Review Article

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Prevalence of Human T-lymphotropic Virus in patients with Multiple Transfusions (Thalassemia, Hemophilia and Hemodialysis)

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ABSTRACT

BACKGROUND AND OBJECTIVE: Human T-lymphotropic virus type I (HTLV-1) is a member of the retrovirus family, which often leads to the asymptomatic infection of individuals. Transmission of this virus is possible through breast-feeding, sexual contact, transfusion of contaminated blood products and use of contaminated needles. This study aimed to review the prevalence of HTLV-1 infection in high-risk patients, particularly those with thalassemia, hemophilia and hemodialysis in Iran and other countries.

METHODS: In order to find related articles, we searched in different sites including Google, Yahoo, PubMed, Irandoc, IranMedex, Magiran and SID using keywords such as HTLV-1, high-risk, transfusion, thalassemia, hemodialysis, Iran and world.

FINDINGS: In total, 45 articles were found in relation to the subject of the study. Based on the specified criteria of the study in the Iranian population, 17 papers conducted in relation to the prevalence of HTLV-1 infection in patients with thalassemia major and hemophilia were collected, 14 cases of which were about patients with thalassemia alone or those with a combination of hemodialysis and hemophilia. As for the studies conducted in other countries, 12 articles were found, 7 cases of which were about thalassemia patients; therefore, they were selected and studied.

CONCLUSION: According to the results of this study, the prevalence of HTLV-1 infection in high-risk patients with thalassemia, hemophilia and hemodialysis in endemic areas was higher than non-endemic areas.

KEY WORDS: Thalassemia, Hemodialysis, Hemophilia, Human retrovirus type I.

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Introduction

Human T-lymphotropic virus type I (HTLV-1) is a member of the retrovirus family, which often causes asymptomatic infection in individuals. The two major diseases triggered by this virus are adult T-cell leukemia/lymphoma (ATL) and paraparesis spastic tropical, also known as HTLV-associated myelopathy or chronic progressive myelopathy, which is known to occur in less than 5% of the infected individuals (1, 2). Among other disorders caused by this virus are *cutaneous* T cell lymphoma, HLV-1-associated arthropathy, uveitis, polymyositis, Graves' disease, chronic lung disease, lymphadenitis and dermatitis (3). The *human immunodeficiency virus* (HIV) and HTLV-2 are the other two members of the retrovirus family, which could also cause long-term infections in humans.

These infections do not often have any basic treatments, and since these infections are normally fatal, no desirable prognosis is available in their case (4). HTLV-1 is divided into three major categories of Melanesian, central African and cosmopolitan, the last of which is classified into three sub-categories of A, B and C. According to statistics, type B is frequent in Japan (80%), while type A is known to be more prevalent in Iran (5, 6). HTLV-1 is transmitted through different ways including breast-feeding, sexual contact, transfusion of contaminated blood products and use of contaminated needles (7). However, the virus is not normally transmitted through products such as fresh frozen plasma (FFP), and cryoprecipitated and coagulation factors (8).

HTLV-1 is an endemic virus in certain regions of the world such as Japan, the Caribbean, Africa, Italy, Taiwan and the United States (9), as well as some areas of the Caspian Sea border. The close phylogenetic relationship between the frequent viruses in Turkmenistan and Khorasan, Iran is the major cause of the transmission of this virus to the northeastern part of Iran (10, 11).

HTLV-1 is regarded as an endemic virus in the northeastern part of Iran, in cities such as Mashhad and Nishabour (12-15). Areas with a higher virus prevalence than 2% are referred to as “endemic areas” (16). Individuals with the chronic form of any infections who require frequent blood transfusions or repeated injections are at a higher risk of HTLV-1 infection; such example is the patients with thalassemia major and hemodialysis (17, 18).

Therefore, the prevalence of HTLV-1 varies in different parts of Iran and other countries in the world. The prevalence of HTLV-1 in the northern part of Iran is extremely rare, even in case of high-risk patients (19, 20), while in patients undergoing hemodialysis, the prevalence varies in different regions depending on the infection. However, the rate of HTLV-1 infection is considered to be higher in high-risk patients compared to the normal population.

The prevalence of HTLV-1 varies from less than 1% to 32.8% in patients receiving dialysis in Japan (21). Immunoassay techniques, such as ELISA, are normally used for the detection of this virus, as well as to evaluate the anti-HTLV-1 stem cells; however, more practical kits with higher sensitivity are required in this regard. In cases with positive ELISA, the infection needs to be confirmed by other methods such as Western blotting or polymerase chain reaction (PCR), which is known to offer higher accuracy.

Individuals with asymptomatic HTLV-1 infection may not require any special treatments, and they might only need to avoid blood donation and lactation. However, in cases of ATL, chemotherapy, radiation therapy with interferon zidovudine and stem cell transplant are occasionally recommended (22). This study aimed to review the prevalence of HTLV-1 in high-risk patients, particularly those with thalassemia, hemophilia and patients undergoing hemodialysis in Iran and compare it with other parts of the world .

Methods

This review was conducted via searching in different sites such as Google, Yahoo, PubMed, Irandoc, Magiran, IranMedex and SID in order to find relevant articles using Persian keywords such as combinations of hemodialysis and HTLV-1, thalassemia and HTLV-1, and hemophilia and HTLV-1, or using English keywords such as HTLV-1 and thalassemia, hemodialysis and HTLV-1, hemophilia and HTLV-1 and Iran. In total, 29 articles were selected and analyzed in relation to the prevalence of HTLV-1 in patients with repeated injections, including thalassemic patients, those with hemophilia and patients receiving dialysis.

In addition, 4 articles in relation to high-risk HTLV-1 patients were investigated for comparison. The collected data from these papers were studied and reviewed in the form of pre-designed forms.

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Result

In total, we found 17 articles in relation to HTLV-1 infection in patients with thalassemia major and hemophilia (table 1), out of which 12 articles were about the prevalence of this infection in other countries (table 2). Moreover, a number of these articles were written on the prevalence of HTLV-1 infection in patients with cardiovascular and multiple sclerosis (MS) diseases (Table 3).

Table 1. Prevalence of HTLV-1 infection in patients with thalassemia, hemophilia and hemodialysis in different regions of Iran

reference	Author	Number of patients	City /province	Type of disease	HTLV-1	Year of publish	Test	
							ELISA	Western
19	Ghaffari	288	Mazanderan (Sari)	Thalassemia major	%1.4	2013	%6.9	%1.4
20	Ghaffari	160	Mazanderan	Hemodialysis	%0.6	2013	%0.6	%0.6
23	Moradi	181	Gorgan	Thalassemia major	%4.4	2008	%14.9	%4.4
24	Sotudeh	160	Shiraz	Thalassemia major	%2.5	1994	%3.12	%2.5
25	Arjmandi	200	Shiraz	Thalassemia major	%3	2001	%6.5	%3
26	Pourkarim	642	Boushehr	Thalassemia ، hemodialysis hemophilia	%3.7	2004	%6.4	%3.7
27	Ghaderi	90	Shiraz	Thalassemia	%25.5	1996	%25.5	---
28	Moradi	190	Sistan-bluchistan	Thalassemia	%1.6	2002	%1.6	%1.6
29	Karimi	357	Chahr-mahal bakhtiary	Thalassemia , hemodialysis	%6.7	2006	%7.6	%6.7
30	Ziayi	80	Birjand	Hemophilia	%1.25	2007	%1.25	%1.25
31	Rostam zadeh	95	Oroumieh	Hemodialysis	%1.5	2008	%2.6	%1.5
32	Abedi	210	Hormozgan	Thalassemia, hemodialysis, hemophilia	%3.06	2009	%3.06	%3.06
33	Mortezayi	150	Isfahan	Thalassemia	%3.3	2012	%4	%3.3
34	Moyyadi	300	Isfahan	Thalassemia	%2.7	1997	%2.7	%2.7
35	Mansouri Torghabe	360	Mashhad	Thalassemia	%6.11	2008	%6.11	%6.11
36	Anaraki Mohamadi	175	Tehran	Thalassemia	%6.3	2005	%6.8	%6.11
37	Rezvan	868	Tehran	Thalassemia, hemophilia	%7.54	1995	%7.54	%7.54

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Table 2. Prevalence of HTLV-1 infection in patients with thalassemia, hemophilia and patients receiving hemodialysis in different regions of the world, except for Iran

reference	Author	Number of patients	Country/ city	Type of disease	HTLV1	Year of publish	Test	
							ELISA	Western
21	Mery	71	Paris	Hemodialysis	%1.4	1992	%1.4	%1.4
38	Mozzi	1305	Italia	Thalassemia	%0.23	1992	%0.23	%0.23
39	Lin	66	Vietnam	Thalassemia	%0.23	1997	%9.1	%9.1
40	Chiewsilp	64	Thiland	Thalassemia	%0	1993	%0	---
41	Prati	1384	Italia	Thalassemia	%0.28	1998	%0.28	%0.28
42	Namie	142	Japan	Hemodialysis	%9.8	1995	%9.8	%9.8
43	Morikawa	1132	Japan	Hemodialysis	%2.6	1988	%2.6	%2.6
44	Hanada	---	Japan	Hemodialysis	%33.8	1989	%33.8	%33.8
45	Farias	351	Brazil	Multiple blood transfusions	%11	1997	%11	%11
46	Mojaat	619	Tunesia	Thalassemia tuberclosis cycle hemodialysis	%0.15	19999	N=2	N=1
47	Dimas	32	--	Thalassemia	%0	1993	%0	---
48	Gastaldeuo	--	Argentina	Hemophilia	%2.8	2004	%2.8	%2.8

Table 3. Prevalence of HTLV-1 infection in patients with cardiac and MS diseases

references	Author	Number of patients	City /province	Type of disease	HTLV-1	Year of publish	Test	
							ELISA	Western
49	Ghaffari	1200	Mazanderan (Sari)	Other patients	%0.08	2011	%0.08	%0.08
50	Heydari	8122	Mashhad	Cardiac patients	%2.59	2008	%2.59	%2.59
51	Saeedi	826	Mashhad	MS	%2.5	2010	%۲,۵	%2.5
52	Hedayati Moghadam	483	Khorasan	Other patients	%7.2	2010	%12.1	%7.2

Discussion

HTLV-1 is the first human retrovirus which was first reported by Gallow in 1978 (53). HTLV-1 infection is known to develop in 1% of the world's population and over 10% of the population of the endemic areas (54). For the first time in Iran, Farid et al. reported positive ATL with HTLV-1in 1992 (55). In Iran, most of the studies in this regard have been conducted on patients with thalassemia major (15 cases out of 17), and the prevalence of HTLV-1 infection ranges from 0.6% in patients undergoing hemodialysis in Sari, to 7.54% in patients with thalassemia and hemophilia in Tehran according to the Western blot test (20, 37). Although an HTLV-1 infection prevalence of 25% has been reported in patients with thalassemia major in Shiraz, all these patients were tested by ELISA, and Western blot or PCR tests were not performed on them. Since the rate of false positive could be rather high in ELISA, the true prevalence of the virus in this area might be noticeably lower (27).

On the other hand, most of the studies conducted in this regard have indicated higher results for ELISA compared to Western blot or PCR; therefore, suspected positive ELISA tests need to be confirmed by Western blot analysis or PCR. In studies performed in Iran, the highest prevalence of HTLV-1 infection was 1.5% in patients receiving hemodialysis or those with hemophilia, while it was reported to be 7.5% in thalassemic patients. Consequently, it seems that thalassemic patients are at a higher risk of this infection compared to patients with hemophilia and those undergoing hemodialysis. However, most of the studies conducted on hemodialysis and hemophilia patients have been performed in non-endemic areas;

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for instance, a study by Ghaffari et al. indicated the prevalence of HTLV-1 infection to be higher in thalassemia cases compared to hemodialysis ones in the non-endemic region of northern Iran (1.4% vs. 0.6%, respectively) (19, 20).

In the southern regions of Iran, the prevalence of HTLV-1 infection has been reported to be comparatively lower,with the exception of Chahar-mahalo-bakhtiary region (≤2.7%), which is due to the increasing prevalence of the infection in the healthy individuals of this endemic region (6.2%) (24-29,32). These differences in the prevalence of HTLV-1 infection might be due to factors such as the patients' age, frequency of injections, transfusion and endemic state of the virus (23).

In Mashhad, Nishabour (located in the region of Khorasan) and Tehran, the prevalence of HTLV-1 infection is detected in higher levels (6.11% and 7.54%, respectively). Khorasan province is one of the endemic areas of Iran and therefore, the higher prevalence of virus infection is not unexpected (35). On the other hand, the higher prevalence of this infection in Tehran is possibly due to the large population of migrants from other provinces (36, 37). Most of the studies conducted on this subject out of Iran date back to before 2000, and recent studies are not available in this regard. The prevalence of HTLV-1 infection in patients receiving hemodialysis ranges between 0% in Thailand (40, 47) to 33.8% in Japan as an endemic area (44). Lack of infection in blood donors in Thailand is the reason for the 0% infection prevalence of this virus. In European countries such as Italy and France (Paris), HTLV-1 infection is comparatively low in patients receiving hemodialysis and thalassemia minor patients, which is due to the non-endemic classification of these areas (21, 37, 41). The high prevalence of HTLV-1 infection in hemodialysis patients in Japan (unlike other countries, including Iran) indicates that the endemic prevalence of this virus is an important issue (42-44). With regard to South American countries, the prevalence of this infection is different in various areas; for instance, it is reported to be 11% in Brazil, and 2.8% in Argentina (45, 48). Other reasons behind the differences in the prevalence of HTLV-1 infection could be the differences in the size of sample populations and research laboratory techniques. The state of being endemic in HTLV-1 is associated with social, health-related behavior and environmental factors in a country (11).

The prevalence of HTLV-1 infection is on an increasing trend due to the rising rate of intrastate traveling, marriages and infective injections in Iran and other countries. Despite the fact that screening tests in non-endemic areas with a low prevalence of this infection are proceeding, regions with a higher prevalence rate than 6% also need to be taken into account according to the protocols of the World Health Organization (WHO).

The prevalence of HTLV-1 infection in high-risk patients (e.g. patients with thalassemia, hemophilia and those undergoing hemodialysis) is believed to be higher in endemic areas compared to non-endemic regions. Therefore, further investigation and screening could decrease the prevalence as well as the potential complications caused by HTLV-1 infection.

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