TRANSFUSION MEDICINE Official Journal of the British Blood Transfusion Society

Transfusion Medicine | ORIGINAL ARTICLE

Seroepidemiology of human T-cell lymphotropic virus among Iranian adult thalassemic patients

M. Keshvari,[1,2] B. Hajibeigi,[1] A. Azarkeivan,[1] H. Keyvani,[3] B. Behnava,[2] S. Y. Saiedi Hosseini,[2] H. Sharafi[2] & S. M. Alavian[2]

[1]*Blood Transfusion Research Center, High Institute for Research and Education in Transfusion Medicine,* [2]*Department of Clinical Hepatology, Middle East Liver Disease (MELD) Center, and* [3]*Department of Clinical Virology, Iran University of Medical Sciences, Tehran, Islamic Republic of Iran*

Received 2 April 2014; accepted for publication 13 June 2014

SUMMARY

Background: A large number of transfusion-dependent thalassemic patients is at a substantial risk for transfusion-transmitted infections. Human T-cell lymphotropic virus (HTLV) is a blood-borne pathogen and can be transmitted via cellular products. We aimed to evaluate the seroprevalence of HTLV in transfusion-dependent thalassemic patients referred to Tehran Adult Thalassemia Clinic.

Methods: From 2008 to 2010, 257 transfusion-dependent thalassemic patients who referred to Tehran Adult Thalassemia Clinic were enrolled. The seroprevalence of HTLV, hepatitis B virus (HBV), hepatitis C virus (HCV), and HIV were assessed using enzyme-linked immunosorbant assay (ELISA). Also, the samples with positive result for anti-HTLVAb (by ELISA) were reassessed using Western blot for HTLV.

Results: Among the 257 transfusion-dependent thalassemic patients who were tested for anti-HTLVAb, 29 (11·3%, 95%CI = 7·8 – 15.6%) were found to be anti-HTLVAb positive by ELISA and Western blot. No case was detected to be HBsAg positive, whereas 16% had HBV seroconversion criteria, and more than 95% had anti-HBsAb in their sera. Also, 103 (40·1%) patients were HCV seropositive, 13 (5·1%) patients of which were co-infected with HCV/HTLV. Among the HTLV-infected patients, 44·8% were co-infected with HCV, whereas 39·5% of HTLV-seronegative individuals were HCV mono-infected ($P > 0·05$).

Conclusion: This study showed that transfusion-dependent thalassemic patients were in higher risk for transmission of different blood-borne pathogens such as HTLV. The screening of HTLV in Iranian blood donors is recommended.

Correspondence: Seyed M. Alavian, MD, Department of Clinical Hepatology, Middle East Liver Disease (MELD) Center, No. 178, Cross Shadab, Sepahbod Gharani Street, P.O. Box 14155/3651, Tehran, Islamic Republic of Iran.
Tel.: +98 21 88945186; fax: +98 21 88945188; e-mail: alavian@thc.ir

Key words: HTLV, Iran, thalassemia.

Human T-cell lymphotropic virus (HTLV) is a human retrovirus that belongs to the genus Deltaretrovirus. Four types of HTLV (HTLV-1, HTLV-2, HTLV-3 and HTLV-4) have been identified. HTLV-1, also called adult T-cell leukaemia/lymphoma (ATLL) virus type 1, a virus that has been implicated in several kinds of diseases including HTLV-1-associated myelopathy/tropical spastic paraparesis (HAM/TSP), Strongyloides stercoralis hyper-infection and ATLL. Among the 20 infected persons, one was estimated to develop cancer as a result of HTLV-1 infection (Proietti *et al.*, 2005). HTLV-2 causes a milder form of HAM/TSP and some inflammatory illnesses. Both viruses (HTLV-1 and HTLV-2) have similar routes of transmission including mother to child via breastfeeding and sexual contact. However, exposure to contaminated blood, either through blood transfusion or sharing of contaminated needles, was mentioned as minor transmission routes of HTLV infection (Khabbaz *et al.*, 1992). Transmission of HTLV-1/2 by blood transfusion occurs with transfusion of cellular products of blood (packed cell, platelet and whole blood), whereas plasma fraction and plasma derivatives from HTLV-infected donors do not have any roles in viral transmission. The importance of various transmission routes was believed to vary geographically. Both viruses are present in all continents. The highest HTLV-1 prevalence in the general population has been found in Southern Japan with 10% prevalence. HTLV-2 is more prevalent among American Indian population (Shindo *et al.*, 2002). Based on the studies among Iranian blood donors, the prevalence rate of HTLV-1/2 infection varied between 0·013 and 2·3% (Karimi *et al.*, 2013). Razavi Khorasan, the Northeastern province in Iran, has been recognised as an endemic area for HTLV-1 infection, and all blood donors have been screened for HTLV since 1995 (Abbaszadegan *et al.*, 2003). At present, the screening of blood donors for HBsAg, anti-HCVAb, HIV Ag/Ab and rapid plasma reagin (RPR) is mandatory in all provinces of Iran, whereas screening for anti-HTLVAb is performed routinely in seven provinces including Razavi Khorasan, North Khorasan, South Khorasan, Guilan, West Azerbaijan, Alborz and Ardebil.

doi: 10.1111/tme.12133

Table 1. Demographic, laboratory and clinical characteristics of the study population

	Anti-HTLVAb negative ($n = 228$)	Anti-HTLVAb positive ($n = 29$)	*P*-value
Sex, *n* (%)			
Male	107 (46·9)	14 (48·3)	0·80[1]
Female	121 (53·1)	15 (51·7)	
Age, mean years ± SD	29 ± 9	30 ± 8	0·71[2]
Anti-HCVAb, *n* (%)			
Positive	90 (39·5)	13 (44·8)	0·57[1]
Negative	138 (60·5)	16 (55·2)	
Date of first blood transfusion, mean years ± SD	25 ± 7	25 ± 7	0·90[2]
Transfusion interval (transfusion number/month), mean ± SD	1·3 ± 4	1·3 ± 4	0·90[2]
Splenectomy, *n* (%)			
Yes	135 (59·2)	17 (58·6)	0·90[1]
No	93 (40·8)	12 (41·4)	

[1]Fisher exact test.
[2]*t*-Test.

Thalassemia, an inherited blood disorder resulting in defective haemoglobin synthesis and anaemia, is found in about 60 countries with the highest prevalence in the Mediterranean region, parts of North and West Africa, the Middle East, the Indian subcontinent, the Southern Far East and Southeastern Asia, together composing the so-called thalassemia belt (Abolghasemi *et al.*, 2007; Aydinok, 2012). The variants associated with beta-thalassemia have high frequency in Iran especially around the Caspian Sea and Persian Gulf. It was estimated that about 25 000 thalassemia patients live in Iran (Rezaee *et al.*, 2012). Patients with thalassemia need regular blood transfusion and are exposed to various blood-borne pathogens such as hepatitis C virus (HCV), hepatitis B virus (HBV) and HTLV. However, other routes of HTLV transmission such as sexual contact and mother to child via breastfeeding among these patients should also be considered as well.

As there is little data regarding HTLV prevalence in transfusion-dependent thalassemic patients in the literature, we aimed to evaluate the seroprevalence of HTLV infection in Iranian transfusion-dependent thalassemic patients who referred to Tehran Adult Thalassemia Clinic from 2008 to 2010.

MATERIALS AND METHODS

Study population

In this cross-sectional study from 2008 to 2010, 257 adult transfusion-dependent thalassemic patients who referred to Tehran Adult Thalassemia Clinic, a referral centre for treatment and follow-up of thalassemic patients from different provinces of Iran, which is under the supervision of Iranian Blood Transfusion Organization (IBTO), were enrolled and their demographic data, transfusion history and previous medical history were obtained by reviewing medical records and interviews. Thereafter, venous blood sample was obtained from each patient before blood transfusion. All study participants provided informed consent, and the study design was approved by the Ethics Committee of Middle East Liver Disease (MELD) Center. The study protocol conforms to the ethical guidelines of the 1975 declaration of Helsinki.

Laboratory studies

All sera were tested using third generation commercially available enzyme-linked immunosorbent assay (ELISA) kits to detect anti-HTLV-1/2 antibody (anti-HTLVAb) (Adaltis, Italy), anti-HCV antibody (anti-HCVAb) (United Biomedical, China), hepatitis B surface antigen (HBsAg), hepatitis B core antibody (anti-HBcAb), hepatitis B surface antibody (anti-HBsAb) (Siemens Healthcare Diagnostics, USA) and anti-HIV antibody (anti-HIVAb) (Biomerieux, the Netherlands). All sera positive for anti-HTLVAb were retested by Western blot (HTLV blot 2.4, MP Diagnostics, Singapore, Singapore) kit as a complementary test. The patients who were found to be positive for anti-HTLVAb by both ELISA and Western blot were considered as HTLV infected.

Statistical analysis

Results were expressed as mean ± standard deviation (SD) for continuous variables and as number and percentage for categorical variables. Comparison between two groups was made using Student's *t*-test for continuous variables and χ^2 or Fisher exact test, when appropriate, for categorical variables. A *P*-value of $<0{\cdot}05$ was considered statistically significant. All statistical analyses were performed using SPSS software for windows (version 17.0; SPSS Inc., Chicago, IL, USA).

RESULTS

Among the 257 transfusion-dependent thalassemic patients who were tested for anti-HTLVAb, 29 (11·3%, 95%CI = 7·8–15·6%)

were found to be anti-HTLVAb positive by ELISA and were confirmed to be HTLV-1 positive by Western blot. Demographic and clinical characteristics of patients are shown in Table 1. Patients' gender and age were not significantly different between HTLV seropositive and seronegative patients ($P > 0{\cdot}05$). None of the patients was found to have anti-HIVAb in their sera. No HBsAg-positive case was detected and 41 (16%) individuals had HBV seroconversion criteria (absence of HBsAg and presence of anti-HBcAb and anti-HBsAb). Patients without anti-HBsAb had received hepatitis B recombinant vaccine series and more than 95% of the patients had anti-HBsAb more than 10 IU mL^{-1} in their sera. Among the 257 thalassemic patients, 103 (40·1%) patients were found to be HCV seropositive, 13 (5·1%) of which were co-infected with HCV/HTLV. In HTLV-infected patients, 44·8% were co-infected with HCV, whereas 39·5% of HTLV-seronegative individuals were HCV mono-infected ($P > 0{\cdot}05$). Liver disease severity was not significantly different between HCV-mono-infected and HCV/HTLV-co-infected patients ($P > 0{\cdot}99$). No significant relation was detected between transfusion interval, the date of first blood transfusion and history of splenectomy with HTLV seropositivity. No case of HAM/TSP and ATLL and also no symptoms related to these conditions was detected among the study population.

DISCUSSION

Thalassemia patients with chronic blood transfusion are one of the most high-risk groups for HTLV-1 acquisition (Ghaffari *et al.*, 2012). Various studies have been performed regarding HTLV prevalence in Iran. The study by Anaraki Mohammadi *et al.* (2005) on thalassemic patients with mean age around 18 years referred to a thalassemia clinic in Tehran reported 6·3% of HTLV seropositivity, whereas the present study showed that 11·3% of transfusion-dependent thalassemic patients were HTLV seropositive, which may indicate a rise in HTLV prevalence among the thalassemia patients. However, we should consider that the patients who were included in this study were around 10 years older and as a result received more numbers of blood products than the patients in the study by Anaraki Mohammadi *et al.* (2005), which can be the cause of higher prevalence of HTLV infection in the patients of this study. The prevalence of HTLV in thalassemic patients was investigated in other provinces of Iran, which showed the HTLV seropositivity rate of 1·6 – 7·2% throughout the country (Fig. 1) (Table S1, Supporting Information). A previous study from Shiraz (Southwest of Iran) in 1996 showed 25·5% of HTLV-1 prevalence among thalassemic patients. This high prevalence rate of HTLV in the

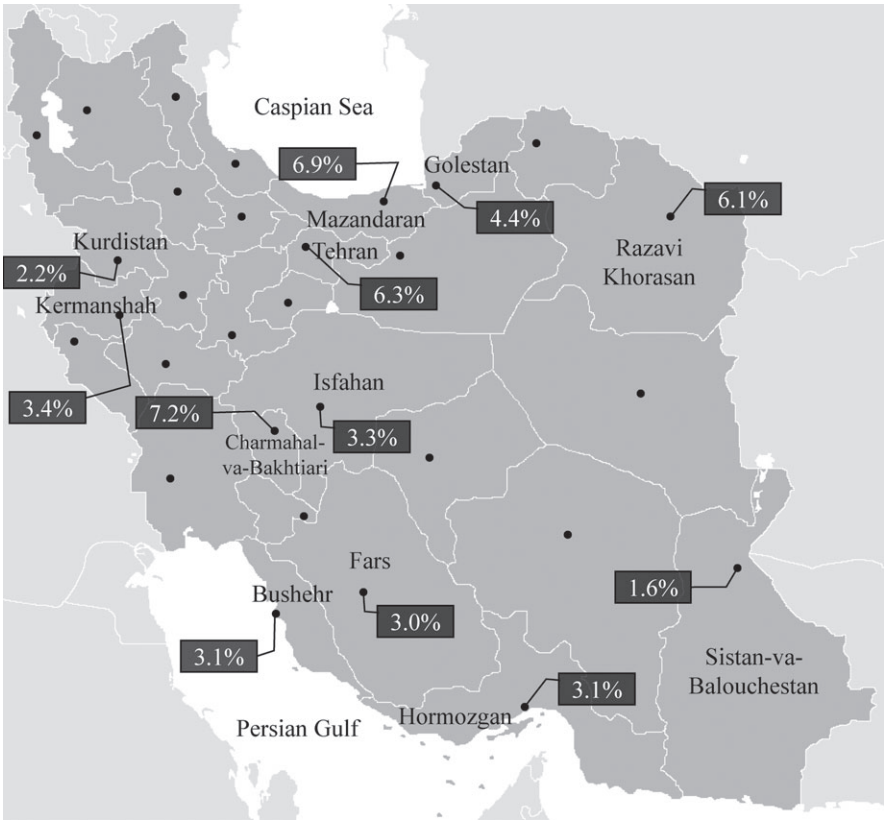

Fig. 1. Prevalence of HTLV infection among Iranian thalassemic patients in different provinces including Mazandaran (Ghaffari *et al.*, 2012), Golestan (Moradi *et al.*, 2008), Razavi Khorasan (Mansouritorghabeh & Badiei, 2008), Tehran (Anaraki Mohammadi *et al.*, 2005), Isfahan (Mortezaie *et al.*, 2012), Kermanshah (Ghadiri *et al.*, 2011), Kurdistan (Ardalan *et al.*, 2013), Sistan-va-Balouchestan (Moradi *et al.*, 2003), Fars (Arjmandi *et al.*, 2002), Charmahal-va-Bakhtiari (Karimi *et al.*, 2007), Bushehr (Pourkarim *et al.*, 2005) and Hormozgan (Abedi *et al.*, 2009).

latter study may be caused by the high false-positive rate of the former laboratory assays (Ghaderi & Habib-Agahi, 1996). Also, another study on thalassemic patients who referred to a hepatitis clinic in Tehran found the prevalence of HTLV-1 among 64 HCV-infected thalassemic cases, which is about 11% (Salimi *et al.*, 2013). Unfortunately, we did not find any studies searching for HTLV prevalence in thalassemic patients in the Middle East countries. Based on the study from Italy on transfusion-dependent thalassemic patients, antibodies to HTLV-1 and HTLV-2 were detected in 0·23 and 0·08% of individuals, respectively (Mozzi *et al.*, 1992). Tseliou *et al.* (2006) found an overall prevalence of 1·1% for HTLV infection among thalassemic patients in Greece. Also, no case with anti-HTLVAb was detected in a group of transfusion-dependent thalassemic patients in India (Chaudhary & Phadke, 2001).

The rate of HTLV seropositivity among blood donors was various in different provinces of Iran (Table S1). The Northeast part of Iran (Razavi Khorasan) has been considered as an endemic area for HTLV-1 infection. Phylogenetic study on HTLV-1 isolates from Mashhad (the capital of Razavi Khorasan province and a pilgrimage centre for the Shia Muslim) showed high degree of similarity between the Mashhad HTLV-1 and the Cosmopolitan HTLV-1 type (isolates from Africa, Europe and America). It was postulated that the virus introduced to this area through pilgrims and slave trade (Safai *et al.*, 1996). Based on the study by Rezvan *et al.* (1996), the prevalence of anti-HTLVAb in Mashhad was estimated to be about 1·9% in blood donors. After the implementation of systematic screening for anti-HTLVAb in Khorasan Blood Transfusion Center, a sharp decrease in HTLV seropositivity among blood donors of this province has been detected (Tarhini *et al.*, 2009). A recent systematic review for the estimation of HTLV prevalence among Iranian blood donors showed the different rates of HTLV prevalence in seven provinces of Iran, and it was concluded that the overall estimation of the HTLV-1 prevalence in Iranian blood donors was 0·12% (Hedayati-Moghaddam, 2013). In different studies, the HTLV seropositivity was associated with female sex, older age and non-white race (Rafatpanah *et al.*, 2011; Chang *et al.*, 2014), whereas no significant association was found between age and gender with HTLV infection among the patients of this study.

Hepatitis B has low prevalence among thalassemic patients (Poorolajal & Majdzadeh, 2009). A multicentre study in transfusion-dependent thalassemic patients from Iran showed the prevalence of HBV infection to be 1·5%, which was lower than the prevalence of HBV infection in the general population (Mirmomen *et al.*, 2006). This study found the prevalence of anti-HBsAb to be about 95%, and also 16% of individuals had anti-HBcAb in their sera. Another study among beta-thalassemia children in Tehran showed that 3·03% of patients were anti-HBcAb positive, 1·01% HBsAg positive and 89·9% anti-HBsAb positive (Milani & Shooshtari, 2010). A study among transfusion-dependent thalassemic patients showed that 10·5% had HBsAg seroconversion and more than 90% of vaccinated patients had anti-HBsAb more than 10 IU mL^{-1} (Azarkeivan *et al.*, 2009). The prevalence of HCV infection in thalassemic patients ranged from 16 to 64% in different provinces of Iran; also, 24·2% of thalassemic patients in Tehran were anti-HCVAb positive (Alavian *et al.*, 2002; Mirmomen *et al.*, 2006). It should be mentioned that after the implementation of HCV screening in 1995 and improvement of exclusion criteria for donation, the prevalence of HCV infection in thalassemic patients has decreased significantly and no new case has been infected after that time. HIV infection is rare among thalassemic patients in Iran, which can be explained by low prevalence rate of HIV infection and screening of all blood units for HIV in Iran.

Dissimilar rates of HCV/HTLV co-infection in thalassemia patients were observed in different studies. This study implied that 5·1% of cases were co-infected with HCV and HTLV, whereas in the study by Mansouritorghabeh & Badiei (2008), 1·94% of the study population were co-infected with HCV/HTLV. In a study among a group of the US thalassemia patients, 1·3 and 18·8% were anti-HTLVAb and anti-HCVAb positive, respectively, and 1 (0·45%) patient was found to be co-infected with HCV/HTLV (Switzer *et al.*, 2013). As HCV and HTLV-1/2 can be transmitted by blood transfusion, the higher occurrence of co-infection is expected in the populations at higher risk of blood-borne viral infections (Milagres *et al.*, 2009). In spite of HTLV-associated illnesses that may occur in infected patients, the HTLV influences chronic hepatitis C outcome. Evidences indicated that HTLV-1 produces a functional impairment of cellular immune response. A study reported that the host and virus interaction can lead to cellular immune dysfunction in HCV/HTLV-co-infected patients, which might impair HCV clearance and lead to hepatitis C aggressive forms consequently (Milagres *et al.*, 2009). As thalassemic patients need chronic blood transfusion that exposes them to different blood-borne pathogens, HCV/HTLV co-infection is prevalent among these patients, and as a result chronic hepatitis C should be treated promptly.

IBTO has established various strategies to decline the prevalence of transfusion-transmitted infections (TTI) including donor questionnaires, efficient donor selection, self-deferral procedure, confidential unit exclusion and increasing in the number of regular donations. Also, educational efforts to increase public knowledge on TTI, improvement in automation and data registry of blood donors with history of positive results for screening tests have been implemented by IBTO. Leukoreduction as a strategy to decrease the rate of TTI has been performed routinely by IBTO on blood units prepared for thalassemic patients since 2008. In spite of the low prevalence of HTLV in western countries, the HTLV screening in blood donors is mandatory in these countries, whereas screening for HTLV infection is not routinely performed in the regions, such as Iran, with high prevalence of HTLV infection. This paradox can be due to the cost of HTLV screening tests in Iran and in developing countries. As Iran is located in the HTLV endemic area, HTLV screening should be implemented in all blood transfusion centres of Iran.

In conclusion, as transfusion-dependent thalassemic patients need lifelong blood transfusion and are exposed to different blood-borne pathogens especially viral particles such as HTLV and because of higher prevalence of HTLV infection in transfusion-dependent thalassemic patients in this study compared with some previous studies, blood donation screening for HTLV should be implemented in all blood donor centres of Iran. General awareness about blood-borne infection and their transmission routes among blood donors should be considered. Also, routine HTLV screening in thalassemia patients who need regular blood transfusion is recommended, and HTLV-infected thalassemic patients should be consulted about the viral transmission routes and screening of their spouses as well. Further study on HTLV seroepidemiology in high-risk groups especially in transfusion-dependent thalassemic patients in all provinces of Iran is needed.

ACKNOWLEDGMENTS

B. H., A. A. and S. M. A. designed the study, M. K., A. A. and B. B. contributed in sample collection, M. K., A. A. and H. K. performed the study, S. Y. S. H. and H. S. analysed the data, M. K., A. A., B. B., H. S. and S. M. A. wrote the paper. We are grateful to Mr Arjangian and Mr Ashour for their assistance in sample and data collection.

CONFLICT OF INTEREST

The authors have no competing interests.

REFERENCES

Abbaszadegan, M.R., Gholamin, M., Tabatabaee, A., Farid, R., Houshmand, M. & Abbaszadegan, M. (2003) Prevalence of human T-lymphotropic virus type 1 among blood donors from Mashhad, Iran. *Journal of Clinical Microbiology*, **41,** 2593–2595.

Abedi, F., Yavarian, M., Shakibzadeh, A., Khalvati, B. & Asadi, A. (2009) A pilot seroepidemiologic study of HTLV in thalassemia, hemophilia, and hemodialysed patients in Hormozgan. *Medical Journal of Hormozgan University*, **13,** 75–80.

Abolghasemi, H., Amid, A., Zeinali, S. *et al.* (2007) Thalassemia in Iran: epidemiology, prevention, and management. *Journal of Pediatric Hematology/Oncology*, **29,** 233–238.

Alavian, S.M., Kafaee, J., Yektaparast, B., Hajarizadeh, B. & Doroudi, T. (2002) The efficacy of blood donor screening in reducing the incidence of hepatitis C virus infection among thalassemic patients in Iran. *Transfusion Today*, **53,** 3–4.

Anaraki Mohammadi, G., Sadeghipour, A., Vossough, P., Nour Mohammadi, I. & Mirnateghi, A. (2005) Assessment of the prevalence of human T-lymphotropic virus type 1 among thalassemic patients with frequent blood transfusion in Tehran in 2003. *Razi Journal of Medical Sciences*, **12,** 19–24.

Ardalan, N., Abdi, M., Zarif, B., Amini, A., Memary, F., Haydari, E. & Ahmadi, A. (2013) Prevalence of human T-lymphotropic virus types I&II among high risk groups in Sanandaj in 2010. *Scientific Journal of Kurdistan University of Medical Sciences*, **18,** 51–57.

Arjmandi, F., Shahriari, M. & Sadeghi Hasanabadi, M. (2002) A comparitive study of the prevalence of HTLV-I infection in leukemia/non-hodgkins lymphoma patients, thalassemic patients and blood donors. *Journal of Shahid Sadoughi University of Medical Sciences and Health Services*, **10,** 25–29.

Aydinok, Y. (2012) Thalassemia. *Hematology*, **17** (Suppl. 1), S28–S31.

Azarkeivan, A., Karimi, G., Shaiegan, M., Maghsudlu, M. & Tabbaroki, A. (2009) Antibody titration and immune response of Iranian beta-thalassemic patients to hepatitis B virus vaccine (booster effect). *Pediatric Hematology and Oncology*, **26,** 195–201.

Chang, Y.B., Kaidarova, Z., Hindes, D. *et al.* (2014) Seroprevalence and demographic determinants of human T-lymphotropic virus type 1 and 2 infections among first-time blood donors – United States, 2000-2009. *The Journal of Infectious Diseases*, **4,** 523–531.

Chaudhary, R. & Phadke, S.R. (2001) Absence of HTLV-I infection in multi-transfused thalassemia patients in North India. *American Journal of Hematology*, **67,** 217–218.

Ghaderi, A. & Habib-Agahi, M. (1996) High prevalence of anti-HCV and HTLV-1 antibodies in thalassemia major patients of Southern Iran. *Iranian Journal of Medical Sciences*, **21,** 2.

Ghadiri, K., Rezaei, M., Payandeh, M. & ErfanZare, M. (2011) Serologic prevalence of human T-lymphotropic virus (HTLV) among major thalassemic patients in Kermanshah 2010. *International Journal of Hematology-Oncology and Stem Cell Research*, **5,** 14–17.

Ghaffari, J., Kowsarian, M., Mahdavi, M., Vahid Shahi, K., Rafatpanah, H. & Tafreshian, A. (2012) Prevalence of HTLV-I infection in patients with thalassemia major in Mazandaran, North of Iran. *Jundishapur Journal of Microbiology*, **6,** 57–60.

Hedayati-Moghaddam, M.R. (2013) A systematic review for estimation of HTLV-I infection in the blood donors of Iran. *Iranian Journal of Basic Medical Sciences*, **16,** 196–201.

Karimi, A., Nafici, M. & Imani, R. (2007) Comparison of human T-cell leukemia virus type-1 (HTLV-1) seroprevalence in high risk patients (thalassemia and hemodialysis) and healthy individuals from Charmahal-Bakhtiari province, Iran. *Kuwait Medical Journal*, **39,** 259–261.

Karimi, G., Gharehbaghian, A., Tafti, M.F. & Vafaiyan, V. (2013) Emerging infectious threats to the blood supply: seroepidemiological studies in Iran – a review. *Transfusion Medicine and Hemotherapy*, **40,** 210–217.

Khabbaz, R.F., Onorato, I.M., Cannon, R.O., Hartley, T.M., Roberts, B., Hosein, B. & Kaplan, J.E. (1992) Seroprevalence of HTLV-I and HTLV-II among intravenous drug users and persons in clinics for sexually transmitted diseases. *New England Journal of Medicine*, **326,** 375–380.

Mansouritorghabeh, H. & Badiei, Z. (2008) Transfusion-transmitted viruses in individuals with β thalassemia major at Northeastern Iran, a retrospective sero-epidemiological survey. *Iranian Journal of Blood & Cancer*, **1,** 1–4.

Milagres, F.A., Duarte, M.I., Viso, A.T. & Segurado, A.C. (2009) Hepatitis C virus and human T-lymphotropic virus coinfection: epidemiological, clinical, laboratory and histopathological features. *Revista da Sociedade Brasileira de Medicina Tropical*, **42,** 363–368.

Milani, S. & Shooshtari, M. (2010) Study on efficacy of hepatitis B immunization in

vaccinated beta-thalassemia children in Tehran. *Iranian Journal of Pediatrics*, **20,** 211–215.

Mirmomen, S., Alavian, S.-M., Hajarizadeh, B. *et al.* (2006) Epidemiology of hepatitis B, hepatitis C, and human immunodeficiency virus infections in patients with beta-thalassemia in Iran: a multicenter study. *Archives of Iranian Medicine*, **9,** 319–323.

Moradi, A., Yaghob-Nezhad, Z., Mohagheghi, A. *et al.* (2003) Seroepidemiology of HTLV-1 antibody in the thalassemic patients in Zahedan and Zaboul cities in 2001. *Journal of Zanjan University of Medical Sciences and Health Services*, **43,** 43–47.

Moradi, A., Mansurian, A., Ahmadi, A., Ghaemi, E., Kalavi, K., Marjani, A. & Moghaddam, E.S. (2008) Prevalence of HTLV-1 antibody among major thalassemic patients in Gorgan (South East of Caspian Sea). *Journal of Applied Sciences*, **8,** 391–393.

Mortezaie, Z., Bouzari, M. & Roghanian, R. (2012) 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. *Iranian Journal of Blood & Cancer*, **1,** 169–175.

Mozzi, F., Rebulla, P., Lillo, F., Varnier, O.E., Biadati, C., Calcagno, L., Melotti, S. & Sirchia, G. (1992) HIV and HTLV infections in 1305 transfusion-dependent thalassemics in Italy. The COOLEYCARE Cooperative Group. *AIDS*, **6,** 505–508.

Poorolajal, J. & Majdzadeh, R. (2009) Prevalence of chronic hepatitis B infection in Iran: a review article. *Journal of Research in Medical Sciences*, **14,** 249–258.

Pourkarim, M., Hajiani, G.R., Khamisipour, G.R., Ardeshirdavani, N. & Tahmasebi, R. (2005) Seroepidemiological investigation of HTLV I, II infection among Busherian multi-transfused patients in 2003. *Blood (Khoon)*, **2,** 99–104.

Proietti, F.A., Carneiro-Proietti, A.B.F., Catalan-Soares, B.C. & Murphy, E.L. (2005) Global epidemiology of HTLV-I infection and associated diseases. *Oncogene*, **24,** 6058–6068.

Rafatpanah, H., Hedayati-Moghaddam, M.R., Fathimoghadam, F. *et al.* (2011) High prevalence of HTLV-I infection in Mashhad, Northeast Iran: a population-based seroepidemiology survey. *Journal of Clinical Virology*, **52,** 172–176.

Rezaee, A.R., Banoei, M.M., Khalili, E. & Houshmand, M. (2012) Beta-thalassemia in Iran: new insight into the role of genetic admixture and migration. *The Scientific World Journal*, **2012,** 635183.

Rezvan, H., Ahmad, J. & Farhadi, M. (1996) A cluster of HTLV-1 infection in northeastern of Iran. *Transfusion Today*, **27,** 8–11.

Safai, B., Huang, J.L., Boeri, E., Farid, R., Raafat, J., Schutzer, P., Ahkami, R. & Franchini, G. (1996) Prevalence of HTLV type I infection in Iran: a serological and genetic study. *AIDS Research and Human Retroviruses*, **12,** 1185–1190.

Salimi, S., Alavian, S.M., Behnava, B., Keshvari, M., Keyvani, H., Mehrnoush, L., Gholami Fesharaki, M. & Karimi, P. (2013) The prevalence of HTLV-I infection in Iranian thalassemic and haemophilic patients with chronic hepatitis C. *Hepatology International*, **7** (Suppl. 1), S399.

Shindo, N., Alcantara, L.C., Van Dooren, S. *et al.* (2002) Human retroviruses (HIV and HTLV) in Brazilian Indians: seroepidemiological study and molecular epidemiology of HTLV type 2 isolates. *AIDS Research and Human Retroviruses*, **18,** 71–77.

Switzer, W.M., Shankar, A., Trimble, S.R. *et al.* (2013) Human T cell lymphotropic virus type 1 infection among US thalassemia patients. *AIDS Research and Human Retroviruses*, **29,** 1006–1009.

Tarhini, M., Kchour, G., Zanjani, D.S., Rafatpanah, H., Otrock, Z.K., Bazarbachi, A. & Farid, R. (2009) Declining tendency of human T-cell leukaemia virus type I carrier rates among blood donors in Mashhad, Iran. *Pathology*, **41,** 498–499.

Tseliou, P.M., Spanakis, N., Spiliotakara, A., Markogiannakis, A., Legakis, N.J. & Tsakris, A. (2006) Prevalence of infection by HTLV-I/II among pregnant women and high-risk groups in the Peloponnese peninsula, Greece. *International Journal of STD & AIDS*, **17,** 543–546.

Supporting Information

Additional Supporting Information may be found in the online version of this article:

Table S1. Prevalence of HTLV infection among Iranian general population, blood donors and thalassemic patients.