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Evaluating the frequency of HTLV-I/II infection among blood donors, major thalassemic patients and individuals infected with hepatitis B and C viruses in Isfahan, Iran

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Abstract

Background: The human T-cell lymphotropic virus type I is the first retrovirus identified in humans. The virus has been associated with adult T-cell leukemia/lymphoma, human T-lymphotropic virus type I, myelopathy/tropical spastic paraparesis, uveitis, arthritis, pulmonary lymphocytic alveolitis, keratoconjunctivitis sicca, and infectious dermatitis. Human T-lymphotropic virus type Iis endemic in Japan, parts of central Africa, the Caribbean basin and South America, Melanesia and Iran (city of Mashhad). The aim of this study was to evaluate serological prevalence of human T-lymphotropic virus type I/IIinfection among blood donors, major thalassemic patients and individuals infected with hepatitis B and C viruses in the city of Isfahan, Iran.

Materials and Methods: Sera were collected from 140 blood donors (440 samples), 150 major thalassemic patients ,150 and individuals with hepatitis B and C and were tested for the presence of human T-lymphotropic virus type I/ IIspecific antibody in a 6 months period in 2007using ELISA and Western Blot tests

Results: Blood donors tested were negative for human T-lymphotropic virus type I/IIinfection, but in major thalassemic patients including 88 males and 62 females, 5 were positive (3.3%). Statistical analyses did not show any significant difference between genders. In individuals with hepatitis one was border line (HCV).

Conclusion: The results indicate a low level of coinfection of human T-lymphotropic virus with HCV in this part of the country. However, the observation of a case with borderline findings, among this group and also positive cases among thalassemic patients, suggests the presence of the virus in blood donor population so this virus could be present in Isfahan but more investigation is needed to evaluate the need for screening tests to detec human T-lymphotropic virus type I among blood donors in Isfahan.

Keywords: HTLV-I/II, Hepatitis C virus, Hepatitis B virus, Thalassemia

Introduction

Human T-lymphotropic virus type 1 (HTLV-I) was the first retrovirus identified in human in 1980. HTLV-I infection is associated with a 1-5% lifetime risk of adult T cell leukaemia/lymphoma, a 0.25% lifetime risk of HTLV-I associated myelopathy, and other inflammatory conditions (uveitis, alveolitis, arthritis, keratoconjunctivitis Sicca and infectious dermatitis). [1,2,3,4,5] There are approximately 10–20 million HTLV-I carriers in the world. Although this virus is distributed worldwide but is endemic (high level), in certain parts of the world such as southwestern Japan, the Caribbean basin, Africa, part of south America, southern Italy, Taiwan, and the United States. [4,6,7,8] In Iran, the first case of adult-Tcell leukemia (ALT) was reported from Mashhad in 1996 and subsequently this city (Northeastern Iran) has been recognized as an endemic area for HTLV-I infection. [9,10,11,12,13]

HTLV-I might infect different types of cells, namely T-lymphocytes, B-lymphocytes, monocytes and fibroblasts.[4] The immune response against HTLV-I is strong. In order to detect specific HTLV-I antibody against virus, screening tests such as enzyme linked immunosorbent assay (ELISA) or

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partial agglutination are performed. Positive results should be confirmed by western blotting (WB).[12] Transmission of HTLV-I occurs through three main routes. Transmission of HTLV-I from mother to child by breast-feeding is one of the main modes of HTLV-I transmission. Another main route is the sexual transmission and the heterosexual transmission is able to introduce HTLV-I infection into previously uninfected groups. Transmission from men to women is more frequent (60%) than women to men (0.4%). Blood transfusion is the third main mode. HTLV-I can also be transmitted by sharing of needles among drug abusers. [1,4,14]

The proviral DNA in donor's blood lymphocytes acts as an infectious agent. The probability of sero-conversion in a recipient of contaminated blood is about 44%. Thus, it is essential to have an efficient blood screening system for HTLV-I in endemic areas to limit the HTLV-I transmission. [14,15]

Due to the variety of diseases caused by the transmission of HTLV virus and harmful sanitary, psychical and social consequences created by this virus, the epidemiological investigation and determining the ratio of the infected people in each society in order to avoid spreading of the infection is needed. As blood transmission is regarded as one of the most basic ways of transmission, therefore, the frequent blood recipients (for example thalassemic patients) are at higher risk. Hence, screening of these patients and blood donors provides useful information about the transmission of the virus and provides information in order to avoid its transmission. The aim of this study was to evaluate the frequency of HTLV-I/II infection among different groups including blood donors, thalassemic patients and individuals infected with Hepatitic B and C viruses in Isfahan, Iran.

Material and Methods

A total of 440 serum samples from healthy blood donors (140), thalassemic patients (150) and individuals infected with hepatitic B (94) and C (56) viruses were obtained for HTLV specific antibody testing during December 2006 to August 2007 and were stored at -20°C until tested. In the case of thalassemic patients the information about age, gender and the number of blood transfusions were collected. The sera were screened for HTLV-I/II using enzyme-linked immunosorbent assay (ELISA; DIA.PRO Diagnostic Bioprobes Srl- Italy) according to manufacturer's guidelines. All repeatedly positive and borderline samples were confirmed and typed by Western blotting (WB; MP Diagnostics (MPD) HTLV BLOT 2.4 kit, Singapore) according to manufacturer's guidelines.

In the case of thalassemic patients, blood smears were prepared to detect any possible morphological changes of the cells. Cell blood count was also performed using Sysmex KX-21N (Japan) apparatus. Chi-square test was used to perform the statistical analyses.

Results

The donors were 139 male and 1 female, with a mean age of 35.73 years (ages ranged between 18 and 64 years). The HTLV-I/II infection test was negative among all healthy blood donors. Among patients with thalassemia major, including 88 males (58.7%) and 62 females (47.3%), with a mean age of 17.74 years (ages ranged between 1 and 49 years), 6 positive and 7 border line cases were detected. All HTLV-I/II-positive and border line cases were checked by Western blotting. Five out of six positive samples by ELISA were also positive by WB. All seven border line specimens were negative. So the prevalence of the infection

Table 1. The frequency of anti-HTLV-I/II antibodies positive cases in different age groups among thalassemic patients.

Age groups	Frequency		Total
	Positive	Negative	
10≥	1(3.7%)	26	27
10-20	2(3.0%)	64	66
20≤	2(3.5%)	55	57
Total	5(3.3%)	145	150

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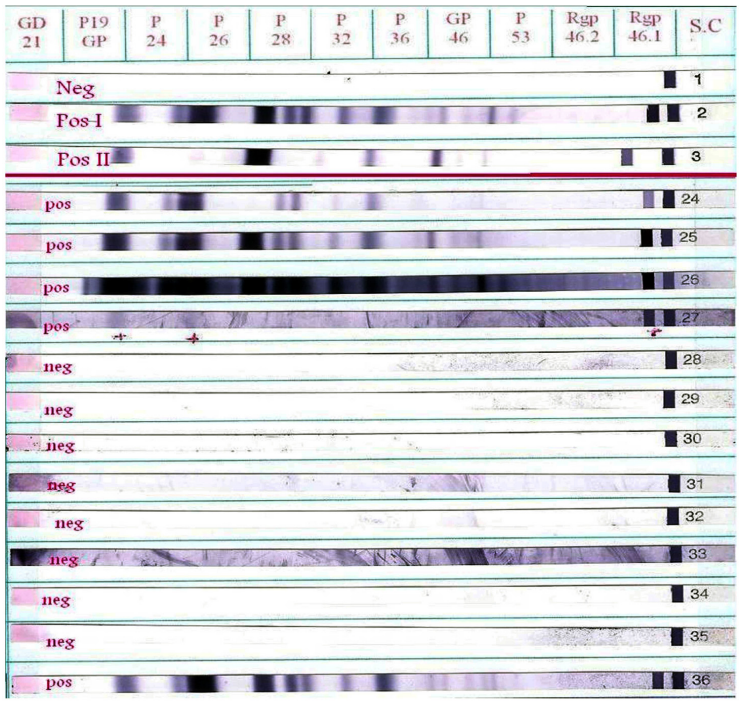
was 3.3% among major thalassemic patients. All the positive cases used to receive packed cell blood monthly, and 33% of these patients received washed blood. Most of the patients received blood since birthday. Statistical analysis did not show any significant correlation between the prevalence of infection and gender. The result of ELISA and Western blotting are shown in table1 and figure1 respectively. Among thalassemic patients, factors such as WBC, RBC, HGB, HCT, MCV, MCH, PLT and PDW were determined, but no significant differences were observed between infected and non-infected cases. Also the evaluation of the blood smears did not show any morphological changes of the cells (flower cell). Of 94 individuals infected with Hepatitis B and 56 individuals with Hepatitis C, 3 (2%) were females and 147 (98%) were males with a mean age of 36.34 years (ages ranged between 18 and 64 years). Using ELISA, one of these patients was positive and was borderline respectively. The results of WB showed that one of the sera from HCV cases was at border-line and there was not any positive case in this group. Regarding these results the prevalence of the infection was not notable. The frequency of anti-HTLV-I/II antibodies in three groups are shown in figure 2.

Discussion

The human T-cell lymphotropic virus type I (HTLV-I) is the first retrovirus identified in humans. It has been responsible for a number of clinical syndromes, most notably adult T-cell leukemia or lymphoma (ATL).Understanding the epidemiology and clinical manifestations of this virus is necessary to properly diagnose and care for patients with HTLV-I infection.[1] There is no defined treatment for patients infected with HTLV-I, but the accurate knowledge of seroprevalence rates in different population groups may be helpful in establishing prophylactic measures to reduce rates of viral transmission from infected individuals. This infection is endemic in certain parts of the world as well as in a northern city of Iran, Mashhad.[10,11,13] A nation-wide sero-epidemiologic survey of adult T-cell leukemia virus (HTLV) has been performed in Japan. Sera from adult donors in 15 different locations were screened for anti-ATL. High incidences (6 to 37%) of antibody-positive donors

Figure 1. Results of Western blotting in thalassemic patients. Strip1: Negative control, Strip2: HTLV-I positive control, Strip3: HTLV-II positive control. Other strips: Tested sera. No reaction with HTLV specific proteins indicates seronegativity. Reaction with GAG (p19 with or without p24) and two ENV proteins (GD21 and rgp46-I) indicates HTLV-I seropositivity and reaction with GAG (p24 with or without p19) and two ENV (GD21 and rgp46-II) indicates HTLV-II seropositivity.



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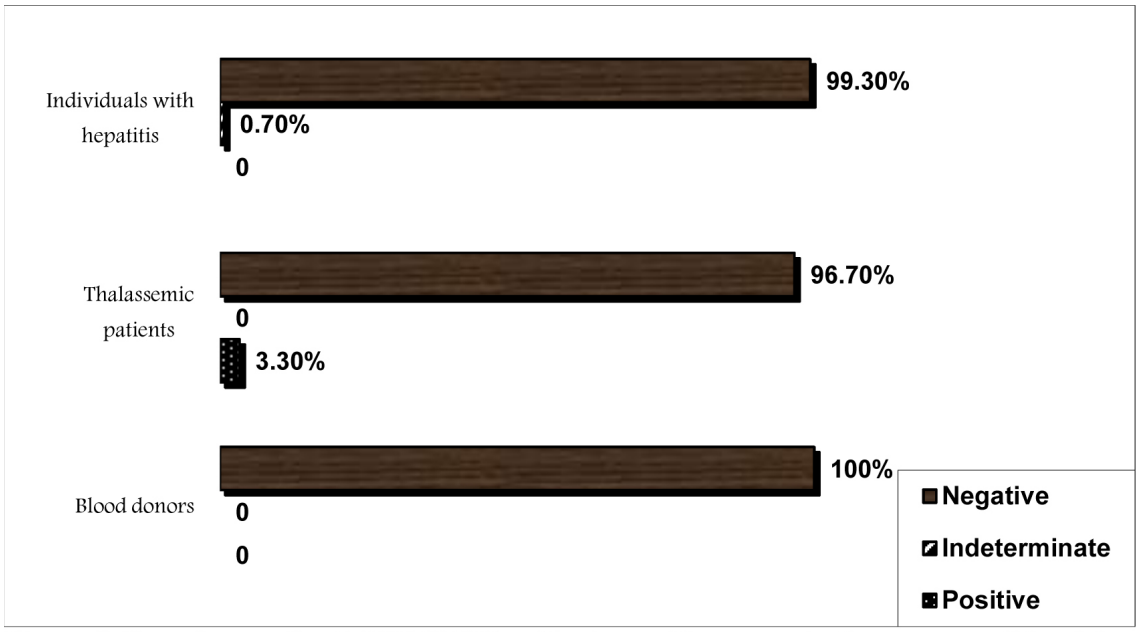
were found in seven regions. These areas were HTLV-endemic areas corresponding to ATL-endemic areas.[6] In 1987 screening for human T-lymphotropic virus type I (HTLV-I) antibodies in the United States showed 0.025% rate of infection.[7] In 1984, the prevalence of infection with the virus was 2/100 000 among Swedish blood donors. It is notable that from 7 positive samples only three of the infected donors were of Swedish origin. The remaining four were originally from Denmark, the United Kingdom, Iran and Chile. The calculated prevalence for donors born in Europe was 1.3/100000 and for donors born in Sweden 1/100000.[16] There are some studies about the seroprevalence of HTLV-I/Π infection in different areas of Iran with the most important studies conducted in Mashhad. The first investigation in Mashhad showed a 3.2% frequency and for the first time it was suggested that the city of Mashhad, the capital of Khorasan, a northeastern province of Iran, is an area where human T-lymphotropic virus type 1 (HTLV-1) infection is endemic.[12] Following this study, in 2003, the prevalence of HTLV-1 infection was 0.77% among blood donors, which confirms the city of Mashhad as an area where the virus is endemic compared to other regions in the world.[10] The incidence was correlated with increasing age, and it was higher in females than males.[10,14] In Shiraz city seroprevalence of the anti-HTLV-I/II antibody was reported to be 0.2%.[17] In the present study, among 140 samples from blood donors in Isfahan, no positive cases were observed but regarding the low number of samples tested, it is suggested that a higher number of blood donors need to be screened.

Thalassemic patients, who are blood transfusion dependent, are the most high risk groups for viral infections such as HIV, HCV, HBV and HTLV-I/II. In 1985, seroprevalence of anti-HTLV-I/II antibody in New York City blood product recipients, including persons with hemophilia (Hem A), beta-thalassemia major and patients with sickle cell anemia (SCA), was evaluated. Three (6.1%) with beta-thalassemia major and one with SCA were antibody-positive. These data suggested that HTLV-I is preferentially transmitted through cellular blood products and that, it is an infection for which cellular blood product recipients in at least some areas of the United States are at risk.[18] In Brazil, the presence of HTLV-I infection in 2.9% of blood transfusions patients was reported.[19] In Italy, HTLV-I infection frequency among thalassemic patients was estimated to be 4.8%.[8] In Iran, also, there is some evidence suggesting relatively high prevalence of the virus in thalassemic patients. Anti-HTLV-I antibody prevalence among thalassemic patients in Isfahan city was 2.7% in 1997.[20] In 1994, the prevalence of HTLV-I/II infection was, 25.55%

Figure 2. Prevalence of anti-HTLV-I/II antibody positive cases in three groups (blood donors, thalassemic patients and individuals with hepatitis) in the present study.



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among thalassemic patients in Shiraz.[21] In 2002, by using more accurate methods, the prevalence of anti-HTLV-I/II antibody was tested in thalassemic patients. In this study 3% positive and 3.5% indeterminate cases were reported that was quite different with previous results in Shiraz[17] and could be correlated to the methods used. In Zabol and Zahedan cities, seroeprevalence of HTLV-I in major thalassemic patients was estimated to be 1.6%.[22] In 2003, in repeated blood recipients (thalassemic and hemodialysis patients) in Boushehr province, only in thalassemic patients, the frequency was 3.07%.[23] In Tehran, the prevalence of infection among thalassemic patients has been reported to be 6.3%.[24] In 2006 the prevalence of HTLV-I/II infection in thalassemic patients of Shahre-Kord, was estimated 6%.[25] In 2008 in a retrospective study of medical records of 360 major β-thalassemic patients in northeastern Iran, sera of 22 individuals (6.11%) were positive for HTLV-I.[13] In the present study, frequency of HTLV-I infection in major thalassemic patients was 3.3%. For ensuring the virus is not transmitted from mother to child, blood samples of the mothers of the positive HTLV-I individuals were tested. Results showed that all of them were negative. As there was no marriage among thalassemic individuals, transmission via sexual contact was also rejected. According to the information collected from thalassemic department of Omid hospital in Isfahan, all the bloods needed for the patients, were obtained through Isfahan blood transfusion center. This may indicate the role of transfusion for transmission of the virus. Comparing with the world level, HTLV-I/II frequency among thalassemia patients in Isfahan (3.3%) was greater than Brazil (2.9%), and lower than the United States (6.1%) and Italy (4.8%). Comparing with other cities of Iran, the prevalence of HTLV-I/II infection was more than Shiraz (3%), Zabol and Zahedan (1.6%), Bushehr (3.07%) and Isfahan in 1997 (2.7%) and less than Tehran (6.3%), Shahre-Kord (6%) and northeastern of Iran (6.11%). Hence, the prevalence of HTLV-I/II infection in thalassemic patients indirectly could be indicative of the prevalence of infection in blood donors and finally in total population studied. So with regard to increasing the rate of anti-HTLV-I/II antibody in thalassemic patients from 1997 to 2007, in Isfahan and high frequency of the virus in Shahre-Kord, capital of Charmahal-va-Baktiari Province, which is in neighborhood of Isfahan Province, this region may be an endemic area for the virus, but the confirmation of this needs more investigations with higher number of samples.

There have been many studies about the coinfection of HTLV-I/II with hepatitis viruses with contradictory results. Coinfection of hepatitis C virus (HCV) and human immunodeficiency virus (HIV) and/or human T-lymphotropic virus type II (HTLV-II) is common among drug abusers. Hisada et al. studied 6570 injection drug abusers from 9 United States cities during 1987-1991. Drug users were divided in two races, white and black. Results showed that HTLV-II infection significantly increased HCV load in white subjects but not in other racial groups.[26] In Shiraz, the prevalence of HTLV-I and HCV coinfection among thalassemic patients was 16.7%.[21] No coinfection of HTLV with hepatitis viruses was observed in Southern Khorassan (Birjand),[11] but in northeastern of Iran 1.94% and 0.55% of the thalassemic patients were coinfected with hepatitis C and B viruses respectively.[13] In this study one of the sera from HCV positive cases was at border-line. The results showed low level of coinfection of HTLV with HCV in this part of Iran. However, intermediate observation of HTLV, among this group as none healthy blood donors, indicates that the virus might be present in blood donors population. These evidences, show that this virus could be present in Isfahan but to consider screening tests for detection of HTLV-I in blood donors in Isfahan more investigations is needed.

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