The Prevalence of *M. Tuberculosis* Infection and Disease in HIV Positive Individuals in Shiraz, Southern Iran

MA Davarpanah¹, GH Rafiee², D Mehrabani¹

¹Gastroenterohepatology Research Center, Department of Internal Medicine, ²College of Nursing and Midwifery, Nemazee Hospital, Shiraz University of Medical Sciences, Shiraz, Iran

Abstract

Background: The emergence of HIV infection and its close association with TB poses an even greater challenge to the health systems and when co-infection is present, it is the most potent risk factor for progression of the disease to an active TB. This study was performed to determine the HIV-seropositive individuals with *Mycobacterial* infection referring to Center for Counseling and Behavioral Modification in Shiraz, southern Iran.

Methods: From January 2004 to December 2006, 459 HIV-positive individuals who referred to Center for Counseling and Behavioral Modification in Shiraz, Southern Iran were enrolled. HIV antibody tests included ELISA and western blot test, and the tests used for *M. tuberculosis* infection were PPD skin test, chest x-ray, Ziehl-Neelsen technique, culture in Lowenstein-Jensen medium and pathological examination.

Results: 28.5% of HIV-positive individuals had a positive PPD skin test, among whom 89.3% showed a latent tuberculosis infection and 10.7% active tuberculosis. 7.9% of HIV positive patients had active tuberculosis including pulmonary (75.8%) and extrapulmonary types (24.2%). Among the latter cases, 62.5% had TB lymphadenitis, 25% pericarditis and 12.5% TB pleuritis. 40% of those with pulmonary tuberculosis and 50% with extrapulmonary TB had a positive PPD skin test.

Conclusion: As tuberculosis is a common opportunistic infection in HIV-positive patients in Iran with a higher prevalence of extrapulmonary type and the complex clinical presentation of disease, HIV-positive patients should be regularly screened for tuberculosis. Early recognition of latent tuberculosis infection and adequate chemoprophylaxis seem to be essential too.

Keywords: HIV; *M. tuberculosis*; Prevalence; Coinfection; Southern Iran

Introduction

Tuberculosis (TB) is a major cause of illness and death worldwide, especially in Asia and Africa. Globally, 9.2 million new cases and 1.7 million deaths from TB occurred in 2006, of which 0.7 million cases and 0.2 million deaths were in HIV-positive people.¹

TB is still an important public health problem, particularly in the developing world, taking a heavy toll of those at their prime of life. The emergence of HIV infection and its close association with TB poses an even greater challenge to the health systems and when co-infection is present, it is the most potent risk factor for progression of the disease to an active TB.²

In countries with high HIV prevalence, up to 80% of TB patients also have HIV infection.³ Preventing and controlling HIV/AIDS and TB requires broad and integrated interventions that address the underlying causes of inequity that result in a poorer health and worse health outcomes.³ The majority of TB infections are limited to the lungs and those with CD4 counts <200 cells/mm³ are more likely to have atypical infiltrates and extrapulmonary (up to 60%) or disseminated TB.⁴ Extrapulmonary TB was reported in
10-20% of HIV-seronegative patients but in 40-80% of those infected with HIV. The increased risk in HIV-infected patients has been associated with advanced immune suppression. The tuberculin test has been used for the past 50 years to support the diagnosis of TB. In HIV-infected patients, an induration of greater than 5 mm on a standard tuberculin skin test is considered reactive. The CD4+ lymphocyte count, using a cutoff level of 500 cells/mm³ allowed us to discriminate between a lack of reactivity to tuberculin due to non-infection with *M. tuberculosis* or to immunodeficiency. The tuberculin test is positive in the majority of patients with pulmonary disease and a CD4 cell count <200 cells/mm³. This study was performed to determine the prevalence of *M. tuberculosis* infection and disease in HIV Positive individuals during 2004-2006.

**Materials and Methods**

From January 2004 to December 2006, 459 HIV-positive individuals having been referred to Center for Counseling and Behavioral Modification in Shiraz, Southern Iran were enrolled in our study. This is a referral center for individuals with a high risk for HIV infection such as IV drug abusers and sex workers. On referral, optional counseling is done for the individual and if he/she gives informed consent, HIV testing is undertaken. In the case of a positive test, the patient is registered in a program including methadone maintenance therapy, opportunistic infection prophylaxis, highly active antiretroviral therapy, etc. The study was approved in the ethics committee of the department.

HIV antibody tests were enzyme-linked immunosorbent assay (ELISA) and western blot test. To determine infection by *M. tuberculosis*, PPD (purified protein derivatives) skin test was done for all HIV infected individuals. In HIV-positive patients, *M. tuberculosis* infection was confirmed by an induration of 5 mm or more. Chest x-ray was provided for all of them. In patients with productive cough, three consecutive samples of the sputum were provided, stained by Ziel-Neelsen technique and studied under microscope and also the samples were cultured, using Lowenstein-Jensen medium. Pulmonary TB diagnosis was based on chest x-ray and a positive acid fast sputum smear or culture. CD4+ T cell count was measured for all individuals. Also, tissue biopsy was done for patients with suspicious extra-pulmonary TB (lymph node, pericardial and pleural biopsy). The diagnosis was based on histological findings (caseating granuloma or acid fast bacilli in tissue samples).

**Results**

Among 459 HIV-positive individuals, 15.2% (70) were female and 84.7% (389) were male. 28.5% (131) of HIV-positive individuals had positive PPD skin test (induration≥5 mm) and 71.5% (328) were negative. Out of 131 HIV-positive individuals with reactive PPD skin test, 117 patients (89.3%) showed a latent tuberculosis infection and 14 (10.7%) had active tuberculosis. 5.7 % (4/70) of the females, and 32.6% (127/389) of the males had positive PPD skin test. The mean induration of PPD skin test in patients with latent tuberculosis was 11.13 mm. 33 out of the total HIV+ patients (7.9%) had active tuberculosis including 25 pulmonary (75.8%) and 8 extrapulmonary types (24.2%), respectively. Among 8 patients with extrapulmonary tuberculosis, 5 of them (62.5%) had TB lymphadenitis, 2 pericarditis (25%) and one TB pleuritis (12.5%). Forty percent (10/25) of the patients with pulmonary tuberculosis, and 50% (4/8) with extrapulmonary TB had positive PPD skin test. The mean induration of PPD skin test in patients with pulmonary and extra-pulmonary tuberculosis was 8.2 and 13.5 mm, respectively. The mean CD4+ T cell counts of the patients with latent tuberculosis infection, pulmonary, and extrapulmonary tuberculosis were 287, 189, and 138, respectively. The mean CD4+ T cell count in HIV-positive individuals with negative PPD test (induration less than 5 mm) was 283 (Table 1).

**Table 1:** Reactivity to PPD skin test and mean CD4 +cell count in HIV-Positive patients referred to Counseling and Behavioral Modification Center in Shiraz, southern Iran.

<table>
<thead>
<tr>
<th>PPD test (mm)</th>
<th>Results No. (%)</th>
<th>Mean CD4 count</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>281 (61)</td>
<td>296</td>
</tr>
<tr>
<td>1-4</td>
<td>47 (10.2)</td>
<td>272</td>
</tr>
<tr>
<td>5-9</td>
<td>71 (15.4)</td>
<td>319</td>
</tr>
<tr>
<td>10-15</td>
<td>37 (8)</td>
<td>303</td>
</tr>
<tr>
<td>&gt; 15</td>
<td>23 (5)</td>
<td>238</td>
</tr>
</tbody>
</table>

**Discussion**

Patients with HIV infection are highly susceptible to *M. tuberculosis*. Regardless of age, induration of 5
mm or more on tuberculin test is considered as positive in HIV-infected patients. In HIV and TB infection, there is a reduction in the proportion of those reacting to tuberculin as the CD4+ T cell count falls. In Markowitz et al.’s study, patients with HIV-infection and CD4+ T lymphocytes/mm3 <400 had a lower prevalence of PPD reactivity than HIV-seronegative controls. In our study, 28.5% of HIV-infected individuals had positive PPD skin test; 89.3% of them had latent tuberculosis and 10.7% developed active tuberculosis. In Iran, similar to our results, Mohraz et al. showed that 25% of HIV-infected patients had tuberculosis infection. It was shown that the rate of progression of TB infection to active disease following the initial exposure was more than 40% in individuals infected to HIV, compared to approximately 5% in HIV negative individuals. They are more likely to develop active rather than latent TB and are also susceptible to reactivation of latent TB with an annual risk of 5-10%. When infection is established and either endogenously or exogenously reactivated, there is usually rapid progression to active disease. Tuberculin-positive co-infected persons have a risk of TB development of 8-10% per year compared to <0.1% annually in those without HIV infection. Of 230 HIV/AIDS patients who were Indian, 38 (16.52%) had TB at some stage of HIV/AIDS infection. Pulmonary TB was seen in 17 patients, proved to be clinically and radio-graphically correlated with a positive sputum smear. Extrapulmonary disease was seen in 19 patients with lymphadenopathy. In our study, out of 131 HIV-positive individuals with reactive tuberculin test, 89.3% showed a latent tuberculosis infection, 10.7% had active tuberculosis and 5.7% of females and 32.6% of males had positive PPD skin test. No patient with active tuberculosis received any prophylaxis. In Murcia-Aranguren et al.’s study, active tuberculosis developed in 3.1% of HIV infected patients with a negative tuberculin skin test after a mean follow-up of 16±11 months. 106 patients had a positive tuberculin skin test. Active tuberculosis developed in seven out of 26 patients not receiving prophylaxis or in whom prophylaxis had to be discontinued. In a cohort study in the United States, 1130 HIV-positive patients were followed for a median of 53 months, active TB being diagnosed in 31 patients from this group and occurring more frequently in persons with CD4+ T cell counts of less than 200/mm3. Mahajan et al. showed that CD4 count was less than 200/mm3 in 73 patients in HIV alone and 20 patients in TB co-infection groups. Sixty patients recorded absolute TLC less than 1200/cm2 in HIV alone group whereas 20 patients recorded absolute TLC less than 1200 mm3 in TB co-infection groups. In our study, mean CD4+ T cell count in patients with extra-pulmonary, pulmonary and latent tuberculosis were 138, 189, and 287/mm3 respectively.

Tuberculosis is a common opportunistic infection in HIV-positive patients in Iran. HIV-related TB shows a higher prevalence of extra-pulmonary type. The increased risk of TB in HIV-positive patients and the complex clinical presentation means that HIV-positive patients should be regularly screened for tuberculosis. Early recognition of latent tuberculosis infection and adequate chemoprophylaxis is essential. Also, due to the high prevalence of negative tuberculin test in HIV infected patients with latent and active tuberculosis, a more reliable test for TB screening among these patients is highly suggested. Quantiferon-TB is a new test for this purpose but it should be evaluated in this group of patients.

Acknowledgement

The authors would like to thank the Office of Vice-Chancellor for Research of Shiraz University of Medical Sciences for financial support, Mr M.J. Tarrahi for statistical analysis and Dr F. Khademhosseini at Gastroenterology and Hepatology Research Center for editorial assistance.

Conflict of interest: None declared.

References


