence density ratio comparing EPTB group to PTB group.

^eOpportunistic infection in which rate in AIDS/EPTB cases was statistically higher than the rate in AIDS/PTB cases. AIDS, acquired immunodeficiency syndrome; EPTB, extrapulmonary tuberculosis; PTB, pulmonary tuberculosis.

time for the EPTB versus the PTB groups is an important finding for which there were no comparable reports found in the literature. Petrukevitch et al.⁴ reports no differences in CD4 declines for two groups of HIV-infected persons with and without TB but reported no data comparing an EPTB/AIDS to a PTB/AIDS group.

The OI incidence rate in our AIDS/EPTB study group is about twice that found in the study by Whalen et al.,² which followed 106 HIV-infected persons with tuberculosis at four U.S. medical centers. The OI rate in our AIDS/PTB study did not differ from the Whalen study,² and the overall OI incidence is comparable in the two studies.

PCP, candidiasis of the esophagus, and *Mycobacterium avium* were the predominant types of OIs identified during the follow-up period for both our study and the study by Whalen et al.², although the numbers of individual OIs identified in our study group are small, resulting in unstable estimates. The finding of *Mycobacterium avium* in both studies is not surprising because as *Mycobacterium avium* is a common pathogen that frequently is associated with EPTB and disseminated disease among AIDS patients.¹¹ With the exception of CMV retinitis and recurrent pneumonia, the OI rates for the EPTB group tended to be higher than those for the PTB group, suggesting that the



| Survival | Comparisons | P-Value |
|----------------|-----------------------------|---------|
| PTB | vs. EPTB | 0.07 |
| PTB | vs. Non-TB Clinical AIDS | <0.0001 |
| EPTB | vs. Non-TB Clinical AIDS | 0.0002 |
| Both TB Groups | vs. Non-TB Clinical AIDS | <0.0001 |
| PTB | vs. Non-TB Immunologic AIDS | 0.06 |
| EPTB | vs. Non-TB Immunologic AIDS | <0.0001 |
| Both TB Groups | vs. Non-TB Immunologic AIDS | <0.0001 |

1. PTB: Pulmonary TB
2. EPTB: Extrapulmonary TB
3. Non-TB clinical AIDS includes persons who developed one or more of the 26 opportunistic infections at the time of an AIDS diagnosis with the exception of pulmonary TB and extrapulmonary TB.
4. Non-TB immunologic AIDS includes persons with CD4 counts of less than 200ul/dl or CD4 percent less than 14, and no AIDS indicator clinical conditions at the time of an AIDS diagnosis.

FIG. 1. Crude survival curves for pulmonary tuberculosis (PTB), extrapulmonary tuberculosis (EPTB), and non-TB/AIDS groups, 1993–1996, Los Angeles County.

EPTB group had a more complicated medical course after a TB diagnosis compared to the PTB group.

The similarities in the mortality profiles for this population-based sample of persons with AIDS with PTB versus EPTB is consistent with other data from a population-based sample of U.S. AIDS cases⁸ and a small sample of 30 men hospitalized in public hospitals in New York City and infected with HIV and TB.¹² In contrast, one European clinic-based study reported a worse survival profile for persons with AIDS and PTB compared to an AIDS/EPTB group,¹² while another U.S. clinic-based study showed a

worse survival profile for HIV-infected persons with EPTB compared to those with PTB² with HIV-infected persons without any TB at all faring the best. If generalization of patterns of disease progression and mortality to the population at large is the goal, however, then use of population-based studies such as this one and that by Jones et al.⁸ may be more useful.

In this study, the better survival profile for the TB/AIDS groups combined compared to the non-TB clinical AIDS groups is consistent with several other population and clinic-based studies.^{2–4,8,13,14} Several studies have shown that TB is diagnosed earlier in the course of HIV

TABLE 4. PROPORTIONAL HAZARDS REGRESSION ANALYSIS CONTROLLING FOR DIFFERENCES IN BASELINE CHARACTERISTICS AND KNOWN PREDICTORS OF SURVIVAL IN 382 PERSONS WITH AIDS AND TB IN LOS ANGELES COUNTY, 1993–1996

| Characteristic | Univariate model | | Multivariate model ^a | |
|--|------------------|----------|---------------------------------|----------|
| | OR for death | 95% CIs | OR for death | 95% CIs |
| Age at AIDS diagnosis, years | | | | |
| ≥40 | 1.5 | 1.1, 2.0 | 1.5 | 1.0, 2.2 |
| <40 | Reference | | Reference | |
| CD4 counts at AIDS diagnosis, cells per microliter | | | | |
| <200 | 3.6 | 2.0, 6.5 | 4.0 | 1.9, 8.2 |
| ≥200 | Reference | | Reference | |
| Antiretroviral therapy | | | | |
| Yes | 0.2 | 0.1, 0.3 | 0.3 | 0.1, 0.6 |
| No | Reference | | Reference | |
| PCP prophylaxis | | | | |
| Yes | 0.3 | 0.2, 0.4 | 0.8 | 0.4, 1.9 |
| No | Reference | | Reference | |
| TB type | | | | |
| EPTB | 1.2 | 0.9, 1.6 | 1.2 | 0.9, 1.8 |
| PTB | Reference | | Reference | |

^aMultivariate model includes all variables listed and all analyses include all persons with AIDS and PTB and AIDS and EPTB.

AIDS, acquired immunodeficiency syndrome; TB, tuberculosis; PCP, *Pneumocystis carinii* pneumonia; OR, odds ratio; CIs, confidence intervals.

disease than other OIs, possibly explaining the longer survival in TB/AIDS patients when compared to non-TB AIDS patients.³ It is also possible that AIDS-defining OIs other than TB portend a poorer outcome due to fewer effective treatment options than those which are available for TB. The other point worth mentioning is that the sample size for the non-TB clinical AIDS cases ($n = 2,656$) in this study is substantially larger than that for the TB groups, suggesting that the survival estimate is likely to be more stable and valid for the non-TB clinical AIDS group than for the TB/AIDS groups.

In this population-based study, CD4 counts at AIDS diagnosis and antiretroviral and PCP prophylaxis use influenced survival among coinfecting persons. This contrasts to the study by Whalen et al.² in which CD4 counts at AIDS diagnosis, a history of a previous OI, and active TB were statistically significant predictors of survival. The findings from the proportional hazards regression analysis in the two studies were similar, although the analysis by Whalen et al.² included HIV-infected persons without

TB and ours did not. Nonetheless, CD4 counts at AIDS diagnosis emerged as the strongest predictor of survival in both groups of HIV/TB infected persons.

Limitations in this analysis include the absence of information on compliance with and response to TB medications and medications other than ARV and PCP prophylaxis that may have influenced HIV disease progression in the TB groups. Analyses were conducted that excluded those with multidrug-resistant TB, and the results were no different for the MDR-TB cases, however. An additional limitation is the absence of OI data on the non-TB/AIDS group, which would have been useful for comparison purposes. In addition, to assess fully HIV disease progression among persons coinfecting with TB of any type fully, HIV viral load measurements are needed before and after the incidence of TB. Finally, the patients included in this analysis were followed prior to the widespread use of highly-active antiretroviral therapy (HAART), which likely would have significantly slowed HIV disease progression in all groups.

CONCLUSION

Using the measures of HIV disease progression available for this population-based sample of AIDS cases, persons with AIDS who were coinfecting with EPTB were more sick with more OIs than those with PTB, however the mortality patterns for the two TB groups were essentially the same.

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