Seroprevalence of Toxoplasmosis in HIV$^+$/AIDS Patients in Iran

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Abstract- *Toxoplasma gondii* has arisen as an important opportunistic agent especially in the central nervous system and in advanced HIV disease can cause significant morbidity and mortality. This study was carried out to determine the seroprevalence of toxoplasmosis among HIV-positive patients in Iran. Blood samples were collected from 201 HIV-positive patients and anti-toxoplasma antibodies were detected by using conventional ELISA. An antibody titer of >3 IU/ml was considered positive. The majority of studied patients were male (male to female ratio: 5 to 1) with the mean age of 36 ± 1 yrs. The seroprevalence of toxoplasmosis in HIV-positive patients was 49.75%. The mean CD4 count in HIV patients with positive toxoplasma serology was 332.5 ± 22.4 cells/µl. Only 1% of the patients had IgM anti-toxoplasma antibodies and 10% of the patients had clinical toxoplasma encephalitis. The mean CD4 count in this group was 66.4 ± 15.5 cells/µl and there was a significant association between CD4 count and rate of toxoplasma encephalitis (P<0.001). Previous reports suggested that toxoplasma encephalitis could be prevented by appropriate chemoprophylaxis. In view of the relatively high prevalence of toxoplasma infection found among the HIV-infected patients in our study, we suggest that routine screening for toxoplasma should be undertaken for all HIV-infected patients in Iran.

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Introduction

Toxoplasmosis is caused by an obligate intracellular parasite *Toxoplasma gondii*. It is a frequent cause of subclinical latent human infection. With the advent of HIV pandemic, toxoplasmic encephalitis has become one of the more frequent opportunistic infections and the most common cause of focal lesions of the brain complicating the course of AIDS (1, 2).

The incidence of *Toxoplasma gondii* in patients depends mainly on the existence of latent anti-toxoplasma antibodies in the affected population (3, 4). Serological studies have demonstrated that 15% to 68% of adults in the United States and 90% of adults in some European communities show latent *Toxoplasma gondii* infection (5, 6). In the United States, it is estimated that 20% to 47% of all patients with HIV develop encephalitis due to toxoplasmosis while the figures are 25% to 50% for Europe and Africa (3-5, 7-9). Because of the risk of damage to the CNS and high morbidity in these patients, we believe it is of utmost importance to find out the prevalence of anti-toxoplasma antibodies in HIV/AIDS patients. However, only a few studies on the seroprevalence of toxoplasmosis have been carried out among HIV/AIDS patients in Iran. The objective of this study was to determine the seroprevalence of toxoplasmosis among HIV/AIDS patients at Imam Khomeini Hospital; a referral center for HIV/AIDS in Iran.

Patients and Methods

A cross-sectional study was conducted by Iranian Research Center for HIV/AIDS affiliated to Tehran University of Medical Sciences, Iran. This study was carried out at the outpatient department and inpatient ward for infectious diseases at Imam Khomeini Hospital which holds 1000 beds and is the largest government referral hospital in Iran. The study was conducted with the approval of the institutional review board of Tehran University of Medical Sciences. We considered the medical records of 201 HIV infected patients admitted from March 2004 to March 2005. Their records were screened using a standardized data collection sheet for demographic characteristics such as age, sex, HIV transmission risk factors and CD4 count. Toxoplasmosis

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was screened by standard ELISA (Both IgM and IgG) commercial kit (AxSYM, Abbott Laboratories, Abbot Park, Illinois, USA) in accordance with the manufacturer`s instructions. A titer of anti-toxoplasma antibody >3 IU/ml was considered as positive. In these patients, CDC (Centers for Disease Control) criteria were applied for the diagnosis of clinical cerebral toxoplasmosis and included: 1) Clinical features of CNS involvement, 2) Raised anti-toxoplasma IgG titers, 3) Typical CNS lesions on CT/MRI imaging, 4) Dramatic clinical response to the treatment within 3-5 days of anti-toxoplasma therapy. Three weeks after initiation of conventional anti-toxoplasma therapy, CT scan was performed again to document the radiological improvement. In this study, AIDS defining illnesses were also based on the 1993 CDC criteria. The data were analyzed using the statistical software SPSS for windows version 11.5 (SPSS Inc, Chicago, USA). All measurements are expressed as mean ± SEM. Statistical analysis was estimated using either Chi-square test or Fishers' exact test and independent *t*-test where appropriate. A *P*-value less than 0.05 was regarded as statistically significant.

Results

Two hundred and one HIV/AIDS patients who had referred to Imam Khomeini Hospital between March 2004 and March 2005 were included in this study. The age range of the patients was between 3-62 years with mean age of 36 ± 1 years. Their mean CD4 count was 357.1 ± 18.1 cells/µl. With respect to gender, 172 patients were male and 29 were female. The seroprevalence of toxoplasmosis among these 201 HIV/AIDS patients was 49.75% (100 cases: 84 males and 16 females). The seroprevalence of toxoplasmosis was 48.8% in males and 55.2% in females (Table 1).

Table 1. Demographic and baseline characteristics of 201 HIV/AIDS patients with and without toxoplasma infection

Demographic & baseline characteristics	**Toxoplasma positive** Number (%)	**Toxoplasma negative** Number (%)	**Total** Number
Sex			
Male	84 (48.8%)	88 (51.2%)	172
Female	16 (55.2%)	13 (44.8%)	29
Marital status			
Single	39 (42.4%)	53 (57.6%)	92
Married	35 (56.5%)	27 (43.5%)	62
Divorced	21 (53.8%)	18 (46.2%)	39
Spouse is dead	5 (62.5%)	3 (37.5%)	8
Occupation			
Clerks	1 (20%)	4 (80%)	5
Merchants	17 (58.6%)	12 (41.4%)	29
Students	1 (33.3%)	2 (66.7%)	3
Unemployed	35 (50%)	35 (50%)	70
Other Jobs	46 (48.9%)	48 (51.1%)	94
Education			
Illiterate	2 (50%)	2 (50%)	4
Elementary School	29 (52.7%)	26 (47.3%)	55
Guidance School	40 (52.6%)	36 (47.4%)	76
High School	18 (34.6%)	34 (65.4%)	52
University Students	11 (78.6%)	3 (21.4%)	14
Highly Active Antiretroviral Therapy (HAART)			
With HAART	47 (51.1%)	45 (48.9%)	92
Without HAART	53 (48.6%)	56 (51.4%)	109

Table 2. Age distribution of HIV/AIDS patients with and without toxoplasma infection

Age groups	Toxoplasma positive	Toxoplasma negative	Total
	Number (%)	Number (%)	Number
≤10 years	0 (0%)	3 (100%)	3
11-20 years	1 (50%)	1 (50%)	2
21-30 years	23 (46.94%)	26 (53.06%)	49
31-40 years	43 (51.2%)	41 (48.8%)	84
41-50 years	27 (50%)	27 (50%)	54
51-60 years	6 (75%)	2 (25%)	8
61-70 years	0 (0%)	1 (100%)	1

These patients had different HIV transmission risk factors including: blood transfusion (8), unsafe sex (16), Injection Drug Use (67), HIV spouse (24), other risk factor (19) like vertical transmission, tattoo and multiple risk factors (67). Seroprevalence of toxoplasmosis was 25% (2/8 cases) for cases that had underwent blood transfusion, 50.7% (34/67) for Injection Drug Users, 56.3% (9/16) for those engaged in unsafe sex, 58.3% (14/24) for those with HIV infected spouses (patients who had sexual contact with a monogamous spouse infected with HIV), 36.84% (7/19) for other ways of transmission (like tattoo and vertical transmission), and 50.7% (34/67) for those with multiple risk factors (Figure 1).

CD4 counts (cells/µl) were categorized into four groups: CD4<100, CD4 100-199, CD4 200-499 and CD4>500. The seroprevalence of toxoplasmosis in patients with CD4<100 was 61.5% (16/26) and figures for the other groups were 45.2% (14/31) in 100<CD4<200, 50.5% (50/99) in 200<CD4<500, and 44.4% (20/45) in CD4>500 (Figure 2).

Seroprevalence of toxoplasmosis was different in different age groups. No antibodies were detected in age ≤10 and 61-70 years while a high seropositivity was observed in the 51-60 age groups (75%) (Table 2).

The mean age and CD4 count of patients with positive toxoplasma serology was 36.8 ± 0.8 years and 332.5 ± 22.4 cells/µl, respectively while the mean age and CD4 count of patients with negative toxoplasma serology was 35.2 ± 1.0 years and 381.5 ± 28.2 cells/µl, respectively.

No significant relationship was observed between seroprevalence of toxoplasmosis and demographic and baseline characteristics of the patients, the HIV transmission risk factors and the CD4 counts (P>0.05, non significant). Ten cases (10%) of HIV/AIDS patients with positive serology of toxoplasma had clinical toxoplasma encephalitis and one case (1%) had IgM anti-toxoplasma antibodies. The mean CD4 count in this group was 66.4 ± 15.5 cells/µl and there was a significant relationship between CD4 count and rate of toxoplasma encephalitis (P<0.001).

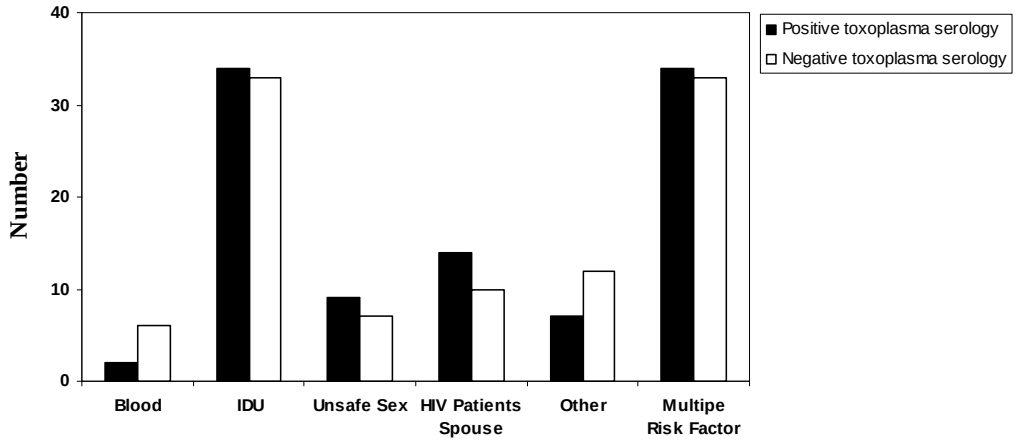

Figure 1. Prevalence of toxoplasma infection in HIV/AIDS patients by risk factors

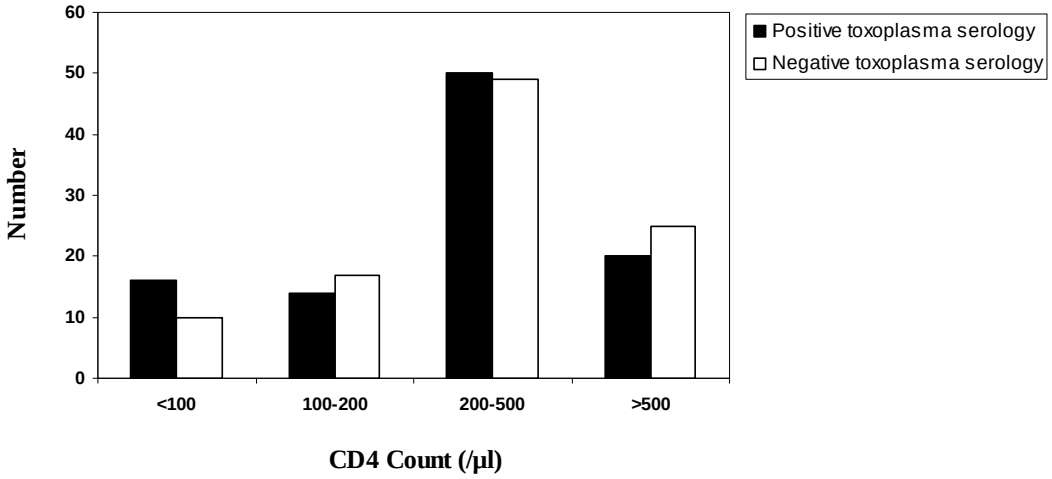

Figure 2. Prevalence of toxoplasma infection in HIV/AIDS patients by CD4 count

Discussion

Seroprevalence studies on toxoplasmosis vary according to geographical location. The global seroprevalence in general population is reported to be 46.1% (10). In Iran, about 51.8% of the population is estimated to have antibodies against the infection (11).

This study has shown that the seroprevalence of toxoplasmosis in HIV/AIDS patients (49.7%) are the same as general population (51.8%) in Iran.

A study by Jones *et al.,* (12) in nine United States cities found that toxoplasma encephalitis in HIV infected patients varied by geographical area. In The United States, 10-40% of adults with AIDS are seropositive for toxoplasmosis (13). In Europe, Latin America and Africa the prevalence of latent toxoplasma infection is between 4-90% (6, 14-17) and in Asia the prevalence of toxoplasma varies from 10-50% (18-21). The overall seroprevalence of toxoplasmosis was found to be 49.7% in our HIV/AIDS patients.

The majority of our patients had anti-toxoplasma IgG antibodies and in only one case (1%) IgM anti-toxoplasma antibodies were detected. These results can be compared to other similar studies: 1% in Mexico (15) and 0% in India (19). So in most of the cases, clinical toxoplasmosis is the outcome of a reactivation of a latent infection (4). However it is possible that some cases of acute toxoplasma infection may have been found negative for IgM particularly in the more profoundly immunodeficient, or where testing was carried out several months after infection has been acquired.

Similar to other studies in Taiwan (20) and India (19), we demonstrated that there is no association between the prevalence of toxoplasmosis and demographic and baseline characteristics.

In our study, 10 cases (10%) of all toxoplasma positive patients had clinical toxoplasma encephalitis with a mean CD4 count of 66.4 cells/µl. This shows that in these patients who have a low number of CD4 cells, the risk of reactivation of latent infection increases.

Toxoplasma encephalitis is reported to occur at CD4 count<200 cells/µl (France) (22), CD4<100 cells/µl (USA) (12) and 35 times more common in those with CD4<50 cells/µl (Edinburgh) (23).

The mean CD4 count was in our HIV positive patients who had clinical toxoplasma encephalitis was 58.1 cells/µl. The risk of cerebral toxoplasmosis seems to be higher in moderately severe immunodeficiency.

Before Highly Active Antiretroviral Therapy (HAART) and chemoprophylactic regimens against toxoplasma, the risk of toxoplasma encephalitis in HIV patients with positive serology of toxoplasma was high. The rates of risk have been reported from a few centers and include 25.4% in France (24) and 30% in Baltimore (25) and 45% in Norway (26).

In some textbooks (27, 28) it has been mentioned that 20-47% or more than 1/3 of all HIV positive patients with positive serology of toxoplasma will develop toxoplasma encephalitis by using HAART therapy and chemoprophylactic regimens against toxoplasma. In our study we had a lower rate of toxoplasma encephalitis among HIV patients with positive serology of toxoplasma (This may be due of

administration of chemoprophylactic regimen and HAART therapy). This figure can be compared with other studies such as 5-10% in USA, 15% in Europe and 14.9% in Indonesia (21). One explanation for these differences might be related to different levels of immunodeficiency as well as different duration of therapy.

Hence, *Toxoplasma gondii* has emerged as an important opportunistic infection in Iran. We propose that measurement of anti-toxoplasma antibodies can be recommended as a screening test in all HIV/AIDS patients to detect the latent infection as this may reduce the risk of toxoplasma encephalitis.

We conclude that toxoplasma is a prevalent infection in HIV positive patients in Iran and all HIV positive patients must be screened for toxoplasma infection using appropriate serological tests.

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