

# The Frequency and Risk Factors of Human T-cell Lymphotropic Virus Type I among Blood Donors in Khorasan-e Razavi, Iran, from 2002 to 2013

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## Abstract

**Introduction:** Human T-cell lymphotropic virus (HTLV-I) is the causative agent for adult T-cell lymphoma/leukemia (ATLL) and HTLV-I-associated myelopathy/tropical spastic paraparesis. The virus is endemic in the parts of Iran. This study is conducted to determine the trends in the frequency of HTLV-I in Mashhad, a city in Khorasan-e Razavi province, Iran, over 11 years. **Materials and Methods:** Blood bank records of blood donors positive for HTLV-I were collected from different blood banks across Mashhad between 2002 and 2013. Obtained data were first entered into paper versions and then were analyzed by SPSS version 11.5. HTLV-I antibody was firstly measured by enzyme-linked immunosorbent assay (ELISA) method and later confirmed by the Western Blot (WB). **Results:** During the study period, 983,000 donors were examined by ELISA and WB, among whom 2921 cases (0.297%) were positive HTLV-I carriers. The highest and lowest frequency of carriers was 0.451% and 0.098%, respectively. The most significant factor was related to marital status (85.2%) and the smallest significant factor was associated with the history of acupuncture (0.3%) according to the different risk factors. **Conclusion:** The frequency of HTLV-I carriers among blood donors was significantly decreased in this period. Screening of blood donors for HTLV-I infection played a significant role in this reduction.

**Keywords:** Blood donors, human T-cell lymphotropic virus Type I, Iran, Khorasan, transfusion

## INTRODUCTION

Since the discovery and isolation of human T-cell lymphotropic virus type I (HTLV-I) from the patients with adult T-cell lymphoma/leukemia (ATLL), studies have been conducted about the effects of this virus on T-lymphocytes and its relationship with some diseases such as ATLL and HTLV-I-associated myelopathy/tropical spastic paraparesis and T-cell lymphoma. HTLV-I is a retrovirus, which belongs to Oncovirinae subfamily. Its genome is double-stranded RNA with positive polarity and approximately 140–110 nm diameter. HTLV-1 has been detected throughout the world. However, HTLV-1 highly endemic locations are the Southwestern part of Japan, the caribbean area, sub-Saharan Africa, South America, and some regions in the Middle East, including Khorasan-e province in Iran with a prevalence of 3% in the general population. Blood injection, breastfeeding, and sexual

contacts are among the main ways of viral transmission. The transcriptional activator (Tax) protein, as an oncogenic protein, has a fundamental role in the pathogenesis of ATLL and contributes in polyclonal infection secondary to viral replication and subsequently clonal replication of infected cells.<sup>1-5</sup>

Evaluating the methods that enable its distribution among people and understanding molecular pathways to infect host

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cells are suggested to control HTLV-I spread in different human societies. Mashhad and Neishabour, two cities of Khorasan-e Razavi province, Iran, are known as endemic areas for HTLV-I by frequency rates from 2.1% to 7.2% in the general population.<sup>6,7</sup> However, factors such as methods of prevention and diagnosis of infection, population growth, increasing tourism in the form of religious pilgrimage, treatment methods, cultural and educational factors, employment status, changing lifestyle, and risky behavior may change the frequency of HTLV-I infection over a long period. Therefore, a retrospective analysis of data from blood banks was performed in the region (introduction is inadequate; methods/routes of transmission, impact on immunity, and sequel without treatment should be discussed).

## MATERIALS AND METHODS

### Population and study design

This study was performed at Mashhad University of Medical Sciences after approving by the Local Ethics Committee in collaboration with Blood Transfusion Organization Research Center of Khorasan-e Razavi province, Mashhad, Iran, between 2002 and 2013.

In the blood transfusion center, before donation, all blood donors were evaluated for some risk factors of blood-borne infectious disease such as history of risky behaviors such as sex with nonwife partner or drug addiction, travelling to HTLV-I endemic areas, areas of malaria endemicity as superinfection agent, and history of certain diseases such as hepatitis. For ethics and security issues, information obtained from the donors was confirmed electronically and confidentially. All samples of volunteers, who had decided to leave the study at this stage, were removed from the study. Collected data were the record of all donors in the various blood donation centers in the region.

### Sampling techniques and test performance

During blood donations, 5 ml of blood was taken from donors, and patients' serum was separated after centrifuging, and hepatitis B surface antigen, HTLV-I, human immunodeficiency virus, and hepatitis C virus antibodies were immediately measured by enzyme-linked immunosorbent assay (ELISA) method (by MP Diagnostics reagent™, USA and ADALTIS reagent™, Canada). All samples with photometric absorption were higher than the cutoff and were considered positive for HTLV-I. According to the instruction of kit, cutoff testing was calculated from negative commercial control used during the test process. We decreased this measured cutoff by about 10% to increase the sensitivity of the method. First, for positive samples, ELISA tests were repeated and a Western Blot (WB) test (MP Diagnostics reagent™, USA) was done as a confirmatory test for those who were positive secondly. Specific HTLV-I antibodies detected by ELISA and WB were anti-gp46-I, anti-gp46-II, and anti-gp21-I. If the WB test is positive, patients will be considered as a definite positive donor for HTLV-I infection, and the confidential file is created for them. This laboratory screening program for HTLV-I infection

has been initiated in this center since 1999. Inclusion criteria included the samples that passed the mentioned steps, and exclusion criteria included those cases in which any of the mentioned processes were negative.

### Data analysis

Data were analyzed by SPSS Inc. Released 2002. SPSS for Windows, Version 11.5. Chicago, SPSS Inc., USA. Initially, descriptive analysis and then comparative analysis of parameters were performed. A Chi-square test was used for comparison.  $P \leq 0.05$  was statistically significant.

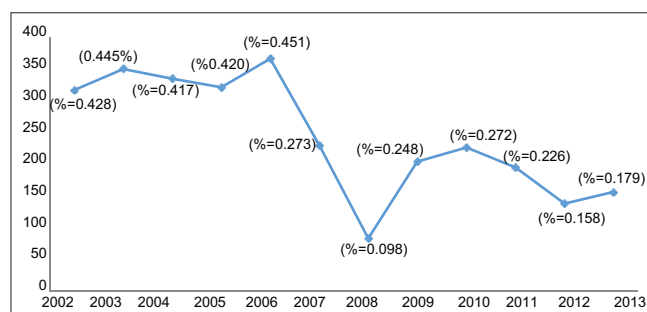
## RESULTS

983,000 blood samples were donated for 11 years between 2003 and 2013. The frequency of the HTLV-I carrier was 0.297 (2921 donors). Table 1 shows information about frequencies of HTLV-I during these years. There was a statistically significant difference in the frequency of HTLV-I between 2002 and 2013 ( $P = 0.005$ ). We also observe a considerable difference between the mean of frequencies of infection between 2002 and 2007 and 2008 and 2013 ( $P = 0.011$ ) so that this might remark a shift for HTLV-I prevalence between the donors. As shown in Figure 1, a remarkable decrease in carriers was observed between 2007 and 2009.

The frequencies of HTLV-I carriers based on demographic variables are shown in Tables 1 and 2. The male carriers were about eight times more than female carriers. The total number of female donors was 62,900 cases, 304 of whom (0.030%) were HTLV-I positive. The total number of male donors was 920,100, in which 2617 of whom (0.266%) were positive. There was a statistically significant difference between male and female carriers ( $P < 0.001$ ). Among all HTLV1 carries, 2406 cases (82.4%) had a history of dental operation, 2877 cases (98.5%) breastfeeding, and 2541 cases marriage (87%) [Table 2]. Indeed, 2202 cases (75.4%) did not mention a history of high-degree education in the university.

## DISCUSSION

The prevalence of HTLV-I carriers in the cities of Mashhad and Neishabour is higher than in other regions of Iran, and Khorasan-e Razavi province has been recognized as an endemic area for HTLV-I infection.<sup>7,8</sup> The study by



**Figure 1:** Changes in human T-cell lymphotropic virus-I carrier frequencies during 2002–2013 in blood donors

**Table 1: The total numbers of donors (including healthy controls and carriers), frequencies of human T-cell lymphotropic virus carriers, and mean age ( $\pm$ standard deviation) of carriers in the blood donors' database of Mashhad city between 2002 and 2013**

Years	The total number of donors	Frequency of male carriers, <i>n</i> (%)	Frequency of female carriers, <i>n</i> (%)	Frequencies of carriers, <i>n</i> (%)	Mean age of carriers $\pm$ SD
2002	74,000	282 (0.381)	35 (0.047)	317 (0.428)	37 $\pm$ 10
2003	78,500	312 (0.397)	38 (0.048)	350 (0.445)	37 $\pm$ 8
2004	80,200	301 (0.375)	34 (0.042)	335 (0.417)	37 $\pm$ 10
2005	76,300	291 (0.381)	30 (0.039)	321 (0.420)	35 $\pm$ 10
2006	81,000	328 (0.404)	38 (0.046)	366 (0.451)	37 $\pm$ 10
2007	84,000	205 (0.244)	25 (0.029)	230 (0.273)	37 $\pm$ 10
2008	84,000	74 (0.088)	9 (0.010)	83 (0.098)	39 $\pm$ 10
2009	82,000	183 (0.223)	21 (0.025)	204 (0.248)	41 $\pm$ 11
2010	83,000	202 (0.243)	24 (0.028)	226 (0.272)	39 $\pm$ 9
2011	86,000	174 (0.202)	21 (0.024)	195 (0.226)	40 $\pm$ 10
2012	87,000	123 (0.141)	15 (0.017)	138 (0.158)	39 $\pm$ 10
2013	87,000	142 (0.163)	14 (0.016)	156 (0.179)	37 $\pm$ 10

SD – Standard deviation

**Table 2: Frequencies of the risk factors among human T-cell lymphotropic virus I carriers during 2002-2013 in blood donors**

Risk factor	<i>n</i> (%)
Dental operation	2406 (82.4)
Breastfeeding	2877 (98.5)
Coinfection with HCV	16 (0.547)
Coinfection with HBV	20 (0.684)
Coinfection with HIV	22 (0.753)
Coinfection with Neisseria Gonorrhoea	35 (1.198)
Positive history in first-degree family members (spouse and parents)	84 (2.875)
IV drug addiction	23 (0.787)
History of blood transfusion	117 (4.005)
History of surgery	591 (20.232)
History of imprisonment	78 (2.670)
Married	2488 (85.2)
History of sex with nonwife partner, <i>n</i> (%)	118 (0.137)

HCV – Hepatitis C virus, HBV – Hepatitis B virus

Hedayati-Moghaddam *et al.*, from February 2009 to July 2010 on 511 samples, reported the prevalence of this virus as 7.2% in the general population of Neishabour, a small town in Khorasan province.<sup>7</sup> The frequency of HTLV-I seropositive carriers was reported as 2.12% in a study by Rafatpanah *et al.* in 2009 on 1678 people from the general population, including 763 males (45%) and 915 female (55%) from 12 residential areas of Mashhad.<sup>6</sup> A study by Catalan-Soares *et al.* between 1995 and 2000 in 27 residential areas from different states of Brazil on blood donors revealed that the frequency of HTLV-I carriers was between 0.04% and 1%.<sup>9</sup> The result of this study is inconsistent with our research; however, Brazil is an endemic area for HTLV-I infection.<sup>10</sup> The common points between the present study and Catalan-Soares survey are the targeted population (blood donors), technical procedures, and the long period of the investigation.<sup>9</sup>

Suspected donors were removed from the system of donation through the blood donors' screening program, including questions about the past medical history of donors and evaluation of risk factors of viral infection and also the self-exclusion of the donors. Furthermore, blood donors are a selected population from the general population. The prevalence of HTLV-I infection among blood donors will be significantly reduced compared to the general population, according to the above mentioned. The role of gender is considered as another reason for reducing the prevalence of infection in our study compared to other studies performed in the general population; as mentioned earlier, men included 77% of the donors in this research. The other studies also indicate that males are the main population participated in the donation. However, the prevalence of HTLV-I infection in the female donors of the general population is more than male.<sup>6,7</sup> While, in the present study among all male donors ( $n = 920,100$ ), 2617 (0.266%) individuals, and of total female donors ( $n = 62,900$ ), 304 (0.030%) were positive for HTLV-I infection. These points can be mainly responsible for the difference of prevalence in the present study compared to the other studies performed in the general population.<sup>6,7,9</sup>

The frequency of HTLV-I carriers was reported to be 0.7% in a study conducted by Abbaszadegan *et al.*, on 28,926 volunteer blood donors in Mashhad in 1999.<sup>8</sup> The most important factors that distinguish the present research from Abbaszadegan research are the study population size (983,000 versus 28,926 volunteers), the duration of investigation (11 years vs. 6 months), and the lack of screening program in 1999 because we noticed that screening blood donors for HTLV-I had a significant effect on decreasing the frequency.

In comparison with other researches, the statistical population (2921 seropositive) and the duration of our

investigation (11 years) are the most critical parameters in the present study. This study also reported a decrease of about 60% in frequencies of carriers from 0.428% in 2002 to 0.179% in 2013. We believe that the most crucial cause for the reduction of HTLV-I carriers among blood donors was related to laboratory blood screening programs that started in 1999. Furthermore, the individuals' growing level of knowledge and education about the transmission routes of the virus (female to male is more facilitated) has been effective in reducing the frequency of the virus during this period. The standard age range to donate blood is between 18 and 60 years according to the standards of the blood transfusion center. The carriers' age distribution in this study revealed that the dominant age of HTLV-I carriers is over 30 years (78%). This finding is consistent with the results of the studies conducted by Rafatpanah *et al.* and Hedayati-Moghaddam *et al.*<sup>6,7,11</sup>

In Rafatpanah *et al.*'s research, the marital status of carriers ( $P < 0.001$ ) and their level of education ( $P = 0.047$ ) had a significant association with HTLV-I infection.<sup>6</sup> As in the present research, the dominant population of carriers was married (85.2%), and they had nonuniversity education (75.4%). This indicates that the marriage may be one of the factors involved in the spread of the virus in the community. It should be noted that the concept of marriage in this study inhibits the virus outbreak on one side and also spreads it on the other side. Moreover, it should be reminded that the marriage could be a significant factor in preventing immoral sexual relationships by creating a commitment regarding ethical and family issues. On the other hand, however, if one partner becomes infected with the virus, with the lower transmission from female to male still, the transmission would be facilitated.

Among many risk factors examined in this study [Table 2], the history of dental operations (82%) and breastfeeding (25.8%) were the most prominent ones. Always, breastfeeding referred to one of the main routes of transmission, and in this study, it also includes a large percentage of the transmission, which was consistent with the results of the previous studies in this issue.<sup>11-13</sup>

It was expected that the actual percentages of history of sex with nonwife and intravenous drug addiction would be more than what was found in the present data. The reason for this issue may result from some self-conservative causes, such as the risk of being fired from the governmental institution where they work, even if these files are confidentially classified. It is recommended to obtain correlations between each of the parameters in this study with a population as an evidence case. Furthermore, in the confidential files of carriers, some questions related to HTLV-I infection were included; more relevant subjects such as a history of skin lesions, tumors, and neurological and movement complications are better to be asked. Due to migration of unaware infected people from Khorasan to different parts of the country, it can also be recommended that screening of blood donors is performed in all provinces of the country.

An absence of information about frequencies of HTLV-I carriers in the other provinces was one of the limitations of the study. At present, blood donor screening for HTLV-I infection is performed only in Khorasan province in Iran, and this screening test is not done in the other provinces of the country. Due to people's movement from Khorasan province to other provinces, transmission risk of the HTLV-I infection to people living in those areas would be increased as a result of blood donation. Therefore, the expansion of HTLV-I screening for blood donors is recommended in the whole country.

## CONCLUSION

The frequency of HTLV-I carriers among blood donors in Mashhad city was significantly reduced for 11 years under the study. Screening of blood donors for HTLV-I infection played a significant role in the reduction of the carriers.

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Nil.

## Conflicts of interest

There are no conflicts of interest.

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