

ORIGINAL ARTICLE

IMMUNOLOGICAL AND CLINICAL FEATURES OF HIV IN A GROUP OF HOSPITALIZED IRANIAN PATIENTS

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Background – HIV infection is found worldwide and the number of cases is increasing rapidly, particularly in developing countries. In recent years, the rate of HIV infection seems to be increasing in Iran, particularly due to the increased number of intravenous (IV) drug abusers who are infected in prisons and rehabilitation centers.

Methods – From September 1998 to April 2000, we reviewed 44 HIV-positive patients who presented to Masih Daneshvari Hospital, Tehran, Iran. Epidemiological factors, immunological status, associated infections and complications were evaluated.

Results – Of 44 patients, 4 (10%) were females and 40 (90%) were males. The mean age was 38 years. The most frequent route of infection was IV drug abuse (75%), followed by heterosexual activity (16%) and blood transfusion (9%). Flow cytometric tests in 39 patients revealed that 16 had lymphocyte CD4+ counts less than 500 cells/ μ L. The purified protein derivative test was positive in 10 of 30 cases (33%). Eight of 39 (21%) patients had hepatitis B surface antigen (HBsAg) and 17 of 39 (44%) had hepatitis B surface antibody (HBsAb); none of these patients had been vaccinated against hepatitis B virus (HBV). Twenty-nine of 39 (81%) cases were positive for antibodies to hepatitis C virus (anti-HCV). Five patients had clinical tuberculosis. Four (9%) patients died.

Conclusion – Our results help to set priorities and to rationalize the availability of prevention and treatment programs in our country, particularly, among IV drug abusers. Multidisciplinary and multilevel approaches, both by government and private health care providers, will have a positive impact on HIV status in Iran.

Keywords epidemiology HIV immunology infection

Introduction

The acquired immunodeficiency syndrome (AIDS) became a clearly defined clinical entity in the early 1980s, since when there has been intense scientific effort to unravel the intricacies of the pathogenesis and dynamics of HIV infection.^{1,2}

At the start of a new millennium, HIV infection has a worldwide distribution and the number of cases is increasing rapidly, particularly in developing countries.³ Experience shows that

the right approaches, applied quickly with courage and resolve, can and do result in lower HIV infection rates and less suffering for those affected.⁴

The increasing incidence of AIDS in less-developed countries is not inevitable.⁵ Yet, unless action against the epidemic is scaled up drastically, the damage already done will seem minor compared with what lies ahead.

Already 42 million people globally are living with the virus (HIV/AIDS), of whom 38.6 million are adults and 3.2 million are children under 15 years;⁶ most of these will die over the next decade or so. The most recent UNAIDS/WHO estimates show that in 2002 alone, 5 million people were

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newly infected with HIV.⁶

In recent years, the rate of HIV infection has increased in Iran, particularly due to more intravenous (IV) drug abusers infected in prisons and rehabilitation centers.^{6,7} High-risk behavior is widespread in this largely male population: about half of users share injecting equipment, and as many are believed to have extramarital sexual relations.⁶

In order to describe the clinical features, immunological status and complications of HIV-positive patients, this survey was performed in Masih Daneshvari Hospital in Tehran, Iran.

Patients and Methods

We reviewed 44 HIV-positive patients who presented to the Masih Daneshvari Hospital of the Shaheed Beheshti University of Medical sciences, Tehran, Iran, from September 1998 to April 2000. Eleven patients were in the clinical stages of AIDS. All serum samples had been tested for HIV-1 infection by the reference laboratory of the Iranian Blood Transfusion Center using two EIAs (electroimmunoassays). Confirmation was provided by Western blot for all patients.

Enrolment of patients was independent of disease stage or degree of immunosuppression. All participants were seen by one clinician, who recorded highlights of the medical history and physical examination of each patient on a detailed questionnaire. All study variables were extracted from these questionnaires. Family members of all married patients were also tested for HIV infection.

All patients had initial routine laboratory evaluations including complete blood count (CBC), erythrocyte sedimentation rate (ESR), liver function test (LFT), uric acid (U/A) and urine acid-creatinine (UA/C). Purified protein derivative (PPD), venereal disease research laboratory (VDRL) and serologic tests for hepatitis B virus (HBV), hepatitis C virus (HCV) and toxoplasma were also performed when possible. HBV serologic tests were performed for 39 (89%) patients, recombinant immunoblot assay (RIBA) for HCV was performed in 11 (25%) patients and polymerase chain reaction (PCR)-based tests were used to detect HCV RNA in 15 (42%) patients. All these tests were performed at Masih Daneshvari Hospital on the basis of routine procedures elsewhere. Radiological studies of the

chest and facial sinuses were performed for all patients.

The immunological status of patients was evaluated using flow cytometric tests. Flow cytometric analysis of peripheral blood lymphocytes was performed using fluorescence-activated cell sorter (FACS) caliber flow cytometry (Becton-Dickinson, Mountain View, California, USA). Pairs of monoclonal antibodies (fluorescent isothiocyanate, phycoerythrin conjugated) against CD3 (total T lymphocytes), CD4 (T helper cells) and CD8 (T cytotoxic cells) were also assessed at Masih Daneshvari Hospital. Further complementary tests were carried out as necessary.

All the patients gave informed consent before entering the study. The characteristics of the patients names remained secret. Outcome variables were measures of epidemiological factors, immunological status, associated infections, therapeutic modalities and complications. The SPSS 9 software was used for statistical analysis.

Results

Characteristics of patients

Of 44 patients, 4 (9%) were females and 40 (91%) were males. The mean age (\pm standard deviation) was 38 ± 10.73 years, with ages ranging between 14 and 55 years. Twenty-three (52%) patients were single and 21 (48%) were married. The most frequent route of infection was IV drug abuse (75%, 33 patients, all males). Other routes of infection were sexual contacts and infected blood products (Figure 1).

Survey of family members of 18 patients showed 3 (16%) infected cases (wives of index cases, all infected by heterosexual contact) while

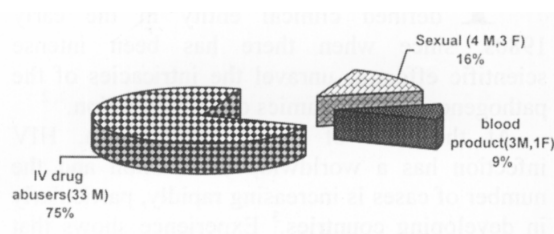


Figure 1. Different routes of infection in 44 HIV-positive patients at Masih Daneshvari Hospital 1998 – 2000. M = male, F = female.

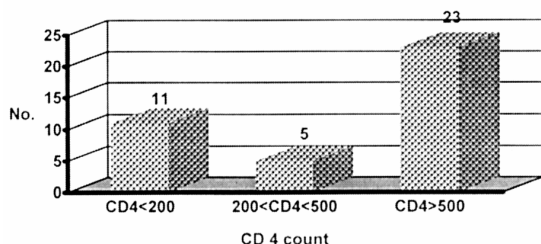


Figure 2. CD4+ count in 39 HIV-positive patients at Masih Daneshvari Hospital, 1998 – 2000.

the remaining (84%) were seronegative.

Of the 39 patients for whom flow cytometric tests were performed, 16 (37%) had a T lymphocyte CD4+ count of less than 500 cells/μL (figure 2). They were encouraged to undergo highly active antiretroviral therapy (HAART).

Opportunistic infections

Of the 30 (68%) patients who underwent PPD testing, 10 (33%) had a positive test (defined for HIV-infected patients as > 5 mm of induration) and received isoniazid prophylaxis. Seventeen (44%) patients were positive for hepatitis B surface antibody (HBsAb) and 8 (21%) for hepatitis B surface antigen (HBsAg). These patients did not undergo liver biopsy.

Of the 36 (82%) patients who underwent HCV screening, using enzyme-linked immunosorbent assay (ELISA), 29 (81%) were positive. The diagnosis of HCV infection was confirmed by RIBA or with HCV RNA in 20 (69%) of the 29 patients with positive ELISA. RIBA for HCV was positive in 8 of 11 patients (73%) and PCR-based tests for HCV RNA were positive in 12 of 15 patients (80%). Liver biopsy was performed in 14 of 29 HCV-positive patients and revealed different degrees of necrosis and disease activity.

Serologic test (immunoglobulin G [IgG]) for toxoplasma was positive in 15 of 27 cases (55%). Serologic test for syphilis (VDRL) was positive in 2 of 26 cases (8%); both were treated.

Five male patients had concomitant clinical tuberculosis (TB) with a combination of different clinical findings; 3 had millary pulmonary TB, 2 had mediastinal lymphadenopathy, 3 had TB pleural effusion and 2 had TB meningitis. Except one patient who died, all were treated successfully.

Four patients had oral candidiasis, one case was affected with necrotizing pneumonitis and

five cases bronchitis and bronchiectasis were detected. All these patients received appropriate treatment. One patient had recurrent herpes labialis and another had hairy leukoplakia; both recovered after institution of HAART.

From 6 months prior to the writing of this paper, 4 of 16 cases (25%) were on regular HAART with zidovudine, lamivudine and indinavir. The T lymphocyte CD4+ count in these patients rose from a mean of 170 to 400 cells/μL. One patient was on a different regimen of antiretroviral therapy from 5 years prior to writing, when his T lymphocyte CD4+ count was undetectable (< 10 cells/μL). With his latest regimen (zidovudine, lamivudine, nevirapine), it reached to more than 1000 cells/μL.

During our evaluation, 4 (9%) patients died. Patient No. 1 was a 44-year-old man with disseminated *Mycobacterium avium* infection, bilateral cytomegalovirus (CMV) retinitis, CMV encephalitis and chronic hepatitis C. Patient No. 2 was a 30-year-old man with chronic hepatitis C, HIV-related dementia, candidal esophagitis and septicemia. Patient No. 3 was a 23-year-old man who died suddenly without any previous history of opportunistic infection, probably because of complications of hemophilia and intracerebral hemorrhage. Patient No. 4 was a 38-year-old man with *Pneumocystis carinii* pneumonia (PCP), disseminated mycobacterial infection and respiratory failure.

Discussion

Because of factors such as HIV subtypes, exposure to endemic diseases, nutritional status and access to medical treatment, the findings of cohorts in resource-rich countries can not be extrapolated to our country. Reports published by the Islamic Republic of Iran's Ministry of Health show that HIV infection in our country is increasing rapidly.⁷ According to these reports, the most common route of infection in 2001 was IV drug abuse (64%).^{6, 7} Comparing this figure with our result (75%) reveals that HIV transmission among drug abusers will be a catastrophe and, if rapid measures are not taken, HIV will explode through the population with remarkable speed and stabilize at very high rates.^{2, 8} Unfortunately, it is hard to know exactly how many people inject drugs and how many share their equipment and even harder to know when they are infected with HIV; thus the exact time of

conversion of HIV infection to AIDS remains unknown.

Drug injection poses a threat of HIV infection not only to the individuals who engage in it but also to their sexual partners. In the USA, it is estimated that 9 out of 10 cases of heterosexual transmission of HIV in New York city are related to sex with a drug user.¹

A good approach to prevent HIV infection among IV drug abusers is treatment.^{1, 9} This includes helping users switch to substances such as methadone, which do not need to be injected. In an 18-month study of 255 drug users in Philadelphia (USA) in the early 1990s, only 3.5% of drug users on stable methadone treatment became infected with HIV, compared with 22% of those who were not being treated.¹ The poor compliance of IV drug abusers with antiretroviral therapy and the high cost of such drugs also present challenges to HIV programs.

No patients had been vaccinated against HBV, and 65% of patients (total of HBsAb⁺ and HBsAg⁺) had been infected. Other studies have shown that the prevalence of HCV and HBV infection in HIV-positive patients is about 50%.¹⁰ Our results revealed that the co-infection rates in our patients were 81% and 65%, respectively. Contrary to the situation in other countries, where the most common route of infection is sexual transmission, IV drug abusers were most commonly infected in our study and also in global reports,⁶ which may explain why we have a higher rate of infection with HBV and HCV. Regarding other routes of infection with HIV, more measures such as detection of associated infections, especially endemic ones such as TB, HBV and HCV, should also be targeted. This will prevent the complications and progression of HIV infection to advanced stages.¹¹

Continued education of the health-care personnel and the public is needed.¹² Better surveillance systems will enable us to accurately track the development of the epidemic and mount effective responses. Isolation of HIV-positive patients in hospitals should be avoided and the reality of AIDS should be illuminated for the public in order to obtain more social support.¹³

Medical treatment programs, particularly HAART, must be available and insurance facilities should be provided to cover its costs. In addition, people with HIV or AIDS need psychological support to cope with the implications of having a life-threatening disease.¹⁴ Sophisticated laboratory centers capable of measuring plasma viral load, flow cytometry and other tests are urgently needed. Current efforts should be applauded, but they must be expanded. Along with such efforts, more information about HIV infection in Iran is needed to allow better planning for the future.

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