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## Respiratory Complications in Iranian Hospitalized Patients with HIV/AIDS

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### ABSTRACT

**Background:** The respiratory tract has been the most commonly affected site of illness in HIV-infected patients. The current study was done to identify the frequency of respiratory complications in a consecutive case series of HIV-positive patients in Iran.

**Materials and Methods:** This study was a retrospective analysis at the national academic reference medical center of Imam-Khomeini Hospital, in Tehran, Iran. The study included 199 new admissions for 177 HIV-infected patients between 2000 and 2005. Demographic characteristics, risk factors for HIV infection, respiratory complications, and CD4+ lymphocyte counts were evaluated in these patients.

**Results:** All patients were males. The mean age was 35 years (age range: 15 to 63 years). Among 34 cases with available CD4+ lymphocyte count results, 70.6% had results <200 cells/mm<sup>3</sup>. Nearly half the patients (47.7%) had respiratory symptoms. The most common pulmonary complications were cough (86.3%), sputum (71.6%), dyspnea (54.7%), and hemoptysis (10.5%). The most common diagnosis was pulmonary tuberculosis (27.1%), followed by other bacterial pneumonias (16.6%) and pneumocystis carinii pneumonia (4.5%). Intravenous drug users who had history of incarceration had the highest risk factors for *Mycobacterium tuberculosis* infection (59%), and other bacterial pneumonias (52%).

**Conclusion:** Our study demonstrates that respiratory complications are highly frequent in HIV patients in Iran and that pulmonary tuberculosis is still a common complication in HIV infected patients, despite the availability of effective treatment. Results suggest the need for more effective preventive and prophylactic measures, wider use of antiretroviral treatment and effective chemotherapy for Iranian patients with HIV/AIDS. (*Tanaffos*2011; 10(3): 49-54)

**Key words:** HIV, Respiratory complications, Tuberculosis, Iran

### INTRODUCTION

Since the original defining outbreak of AIDS, HIV-infected individuals have been repeatedly

shown to be predisposed to respiratory infections, complications and symptoms (1-3). Nearly two-thirds of patients infected with HIV will present with pulmonary involvement as their first clinical manifestation of the syndrome and approximately four-fifths will develop some kind of pulmonary involvement over the course of their disease (4). In

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addition, HIV infection is a dynamic condition in which the immune state and the risk of exposure to specific etiologic agents change over time and by stage of disease (5).

The most common manifestation of pulmonary disease in HIV-seropositive individuals is pneumonia. The most common cause of pneumonia is bacterial infection, including and especially mycobacterium. Other major causes of pulmonary infiltrates include fungal infections (*Pneumocystis carinii*), nonspecific interstitial pneumonitis, Kaposi's sarcoma (KS), and lymphoma (6).

The types of pulmonary complications that develop depend on the degree of immunosuppression, HIV transmission category and geographical location (7). Knowledge about the types of pulmonary complications in patients with HIV infection will help clinicians to apply better diagnostic, therapeutic and preventive approaches. To date, the specific respiratory complications of HIV/AIDS patients in Iran have not been systematically documented. This article describes the frequency of respiratory complications detected in a consecutive sample of 199 HIV- infected patients during their hospitalization.

## MATERIALS AND METHODS

This study was a retrospective case series conducted at a university teaching hospital which serves as the national referral center for infectious diseases in Iran and especially for HIV/AIDS (The Imam-Khomeini Hospital in Tehran). The study included 199 consecutive admissions for 177 patients with HIV infection (in the event all were men) during five years from January 2000 to February 2005. Repeated admissions for the same diagnosis were excluded from the study and each patient's data was considered once using the date of their first admission for a new diagnosis during the study period. Patients were identified from the hospital's admission logbooks. Infection with HIV had been

detected by a positive enzyme-linked immunosorbent assay and confirmed by Western blot following the standard hospital laboratory procedures. The study protocol was approved by the internal review board of Tehran University of Medical Sciences.

Data were obtained from patient's medical records and included age, exposure category for HIV infection, CD4+ lymphocyte counts, body temperature, white blood cell count and any objective documentation of weight changes or respiratory complications. Diagnoses of pneumonia were based on the development of new or progressive pulmonary infiltrates together with at least two of the followings: fever, cough, production of sputum, leukocytosis or leukopenia. The diagnosis of pneumonia was confirmed by the isolation of specific etiologic agent, including positive culture of pleural fluid, positive blood cultures or isolation of *M. tuberculosis* from respiratory samples. Diagnosis of *P. carinii* was based on the clinical presentation of cough and dyspnea for one week with a reticular pattern in chest-x ray and good response to co-trimoxazole.

All the collected data were entered the computer and statistical analysis was performed using SPSS version 11.5 software (SPSS Inc., Chicago, IL, USA).

## RESULTS

The 177 HIV-infected patients were all men with a mean age of 35 years (range 15-63 years). Final diagnosis for the hospital admissions and exposure category for HIV infection of patients are listed in Table 1. The single most common reason for hospitalization was pulmonary tuberculosis, reported in 54 cases (27.1%) followed by other bacterial pneumonias in 16.6% of cases. Nine cases (4.5%) presented with *P. carinii* pneumonia (PCP). By exposure category, the majority of patients (61.3%) were intravenous drug users (IDU), with the dual exposure category of being IDU and history of incarceration (38.2%).

**Table 1.** Diagnoses and exposure categories for 199 male, HIV-infected patients admitted to the hospital.

Variable	No. of patients (%)
<b>Final diagnosis for hospitalization</b>	
Pulmonary TB	54 (27.1%)
Extra pulmonary TB	8 (4%)
<i>P. carinii</i> pneumonia (PCP)	9 (4.5%)
Other bacterial pneumonias	33 (16.6%)
Cerebral toxoplasmosis	8 (4%)
Others	87 (43.7%)
<b>Exposure category</b>	
Intravenous drug use (IDU)	46 (23.1%)
Incarceration	3 (1.5%)
Blood transfusion	12 (6%)
Sexual contact	5 (2.5%)
Dialysis	1 (0.5%)
IDU & Incarceration	76 (38.2%)
Others	56 (28.2%)

Frequency of respiratory symptoms in HIV infected patients is listed in Table 2. Among 95 patients with pulmonary complications, 82 (86.3%) had cough, 77 (81%) fever, 68 (71.6%) sputum, 52 (54.7%) dyspnea, 46 (48.4%) chills, 42 (44.2%) tachypnea, and 10 (10.5%) hemoptysis. Of the 54 patients hospitalized due to tuberculosis, 39 (72.2%) reported to have fever, 46 (85.1%) cough, and 33 (61%) weight loss.

**Table 2.** Frequency of respiratory symptoms in 199 male, HIV-infected patients admitted to the hospital.

Diagnosis	Respiratory symptoms								
	Fever	Chill	Cough	Sputum	Hemoptysis	Dyspnea	Wheezing	Weight loss	Night sweat
Pulmonary TB (n=54)	39 (72.2%)	26 (48.1%)	46 (85.2%)	34 (63%)	2 (3.7%)	29 (53.7%)	49 (90.7%)	33 (61.1%)	27 (50%)
Extra pulmonary TB (n=8)	7 (87.5%)	5 (62.5%)	-	-	-	1 (12.5%)	3 (37.5%)	4 (50%)	2 (25%)
<i>P. carinii</i> pneumonia (n=9)	7 (77.8%)	4 (44.4%)	9 (100%)	8 (88.9%)	1 (11.1%)	7 (77.8%)	9 (100%)	4 (44.4%)	3 (33.3%)
Other bacterial pneumonias (n=33)	31 (93.9%)	16 (48.5%)	27 (81.8%)	26 (78.8%)	7 (21.2%)	16 (48.5%)	31 (93.9%)	17 (51.5%)	6 (18.2%)
Others (n=87)	43 (49.4%)	24 (27.6%)	43 (49.4%)	26 (29.9%)	1 (1.1%)	18 (20.7%)	47 (54%)	39 (44.8%)	14 (16.1%)

**Table 3.** Risk factors for pneumonia in 199 male, HIV-infected patients admitted to the hospital.

Diagnosis	Risk factors				
	IDU	Incarceration	IDU and incarceration	Blood transfusion	Sexual contact
Pulmonary TB	12 (35.2%)	1 (2.9%)	20 (59%)	-	1 (2.9%)
<i>P. carinii</i> pneumonia	1 (14.3%)	-	3 (42.9%)	1 (14.3%)	2 (28.5%)
Other bacterial pneumonias	8 (32%)	-	13 (52%)	4 (16%)	-

Data were available for CD4<sup>+</sup> count of 34 patients with respiratory complications. The mean rate was 234 cells/mm<sup>3</sup>; 24 (70.6%) had CD4<sup>+</sup> cell counts under 200 cells/mm<sup>3</sup>; 6 (17.7%) had CD4<sup>+</sup> cell counts between 200 and 500 cells/mm<sup>3</sup> and 4 (11.7%) had CD4<sup>+</sup> cell counts greater than 500 cells/mm<sup>3</sup>. By diagnosis, 72.2% of the patients with tuberculosis had CD4<sup>+</sup> counts under 200 cells/mm<sup>3</sup>; 66.7% of the patients with bacterial pneumonias had CD4<sup>+</sup> counts less than 200 cells/mm<sup>3</sup>; and 66.7% of the patients with PCP had CD4<sup>+</sup> counts under 200 cells/mm<sup>3</sup>.

Among 38 chest x-ray reports available for patients with tuberculosis, 1 case (2.6%) had a normal chest x-ray while the remainder (97.4%) had an abnormality. Of those with any abnormality on chest x-ray, only 3 (8.1%) had cavitory lesions. Among 43 reports of sputum smears and 6 reports of sputum culture, 23 (53.5%) and 2 (33.3%) were positive for tubercle bacilli, respectively.

Table 3 shows the frequency of risk factors for pneumonia in HIV infected patients. Intravenous drug users who had a history of incarceration had the highest risk of pulmonary tuberculosis (59%), other bacterial pneumonias (52%), and *P. carinii* (42.9%).

## DISCUSSION

Over the course of the epidemic, pulmonary complications have been an important source of morbidity and mortality in patients with HIV/AIDS. Both infectious and noninfectious complications have been well described in other parts of the world (8, 9). This study describes the respiratory complications detected among 199 hospital admissions of 177 adult patients with HIV infection in Iran.

In our study, the most common respiratory symptoms in hospitalized patients with pulmonary complications were cough, sputum and dyspnea, reported by the majority of patients. These findings are similar to the results of Diaz et al. which found the respiratory symptoms of dyspnea, cough and phlegm production to be more common in HIV-infected patients than in HIV-negative patients in the US (10). According to a study by Wong et al. in China, cough for a mean of 75 days with sputum production and dyspnea were the most common respiratory symptoms in HIV patients (11). The most common causes of chronic cough found in 21 patients were bronchopulmonary infections, Kaposi's sarcoma and sinus infections, in order. According to their results, patients with sinopulmonary infections tended to have longer duration of cough and had low CD4 levels. They concluded that chronic cough is a heterogeneous clinical problem in advanced HIV-infected patients, most commonly caused by an infective process (11).

Our data are consistent with other reports demonstrating an unusually high prevalence of unexplained dyspnea in the HIV-infected patient population (1, 2). Of interest is the study of Johnson and colleagues (12), who noted a high incidence of unexplained dyspnea among otherwise healthy military recruits with HIV. Based on the results of cardiopulmonary exercise testing, they hypothesized that a limitation in oxygen delivery to exercising

muscles secondary to cardiac limitation was the most likely cause (13). Another possible explanation may be skeletal muscle dysfunction, including weakness of the respiratory muscles that might be an important contributor to dyspnea development in HIV infected patients (14).

Our observations also suggest that the HIV transmission category, an indicator of varying exposures, influences the types of pulmonary complications developing in patients with HIV (15). In Iran, drug users with history of incarceration comprise the major HIV transmission category while homosexual men are the major HIV transmission category in the US (15).

Pulmonary tuberculosis was the most common bacterial pulmonary complication caused by a single organism in our study, a finding more similar to that of developing and some middle-income countries than developed ones. In Spain, Danés et al. reported bacterial pneumonia as the most frequent diagnosis in HIV-positive patients with respiratory symptoms (63% of cases) (16). In a Brazilian study by Silva et al., the most common etiologic agents were *P. jiroveci* (46.7%), pyogenic bacteria (33.5%) and *M. tuberculosis* (16.7%) in HIV-positive patients (17). Another Brazilian study has shown a higher prevalence of pneumocystosis in this population and pyogenic bacteria were not prevalent etiologic agents (18).

Intravenous drug use has been a risk factor for bacterial pneumonia in many cohorts of HIV-infected patients (19-22). In our study, a history of intravenous drug use and incarceration was associated with a higher risk of pulmonary tuberculosis, followed by other bacterial pneumonia.

This study has several limitations. As a retrospective study, it was not possible to systematically use a standardized protocol for the assessment of HIV-infected patients with respiratory symptoms. Other important data, such as smoking

history and the use of chemoprophylaxis, were not collected. The diagnostic approaches varied according to the patients' primary physicians. Because we were unable to document the patients' antiretroviral therapy, previous antimicrobial treatment or chemoprophylaxis, we could not assess their impact on the incidence, etiology, and outcome of pulmonary infection. In many patients, the medical records were incomplete. Finally, because the study was limited to a single referral center, the results may not apply to other patient populations.

Nonetheless, this study demonstrated the high frequency of respiratory symptoms, infections, and complications in a large consecutive case series of Iranian HIV patients. We showed that pulmonary tuberculosis is still a frequent complication in HIV-infected patients, despite the availability of chemotherapy. Overall findings suggest the need for more effective preventive measures, including the implementation of the guidelines for antiretroviral treatment and prophylaxis in Iran.

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