

# CHARACTERISTICS OF HIV-INFECTED TUBERCULOSIS PATIENTS IN KOTA BHARU HOSPITAL, KELANTAN FROM 1998 TO 2001

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**Abstract.** To characterize the demographic profiles, clinical features, radiological patterns and outcomes of treatment of HIV-infected TB patients, a descriptive study was carried out on 149 HIV-infected TB cases diagnosed from 1998 through 2001 at Kota Bharu Hospital, Kelantan, Malaysia. The majority of the patients were males (94.6%), single (45.0%), ethnic Malay (94.0%) with a mean age of 34 years (standard deviation 7.8, range 18-76). The most common HIV transmission category was through injecting drug use (73.8%) and being the inmates or former inhabitants of drug rehabilitation centers and prisons were the commonest high-risk groups. One hundred and seventeen patients were diagnosed as having pulmonary TB, while about 20% were extra-pulmonary in type with 9 cases of millitary TB. The majority (45%) presented with cough symptoms while only 51% had a positive sputum smear. Fifty-five percent were found to have pulmonary lesions on chest x-ray, such as localized, millitary or diffuse pulmonary infiltrates, or opacities. Eight (5.4%) had pleural lesions while another 8 cases had hilar or mediastinal lymph node lesions. Overall, fifty-eight (38.9%) patients had died by the completion of data collection. The median weeks or survival from the time of starting TB treatment was 13.5 (range 1 - 56) and the majority of them (74%) died without completing the 6-month regime of treatment.

## INTRODUCTION

According to the World Health Organization (WHO), one third of the world's population is already infected with *Mycobacterium tuberculosis*, which is causing about 3 million deaths each year (Raviglione *et al*, 1995). Approximately, seven to eight million people develop tuberculosis (TB) each year with a death toll of around 3 million people annually. At the same time, the human immunodeficiency virus (HIV) pandemic is increasing rapidly in many communities worldwide; more than 30 million people are currently infected and 1.5 million deaths are estimated to have occurred in 1996. Nearly 14 million people were estimated to have both infections by the year 2000 (WHO, 1998). The effects of HIV on TB will be greatest where the two diseases overlap, which is at present, principally in Africa (Colebunders *et al*, 1989; Elliot *et al* 1990). The incidence of HIV-associated TB has been increasing worldwide since the beginning of the AIDS epidemic and is expected to increase even further, especially in developing countries.

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In Malaysia, the annual reported cases of HIV infections and AIDS has shown an increasing pattern for the last ten years. HIV infections have increased from 778 in 1990 to 5,107 cases with 1,168 reported AIDS cases in 2000. The trend of TB with HIV co-infection has also increased and has contributed to nearly 5.0% of the total TB cases in the country (MOH, 2001).

## MATERIALS AND METHODS

This cross sectional study was done at the Chest Clinic, Kota Bharu Hospital, Kelantan (a northeastern state of Malaysia) which provided a mix of city and rural TB patients to reflect the general population of the state. The registry of all TB cases with HIV co-infection at the clinic was reviewed for the years 1998 through 2001. The HIV-related TB cases included all cases smear positive or negative for pulmonary TB, extra pulmonary TB or a mixed type. The HIV status was confirmed from the results of ELISA tests or through the medical history noted on the TB form of the patients.

Data, which were collected on the standardized forms for all cases, includes socio-demographic characteristics, risk factors for HIV in-

fection, presenting symptoms of TB, history of contact of TB, results of microbiology, CD4 counts, and chest x-ray, and also the death outcome of the patients. The data were entered into the computer and analyzed using SPSS version 9.0 software. Descriptive statistics and cross-tabulations were used to explore all the data. Chi-square and Fischer's exact test were used to evaluate the differences between categorical variables. Continuous variables analysis was by means and standard deviations or the median by appropriate tests. A p-value of less than 0.05 was considered significant.

## RESULTS

On the completion of the study, one hundred and forty-nine HIV-infected TB patients were identified from the years 1998 through 2001. Male patients presented the majority of the cases (94.6%) while the Malay race constituted about 94%, Chinese (4.0%) and others (2.0%) of the cases. Their mean age was 34 years (standard deviation 7.8, range 18 to 76 years). Of these patients, most of them had received a secondary education and the majority of them were single (45%), with only 34% being married.

In terms of high-risk sub-groups for HIV infection, this study identified that the majority of the patients (110/149) were injecting drug users (IDUs). Eight cases reported having multiple sexual partners, including promiscuity, two cases of homosexuality while four cases were combined IDU and promiscuity. Three out of eight female patients developed their HIV infection from their husbands who were current or ex-IDUs. Since most of the HIV-infected TB patients were IDUs, it was found that most of them were either inhabitants or former inmates of local prisons or drug rehabilitation centers (Pusat Serenti). Thirty-six patients were from prisons while seven patients were diagnosed with TB while they were at Pusat Serenti. The study also showed that thirty patients (20.1%) were diagnosed as AIDS cases when TB was first diagnosed.

### TB sites

One hundred and seventeen patients (78.5%) had been registered as pulmonary TB patients while an additional four patients (2.7%) had both pulmonary and extra-pulmonary TB. Twenty-eight cases (18.8%) had extra-pulmonary disease, including nine cases of millitary TB (Fig 1).

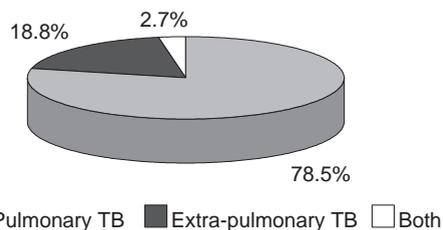


Fig 1—Tuberculosis (TB) sites among HIV-infected TB patients in Kota Bharu Hospital, 1998-2001.

### Clinical and laboratory findings

The majority of the patients presented without cough symptoms (45.0%) with a median duration of cough of 4 weeks. Out of these, about 76% had pulmonary TB; and the difference was significant ( $p = 0.02$ ). One hundred and twenty-nine (86.6%) patients had sputum smears for acid-fast bacilli (AFB) results, of whom 51% (76/129) had a positive smear. Sputum culture or cultures from other sites were not available in most of the patients. Ten patients (6.7%) had a documented history of previous TB disease and treatment. It was not certain whether they finished the treatment regime or not. Fourteen cases (9.4%) claimed to have had contact with a known case of TB, but the data on the year of diagnosis or contacts were not available. BCG scars were present in most of the patients (89%). Regarding tuberculin skin test, only twenty-five cases (16.8%) had a documented history of the test being done, with median of 6.0 mm, ranging from 0 to 25 mm. Out of these, 10 (40%) had a reaction of 10 mm or more while 16 (64%) had more than 5 mm of induration.

Initial chest x-ray findings are also noted in this study. Sixty-five cases (43.6%) presented with minimal chest lesions in their early x-ray results, while fifty-three cases (35.6%) were classified as moderately advanced or far advanced lesions. Fig 2 shows that about 8.0% of the cases had either solitary or multiple cavitations on the chest x-rays while the majority of the cases (55.0%) were found to have either typical or atypical pulmonary lesions, such as localized, millitary or diffuse pulmonary infiltrates or opacities. Eight cases (5.4%) had pleural lesions, while another 8 cases had hilar or mediastinal lymph nodes lesions. Characterization of chest lesions as either post-primary or reactivation patterns were not evaluated in this study.

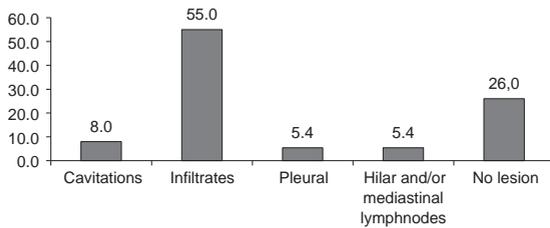


Fig 2—Percentage of chest x-ray lesions in HIV infected TB patients in Kota Bharu Hospital, 1998-2001.

Only fourteen (7.4%) cases had documented results of CD4+ lymphocyte counts. Out of these, eleven cases were noted to have CD4+ count less than 200/mm<sup>3</sup> and were analyzed. Fischer's exact test showed that there were no significant differences in demographic and clinical features between patients whose counts were < 200/mm<sup>3</sup> vs > 200/mm<sup>3</sup> (data not shown). The relationship between the CD4+ count and the clinical features or chest lesions could not be further analyzed because of limited data on the CD4+ count results.

#### Death outcomes

Overall, fifty-eight patients (38.9%) had died by the completion of data collection. The median weeks of survival from the time of starting treatment was 13.5 (range 1 -56 weeks). The majority of them (74%) died without completing the 6-month regimen. Out of these, six patients (10.3%) were diagnosed as having disseminated millitary TB; 1 patient was reported as having toxoplasmosis and cryptococcal infections while the rest were due to TB disease who had not completed the treatment, or from other causes not stated in the patient notes.

#### DISCUSSION

The characteristics of HIV-positive patients in this study may represent the actual scenario in this country, where majority of them are injecting drug users (IDUs), ethnic Malay, males and from younger age groups. The latest statistics from the Ministry of Health of Malaysia show that injecting drug users remain the largest group (74.7%) among risk categories, while 69.6% were Malay, 94.7% were male and 75.4% were age 20-39 years old (MOH, 2001). It is possible the frequency of the sexual modes of HIV transmission reported in this study may be underestimated. Attending doctors or the patients themselves might not have discussed high-risk sexual practices.

In many developing countries, TB has now emerged as the most common opportunistic disease associated with HIV infection. This study was able to show that there were a number of patients who were reported to have a prior AIDS diagnosis or a low CD4+ count before being diagnosed as having TB. This study was able to show that the majority of HIV-infected TB patients presented with either a typical or an atypical TB disease pattern. Many of the pulmonary TB patients presented without cough symptoms and negative sputum smears. Harries (1990) quoted that many studies in African countries in the early HIV epidemic showed that patients seem to produce no sputum, or having negative sputum smears; chest x-rays may show little change or there may be diffuse pulmonary infiltrates without cavitation. Atypical extra-pulmonary TB disease was also common in this group of patients. TB presentations that were previously uncommon, such as millitary disease, pleural and mediastinal lymphadenitis appeared to be more common. Daley (1995) demonstrated the associations of certain chest x-ray findings with HIV disease stage. He showed that hilar or mediastinal adenopathy were significantly associated with a CD4+ count of less than 200/mm<sup>3</sup> while those counts that were more than 200/mm<sup>3</sup> were frequently associated with cavitations. These changes in disease patterns have made the diagnosis of TB more difficult, although a high index of suspicion usually means that these patients are said to have TB and receive empiric antituberculous chemotherapy, usually with good effect.

Fourteen of the patients in this study reported prior contact with people who have active TB, while 64% of them had a tuberculin reaction of more than 5 mm, which might indicate the presence of TB infection before the diagnosis of TB was made. Since isoniazid chemoprophylaxis in patients with HIV and TB co-infection has shown to decrease the incidence of active TB, some of them could have been prevented if they were assessed on skin reaction for TB infection and isoniazid therapy was offered.

Regarding mortality in HIV-infected TB patients, Perriens *et al* (1991) stated that although they respond as well to anti-tuberculosis chemotherapy as HIV-negative TB patients, they may have a higher short-term mortality. This study indicated a case-fatality rate of 28.9% during the

6-months after diagnosis and starting treatment. A study in Zaire (Perriens *et al*, 1991) showed a similarly high rate, while a retrospective cohort study done in 1997 in Thailand showed a mortality rate of 12% among those who received 6-months of therapy (Poprawski *et al*, 2000).

Some limitations were noted in this study. Predictors and risk factors for treatment failure and death among the patients were not thoroughly evaluated because during data collection we were unable to establish many confounders and effect modifiers. Furthermore, a cohort study or survival analysis may be appropriate to see the associations and risk estimations. Lack of CD4+ count information and the status of AIDS prior to diagnosis might have affected the assessment for associations between the degree of immunosuppression and clinical or radiological findings. An accurate description of chest x-ray findings might be questioned, thus, an evaluation by a blinded observer radiologist, especially for the atypical lesions, is needed in future studies.

### Conclusions and recommendations

The demographic profiles of patients with TB who have HIV infection show that they are mostly male, ethnic Malay, single and age 20 to 39 years old. Injecting drug use was a greater risk factor than sexual transmission, with most of them being either inhabitants or former inmates of prisons or drug rehabilitation centers. Pulmonary TB was still the major type of presenting disease but many extra pulmonary TB lesions were found, such as pleural and millitary disease. This was further supported by chest x-ray findings where the majority were found to have mixed typical and atypical lesions. Standard anti-tuberculosis regimens may have cured most of the surviving patients but many died without completing treatment, due to TB and AIDS-related complications during the course of treatment.

Screening for HIV infection among newly diagnosed TB patients is routinely done in health facilities in Malaysia, but screening for TB infection in groups at high risk for co-infection is not commonly done. Resources may be targeted to appropriately screen and evaluate carefully for TB infection and diseases. Even though issues of cost-benefit, compliance and adverse reactions in chemoprophylaxis for TB in HIV-infected patients may surface, especially in developing countries,

such as Malaysia, fatal TB disease in some HIV patients may be reduced or prevented. Implementation of directly observed therapy (DOTS) for all TB cases regardless of HIV status may reduce the likelihood of drug resistance and treatment failure (De Cock and Chaisson, 1999).

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