Seroprevalence of Cytomegalovirus and Toxoplasma in People Living With HIV Referred to the Behavioral Diseases Counseling Center in Tehran

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Abstract- According to data from the WHO and CDC, Toxoplasma gondii is found worldwide, with a higher prevalence in regions with warm, humid climates; the highest reported rates in the general population reach 90%. The prevalence of cytomegalovirus infection among the general population of Iran has been estimated at 5.2%. According to the existence of insufficient data on the seroprevalence of Cytomegalovirus (CMV) infections in Tehran and the Center for Behavioral Diseases of human immunodeficiency virus (HIV)+ and toxoplasmosis among the people of Imam Khomeini Hospital, as well as the grave and fatal complications that threaten these infections, to identification, prevention and timely treatment of People Living with HIV (PLWH), general knowledge of its prevalence in our country is essential. This project was a cross-sectional study of PLWH referred to the Behavioral Diseases Counseling Center of Imam Khomeini Hospital in Tehran in 2018. A number was assigned to each patient who visited this year, and 348 were selected from this group. Anti-Cytomegalovirus Immunoglobulin G (IgG Anti CMV), and Anti-Toxoplasmosis Immunoglobulin G (IgG Anti-Toxoplasmosis) levels in serum were measured alongside demographic information, HIV transmission routes, disease duration, cluster of differentiation 4 (CD4) count, viral load, and Hepatitis B Virus and Hepatitis C Virus status of participants. The collected data were entered into IBM SPSS Statistics software version 25. The data were extracted from the patients' files to support the research aim. The seroprevalence of cytomegalovirus and toxoplasmosis was 99.4% and 41.7%, respectively. Due to cytomegalovirus's high prevalence, it has been impossible to investigate the impact of influential factors, and the efforts have been ineffective. A statistically significant relationship was seen between factors of hepatitis B serum level and marital status with the prevalence of toxoplasmosis; more than half of participants who were married were infected with Toxoplasma in comparison with the unaffected 28.2% (P<0.001). A larger portion of participants with positive HBV test results were infected with Toxoplasma, in contrast to 39% in the HBV-negative group (P=0.017). But no relationship with gender was observed (42.8% vs 39%). In this study, a significant association was observed between serum levels of positive hepatitis B (Hepatitis B Surface Antigen or Hepatitis B Core Antibody) and anti-toxoplasmosis antibody. Given the 99%

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prevalence of CMV in the population, it is recommended to conduct further research on demographic factors, such as residence and income level, or on the reliability and accuracy of the laboratory testing kits at this facility.

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Introduction

Cytomegalovirus (CMV) is a deoxyribonucleic acid (DNA) from the Beta Herpesviridae sub-branch and the Herpesviridae family. It is one of the most common viral infections in the world. The WHO reports that CMV infection is found in approximately 60%-100% of the general population. Symptoms vary based on the level of immunity, ranging from asymptomatic in people with a healthy immune system to the most severe symptoms in people with a suppressed immune system for any reason (fetal-neonatal period, after transplant, and also human immunodeficiency virus (HIV) infection). In a United States study, the prevalence was estimated at 50.4% (1). In another study, the prevalence of CMV in males and females living with HIV was 79.7% and 78.5%, respectively, compared to 50% and 61.4% in HIV-positive people, indicating a higher prevalence in immunosuppressed people (2). It should be noted that in developed countries, 10-20% of children are infected with CMV before puberty. As mentioned earlier, the prevalence of infection varies by a country's safety status and economic level, as well as by the health system. Hence, CMV prevalence is higher in developing countries than in developed countries. This virus is the leading congenital viral infection, with an incidence of 0.2-2.2% in live births. Also, its prevalence is close to 50-90% in transplant patients and 100% in People Living with HIV (PLWH). Due to the broad age range of involvement, the course of symptoms is also variable, so congenital CMV infection with symptoms such as Premature birth, Low birth weight, Hepatosplenomegaly, Prolonged jaundice, Microcephaly, Convulsions, and other complications of infection with this virus include infectious mononucleosis, vision-threatening retinitis, involvement of the nervous system in the form of polyradiculopathy and meningoencephalitis, gastroenteritis, and pneumonia (3).

Toxoplasmosis is an infection caused by a protozoan called Toxoplasma gondii. Depending on the level of immunity, the course of symptoms ranges from asymptomatic to weakness, fever, and lymphadenopathy in healthy people to life-threatening encephalitis in PLWH (4). Toxoplasmosis infection is widespread in hot, humid climates, with prevalence rates reaching up to 90% in some regions around the world, according to the WHO. Its prevalence has been estimated at 22.5% of the total population in the United States and 44.8% in the PLWH (5,6).

In the studies conducted in America about the incidence of toxoplasmosis infection, approximately 225,000 cases of toxoplasmosis infection have been reported per year, of which 5,000 cases lead to hospitalization and about 750 cases lead to death (7).

These cases make toxoplasmosis infection the third most common cause of foodborne death. Considering the existence of insufficient data on the prevalence of cytomegalovirus and toxoplasmosis infections among PLWH in Tehran and the Center for Behavioral Diseases of Imam Khomeini Hospital, as well as the grave and fatal complications that these infections threaten PLWH, the correct allocation of resources to identify, prevent and treat it in time, the general knowledge of its prevalence in our own country is essential.

In other words, the importance of knowing the serology of these infections is that, when a patient presents with a clinical syndrome consistent with reactivation of these infections, such as CMV retinitis, CMV colitis, or cerebral toxoplasmosis, we can take steps toward diagnosis and treatment with prior information on the serology status. Also, knowing the seroprevalence will help us determine how many are susceptible to these infections and who should follow preventive measures. Therefore, this study aimed to investigate the seroprevalence of cytomegalovirus and toxoplasmosis among an HIV+ population and the factors that affect it.

Materials and Methods

Study design

This study was a cross-sectional, with the primary

purpose of assessing the prevalence of cytomegalovirus and toxoplasmosis infections in 2018.

Study population

The study population was PLWH admitted to Tehran's Behavioral Diseases Counseling Center of Imam Khomeini Hospital in 2018. The target sample was included in the study based on the judgment of the serum levels of Anti-Cytomegalovirus Immunoglobulin G (IgG Anti-CMV) and Anti-Toxoplasmosis Immunoglobulin G (IgG Anti-Toxoplasmosis). Considering the descriptiveness of the study, the research variables included age, sex, occupation, marital status, HIV transmission route, disease duration, cluster of differentiation 4 (CD4) level, viral load level, and association with Hepatitis B Virus (HBV), and Hepatitis C Virus (HCV) as independent variables, and seroprevalence of toxoplasmosis, and cytomegalovirus were investigated as dependent variables. A trained researcher collected the required data from the Center for Behavioral Diseases' electronic archive, using a researcher-developed questionnaire and a code for each patient to protect patient rights.

Implementation method

For toxoplasmosis, cytomegalovirus, HBV, and HCV, serum levels were recorded in the electronic system as positive (+) or negative (-) results, with their status directly entered into the database. For toxoplasmosis, a level higher than 12 IU/mL was considered positive. Regarding CMV, a level above 3 IU/mL was considered positive. After selecting the desired sample, the necessary data were collected from the center's electronic archive.

The HBV variable was considered positive if the person tested positive for Hepatitis B Surface Antigen (HBS Ag) or Hepatitis B Core Antibody (anti-HBc). Similarly, the HCV variable was defined as positive if the person tested positive for Anti-Hepatitis C Virus (anti-HCV) or through Hepatitis C Virus Polymerase Chain Reaction (HCV PCR). Age was categorized into three groups: ≤40, 41-60, and ≥61. Occupation was divided into unemployed, other jobs, and high-risk employees (such as police, prison, and medical personnel). Gender was classified as male or female, and marital status was never married, married, widowed, or divorced. The transmission route was divided into four categories: sexual contact, injection, unknown, and needle stick. CD4 levels were grouped into three categories: ≤200, 201-500, and >501.

If more than one test was performed for each variable in 2018, the last test served as the evaluation criterion.

The ethical considerations of this study included not disclosing patients' names and surnames, and data were collected anonymously by assigning a code to each selected case. This study was approved by the ethical committee of Tehran University of Medical Sciences (ethical approval number IR.TUMS.IKHC.REC.1397.356).

Statistical analysis

After collecting the data, they were entered into IBM SPSS Statistics version 25. The normality test was performed using the Kolmogorov-Smirnov test. Based on the results, the related statistical tests, the Chi-square and Independent t-test, were used, with a significance level of 0.05.

Results

The demographic profile of PLWH is as follows: for the age variable, the median was 39 and the majority of participants (92%) were 60 or under, with the majority of patients in the 20-41 age range (50.6%). Participants mainly were primarily male (69.8%) and employed (52.6%). Nearly half had permanent marriage status, 37.6% were single, and 12.9% were divorced, with the rest being widowed. The most prevalent transmission route of HIV disease was sexual contact (71.0%), followed by injection, unknown source, affected mother, and needle stick, respectively (Table 1, 2 based on the variables). The prevalence of CMV in these patients was 99.4% (95% CI: 98.6%-100%), and that of toxoplasmosis was 41.6% (95% CI: 36.4%-46.8%).

There was a significant relationship between the seroprevalence of toxoplasmosis and the variables of marital status, HBV serological status, and age. Hence people who are married have a higher prevalence (53.8%) than people who have never married (28.2%). The seroprevalence of toxoplasmosis in HBV+ patients (55.2%) was higher than its prevalence in HBV negative patients (39%) with a significant level (P=0.017), which deserves more attention and investigation considering the transmission route of each.

The seroprevalence of toxoplasmosis was higher in the age group 41-60 (56.2%) and, after that, in patients aged 61+ (53.6%) (P<0.001). The variables of gender (P=0.29), occupation (P=0.87), HIV transmission route (P=0.07), and HCV serological status (P=0.32) did not show any significant relationship. Also, there was no relationship between CD4 level and seroprevalence of toxoplasmosis (P=0.97) (Table 1). The examination of

toxoplasmosis seroprevalence based on quantitative variables revealed that for HIV duration, 203 individuals tested negative for toxoplasmosis with a mean duration of 3.28 years, while 145 individuals tested positive with a mean duration of 3.27 years, resulting in a *P* of 0.96. Regarding viral load, 202 individuals tested negative, with a mean viral load of 75,793,37 copies/mm³, whereas 145 tested positive, with a mean viral load of 16,739,50 copies/mm³, yielding a *P* of 0.097.

The examination of CMV seroprevalence based on quantitative variables revealed that for HIV duration and viral load. For HIV duration, the serology results show that the negative group has a frequency of 2 with a mean duration of 3 years, while the positive group has a frequency of 346 with a mean duration of 3.28 years. Regarding viral load, the negative group has a frequency of 2 with a mean viral load of 112,350 copies/mm³, whereas the positive group has a frequency of 346 with a mean viral load of 50,761 copies/mm³. The highlighted rows for the positive groups indicate their significance.

Table 1. Serological prevalence of toxoplasmosis based on research variables

Variable	N	Toxoplasmosis Prevalence, n (%)	*P*
Age (Year)			
≤40	190	57(45.6)	<0.001
41-60	130	73(56.2)	
≥61	28	15(53.6)	
Gender			0.29
Male	243	104(42.8)	
Female	105	41(39.0)	
Occupation			0.874
Unemployed	156	65(41.7)	
High-risk employees	9	3(33.3)	
Other-jobs	183	77(42.1)	
Marital status			<0.001
Single	131	37(28.2)	
Married	158	85(53.8)	
Widowed	14	6(42.9)	
Divorced	45	17(37.8)	
HIV- transmission route			0.07
Sexual-contact	247	101(40.9)	
Injection	54	24(79.1)	
Affected mother	12	1(8.3)	
Unknown	35	19(54.3)	
HBV – serologic status			0.017
Positive	58	32(55.2)	
Negative	290	113(39.0)	
HCV- serologic status			0.317
Positive	48	22(45.8)	
Negative	300	123(41.0)	
CD4			0.974
≤200	51	22(43.1)	
201-500	123	51(41.5)	
≥501	174	72(41.4)	

Table 2. Serological prevalence of CMV based on research variables

Variable	CMV prevalence, n (%)	N
Age (year)		
≤ 40	188(92.3)	190
41-60	130(100)	130
≥61	28(100)	28
Gender		
Male	241(99.2)	243
Female	105(100)	105
Occupation		
Unemployed	155(99.4)	156
High-risk employees	9(100)	9
Other jobs	182(99.5)	183
Martial – status		
Single	129(98.5)	131
Married	158(100)	158
Widowed	14(100)	14
Divorced	45(100)	45

Cont. table 2

HIV –transmission route		
Sexual-contact	246(99.6)	247
Injection	48(100)	48
Affected mother	11(91.7)	12
needle stick	6(100)	6
Unknown	35(100)	35
HBV – serologic status		
Positive	58(100)	58
Negative	288(99.3)	290
HCV – serologic status		
Positive	48(100)	48
Negative	2	300
CD4		
≤200	50(98)	51
201-500	123(100)	123
≥501	173(99.4)	174

Discussion

This study was conducted on 348 PLWH referred to the behavioral diseases counseling center of Imam Khomeini Hospital in Tehran to investigate the prevalence of toxoplasmosis and CMV. The seroprevalence of CMV in this sample was 99%, which was much higher than the prevalence in previous studies. A study conducted across various regions of the United States showed the prevalence of CMV in males and females living with HIV to be 79.7% and 78.5%, respectively, against 50% and 61.4% in the HIV population (2). Also, a similar study conducted in Iran reported this prevalence at about 70% (8). The high prevalence of CMV infection can be explained by the study population's demographic characteristics, the use of different diagnostic methods (PCR- or ELISA-based), and epidemiologic differences related to the time and place of the study. Also, due to the high prevalence, statistical tests such as the chi-square test, which are used to relate two qualitative variables, could not be used in this study because the default was not met.

The seroprevalence of toxoplasmosis in this sample was 41.7%, which was similar to the prevalence reported in previous studies (44.8%) (6). There was a significant relationship between the seroprevalence of toxoplasmosis and the variables of age, marital status, and HBV serological status, so that with increasing age (the highest prevalence in the group of 41-60 years old), permanent marital status (53.8%), and finally, people with co-infected HBV (55.2 %) had a higher prevalence of toxoplasmosis.

In a similar study by Dr. Mohraz *et al*., about marital status, the highest prevalence of toxoplasmosis was found in widows (62.5%), followed by married people with 56.5%, and the lowest prevalence in single people with 42.4% (9). Our study has similar results, with the lowest prevalence of 28.2% among single people and the highest prevalence of 53.8% among married people.

Regarding the age variable, the 41-60-year-old group had the highest toxoplasmosis seroprevalence in both studies. Unlike study conducted by Dr. Mohraz *et al*., and similar studies in India and Taiwan, which did not find a significant relationship between demographic factors including age, gender, occupation, and marital status with toxoplasmosis serology, this significant relationship between age variables and marital status, the class of demographic factors was obtained by the serum level of toxoplasmosis (9-11). Similarly, no significant relationship was found with job or gender.

Similar to the previous studies, no statistical relationship was found between the prevalence of toxoplasmosis and CD4 levels in our study (P>0.05). In a study conducted in Jahrom and Yazd on 90 PLWH in relation to the seroprevalence of toxoplasmosis and factors affecting it, the prevalence of toxoplasmosis in this study was 21.1%. Also, the age range and CD4 levels are significantly related to the prevalence of the disease, so that more than half of the patients (52%) in the range of 30-40 years had a positive toxoplasmosis serum level (P=0.05), and about 33.4% of the patients with CD4<100 had positive toxoplasmosis serum level. Gender, marital status, and disease duration were not significantly associated with the prevalence of toxoplasmosis (12). In this study, age was significantly associated with the prevalence of toxoplasmosis infection. In contrast, marital status and CD4 level differed between the two studies. Other factors, including the disease duration, had no significant relationship in both studies.

Limitations

The main limitation of this study is the incomplete

medical records of some patients, which can hinder accurate analysis and conclusions. Additionally, interpreting Hepatitis B Virus (HBV) status is challenging because it can take multiple forms and is influenced by antigen and antibody levels. When patients provided multiple responses to a single variable, researchers selected a single response to simplify hypothesis testing, potentially affecting the study's validity.

We found a significant relationship between serum levels of hepatitis B (HBV) and toxoplasmosis, despite these infections not sharing a standard primary transmission route. Given this finding, along with the 99% prevalence of CMV, it is recommended that future research be designed to explore potential contributing factors, such as socioeconomic status and geographic location, as well as the accuracy of the laboratory kits used in this study. Additionally, considering the link between HBV status and the seroprevalence of toxoplasmosis, further investigation is needed to understand the underlying causes of this relationship.

From a public health perspective, several important points can be drawn. The strong association between HBV and toxoplasmosis suggests that having one infection may increase the risk of acquiring the other, which is especially concerning for people living with HIV (PLWH). This population is already immunocompromised and more vulnerable to opportunistic infections, underscoring the need for future research in this area.

The results underscore the necessity for focused screening and preventive measures for both HBV and toxoplasmosis in at-risk populations, especially in areas with high prevalence. Early detection and management of co-infections could help reduce morbidity and mortality rates associated with these diseases. Additionally, the study emphasizes the importance of educating healthcare providers and at-risk groups about the dangers of co-infection, as greater awareness can lead to improved health-seeking behaviors and better adherence to treatment protocols. The study also advocates for further research to understand the underlying mechanisms linking these infections, as insights into how HBV might affect the prevalence or severity of toxoplasmosis can help improve clinical practices and public health strategies. Given the high prevalence of CMV and the notable rates of toxoplasmosis observed, it is crucial to develop comprehensive preventive strategies that include vaccination, screening, and education about transmission routes and risk factors. The study's findings can influence policy changes that improve screening, resource distribution, integrated care, public health education, research efforts, and clinical practice guidelines, ultimately leading to better health outcomes for PLWH. Future researchers should investigate the high CMV seroprevalence found in the study, examine demographic factors influencing toxoplasmosis seroprevalence, assess the reliability of diagnostic tests, and explore the relationship between HBV and toxoplasmosis. Policymakers are recommended to implement routine screening protocols for CMV and toxoplasmosis among PLWH, allocate resources for integrated care models, develop public health education campaigns, and support further research initiatives to improve health outcomes for this vulnerable population.

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