Provided for non-commercial research and education use.

Not for reproduction, distribution or commercial use.



This article was published in an CASRP journal. The attached copy is furnished to the author for non-commercial research and education use, including for instruction at the authors institution, sharing with colleagues and providing to institution administration.

Other uses, including reproduction and distribution, or selling or licensing copied, or posting to personal, institutional or third party websites are prohibited.

In most cases authors are permitted to post their version of the article (e.g. in Word or Tex form) to their personal website or institutional repository. Authors requiring further information regarding CASRP's archiving and manuscript policies encouraged to visit:

http://www.casrp.co.uk/journals

© 2016 CASRP Publishing Company Ltd. UK.



Available online at www.casrp.co.uk/journals



International journal of Advanced Biological and Biomedical Research 4(2) (2016) 152–157



Original Article

Open Access

Relationship between the human T- lymphotropic virus and myeloid leukemia, mycobacterium tuberculosis

Saman Ayoubi¹, Mohammad Sadegh Hashemzadeh², Omid Lakzaie Azar³, Fatemeh Naeimpour⁴, Nasim Padasht⁵, Bashir Mirtajani⁵, Jafar Aghajani⁵, Mahdi Tat², Mojtaba Sharti², Ruhollah Dorostkar^{2,*}

¹Mycobacteriology Research Centre, National Research Institute of Tuberculosis and Lung Disease (NRITLD), Shahid Beheshti University of Medical Sciences, Tehran, Iran.

²Applied Virology Research Center, Baqiyatallah University of Medical Sciences, Tehran, Iran.

³fajr Milk, Industry Co., Golestan Sabah, <mark>Sabah, Gonbad, Iran.</mark>

⁴Department of Mycology, Fac of Vet. Med, Science and Research Branch Of Islamic Azad University, Tehran, Iran. ⁵Department of biotechnology, Faculty of Basic Sciences, Lahijan Branch, Islamic Azad University (IAU), Lahijan, Iran.

Abstract

Research, Service, Publication

Human T-cell lymphotropic virus type 1, 2 (HTLV-1, 2) is endemic in Particular Areas of the world in which it is associated with myeloid leukemia. In this study, we described the prevalence of HTLV-1, 2 in myeloid leukemia and Mycobacterium Tuberculosis in Iran. We have worked with tissue and blood samples for 2 years. These were the same samples which were positive for myeloid leukemia, *Mycobacterium tuberculosis*, HTLV and were collected from Imam Khomeini hospital in Tehran, Iran. 100 cases were investigated (58% males, 42% females), the age of these samples were within 5 to 89 years old. In 65.7 percent of the leukemia rate HTLV-1 has been positive. Five cases (54%) were myeloid leukemia, 36.4% cases were not myeloid leukemia and 3 out of 8 cases (27.9%) unclassified lymphomas, were positive respectively. All 6 cases (100%) were adults with acute T-cell leukemia/lymphoma (ATLL) and *Mycobacterium tuberculosis* were positive. Among all cases, just one case has been positive for chronic myeloid leukemia and myeloproliferative disruption. Positive HTLV-1- show more in older ages than younger one. At younger ages offers less than negative items. According to our results, in Iran HTLV-1, 2

^{© 2016} The Authors. This is an open access article under the terms of the Creative Commons Attribution-Non Commercial- No Derives License, which permits use and distribution in any medium, provided the original work is properly cited, the use is non-commercial and no modifications or adaptations are made.

Received 19 March 2016	Accepted 18 April 2016	Available online 25 April 2016
iThenticate screening 22 March 2016	English editing 15 April 2016	Quality control 21 April 2016
Thenticate screening 22 March 2010	Linglish Editing 15 April 2010	Quality control 21 April 2010

^{*} Corresponding author: Applied Virology Research Center, Baqiyatallah University of Medical Sciences, Tehran, Iran.

is dramatically related to myeloid leukemia, and more studies are required for accurate connection with myeloma diseases and this area.

© 2016 Published by CASRP publishing company Ltd. UK. Selection and/or peer-review under responsibility of Center of Advanced Scientific Research and Publications Ltd. UK.

Keywords: HTLV-1, 2, Myeloid leukemia, Myeloma.

1. Introduction

Family of human T-lymphotropic viruses or human T-cell lymphotropic viruses (HTLV), are a group of human retroviruses that are known to cause a type of cancer, called adult T-cell leukemia/lymphoma and a demyelinating disease called HTLV-I associated myelopathy/tropical spastic paraparesis (HAM/TSP). The HTLVs belongs to a large group of primate T-lymphotropic viruses (PTLVs) (Manns et al., 1999). Members of this family that infect humans are called HTLVs, and the ones that infect Old World monkeys are called Simian T-lymphotropic viruses (STLVs) (Clark et al., 1985). Today, four types of HTLVs (human T-lymphotropic virus 1 [HTLV-I], human T-lymphotropic virus 2 [HTLV-II], HTLV-III, and HTLV-IV) and four types of STLVs (STLV-I, STLV-II, STLV-III, and STLV-V) have been identified. The HTLVs are believed to originate from intraspecies transmission of STLVs (Zhang et al., 1995). The original name of HIV, the virus that causes AIDS, was HTLV-III; this term is no longer in use (Bartman et al., 2008). The knowledge about HTLV-1 epidemiology is limited (Mori et al., 2002). The high prevalence was detected in Japan where more than 10% of the population are infected. The reasons for this extremely high prevalence has not been known. In some countries like Taiwan, Iran, and Fujian (a Chinese province near Taiwan), the prevalence is 0.1–1%. The infection rate is about 1% in Papua New Guinea, the Solomon Islands, and Vanuatu, where the genotype C is predominated (Einsiedel et al., 2011). Although it is present in some high-risk populations, including immigrants and intravenous drug users, in Europe HTLV-1 is still uncommon (Edlich et al., 2003). Among Americans, the virus is found in indiogenous populations and in descendants of African slaves from where it is thought to have originated (Beilke et al., 2003). The general prevalence is from 0.1 to 1%. In Africa the prevalence is not well known, but it is about 1% in some countries (Zeeb et al., 2004).

Acute myeloid leukemia (AML) is a type of blood cancer. AML usually develops from cells that would turn into white blood cells (other than lymphocytes) (Olière et al., 2001). Sometimes, though, it can develop from other types of blood-forming cells (Andrada-Serpa et al., 1989). Here is a basic information about the symptoms, risk factors, survival rates, and treatments for AML. Acute myeloid leukemia starts in the bone marrow, the soft inner parts of bones (Schuurman et al., 1989). With acute types of leukemia such as AML, bone marrow cells don't mature the way they're supposed to. These immature cells, often called blast cells, just keep building up (Garlet et al., 2010).Acute myeloid leukemias (AMLs) are infrequent yet, so virulent neoplasms are responsible for a large number of cancer-related death (Henry et al., 2007).

Mycobacterium tuberculosis is an obligate (Delacrétaz et al., 1987) pathogenic bacterial species in the family of Mycobacteriaceae and is the causative agent of most cases of tuberculosis (Tang et al., 2012). Tuberculosis is a most important global health problem, According to the report of WHO, "In 2012, an estimated 8.6 million people developed TB and 1.3 million died from the disease" (Tang et al., 2012; Sarvi et al., 2016).

At first, it is discovered in 1882 by Robert Koch. *M.tuberculosis* has an unusual, waxy coating on its cell surface (primarily due to presence of mycolic acid), which makes the cells impervious to Gram staining; M. tuberculosis can appear gram-negative and gram-positive in clinical settings (Laurian et al., 1986). So Ziehl-Neelsen stain, or acid-fast stain, is used instead (Stahl-Hennig et al., 2009). The physiology of *M. tuberculosis* is highly aerobic and requires high levels of oxygen. It is a primarily pathogen of the mammalian respiratory system which infects the lungs (Araújo et al., 2002). The most frequently diagnostic methods used for tuberculosis are tuberculin skin test, acid-fast stain, and chest radiography (Scoazecetal et al., 1988).

The relationships between retroviruses and hematologic cancer is better described in HTLV-1 and HIV infections. HTLV-1, 2 are the first human retroviruses discovered by Poiesz et al (Hayashi et al., 1990). There are case reports of HTLV-1 in non-AML myeloid malignancies (Altafulla et al., 1989). Myeloid malignancies and Tuberculosis can be seen in our hospital to HTLV-1. HTLV-1, is endemic in Iran, where there are prevalent of

unsigned blood donors and 33.15% chosen hospitalized patients, clinically suspicious to have 4.66% HTLV-1 related diseases, so we are going to study the prevalence of HTLV-1 in myeloid malignancies in Iran over 10 years.

2. Materials and methods

During the two years of blood samples from patients suspected myeloid leukemia Mycobacterium Tuberculosis bacteria collected from Tehran Imam Khomeini hospital. And also check records HTLV-1 and serology HIV tests by blood transfusion unit, and determine the hematologic malignancies and tuberculosis were examined at the same time. Diseases were examined by ELISA, and positive serum was tested by the Western blot method in a revered center. Myeloma was classified as myeloid leukemia. Immunophenotyping was not available.

3. Results and discussion

100 cases of histologically recorded hematologic malignancies and Tuberculosis (Table I) are composed of 58 males (59%) and 42 females (41%). The average range and sex distribution of any type was given in Table II. There was an age variability in positive HTLV-1. In this study the Myeloma and the acute form of AML make 63.7% of histologically recorded hematologic malignancies and myeloma is the most common hematologic malignancy in Iran. There was a significant relationship between positive HTLV-1, 2 and Myeloma here, from 76% of TB disease, 72.2% of TB, and all 6 cases of acute AML (63%) were positive HTLV-1. In Iran, the serum prevalence of HTLV-1, 2 in unsigned healthy blood donors is 57.2%. The positive HTLV-1, 2- items of TB may feature constitution of the Myelomatous kind of AML. In this study found an HTLV-1 spread of 86.1% in 88 cases of TB in Iran, an endemic HTLV-1 region.

In this study the Myeloma and the acute form of AML make 63.7% of histologically recorded hematologic malignanciesand myeloma is the most common hematologic malignancy in Iran. There was a significant relationship between positive HTLV-1, 2 and Myeloma here, from 76% of TB disease, 72.2% of TB, and all 6 cases of acute AML (63%) were positive HTLV-1. In Iran, the serum prevalence of HTLV-1, 2 in unsigned healthy blood donors is 57.2%. The positive HTLV-1, 2- items of TB may feature constitution of the Myelomatous kind of AML. In this study found an HTLV-1 spread of 86.1% in 88 cases of TB in Iran, an endemic HTLV-1 region. The average age of 46 years old is accordance with the average age of 43 years recorded in Tehran, Iran (Sharief et al., 1991), but less than from the average age of 56 years observed in the Japan. The average age of this study shows thatearly life is more likely exposed to the virus, such as by mother-to-child transferring. Early childhood infection is considered critical in development of HTLV-1, 2-associated CML/AML since leukemogenesis may take 20-40 years to develop.like this study, US found the same relationship between positive HTLV-1,2 and Myeloma disease, although the number of cases was small. Myeloma disease is highly connected with Epstein-Barr (EB) virus infection, as EB virus was seen in 87.7% of cases of Myeloma disease studied by (Starkebaum et al., 1987). It is not known whether chronic immunosuppression by HTLV-1, 2 virus may predispose individuals to malignancies such as Hodgkin disease or not. Further study, including identification of proviral DNA in tissue, will be needed to establish a definite causal relationship between HTLV-1 and Hodgkin disease. The three cases were not specific for any histologic subtype, as there was 1 case of nodular sclerosing HD, 1 case of lymphocyte predominant HD, and one mixed cellularity HD.

	The relationship between human lymphotropic virus and malignant diseases.					
		Diseases	HTLV1	HTLV2	Age	Sex
1.		ANL	25.23	14.12	25.12	74
2.		CML	47.12	35.1	47.23	84
з.		Myeloma	65.14	74	65.23	15
4.	hairy cell	leukemia	35.2	58.23	85.12	25
5.		тв	56.2	32.25	35	65

Table 1

154

	. ,			0	
Variable	Obs	Mean	Std. Dev.	Min	Max
AML	5	63.786	18.45407	36.12	85.12
CML	5	70.92	22.9826	35.12	95.12
Myeloma	5	76.444	20.58166	45.74	95.12
hairycell	5	58.296	29.34749	25.12	95.12
тв	5	72.924	23.75126	35.12	95.12

Teble 2
Estimates the frequency of connections between the HTLV virus and malignant diseases.

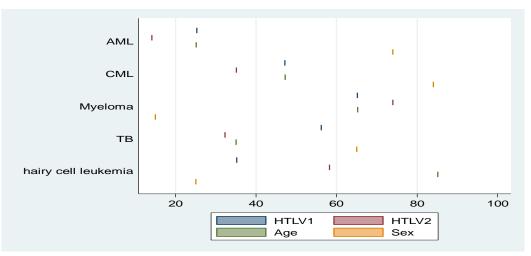


Fig. 1. Relationship between human T-lymphotropic virus and malignant diseases.

4. Conclusion

From the two seropositive chronic leukemias, one case is chronic lymphocytic leukemia and another is chronic myeloid leukemia. There is also a 65-year-old female with myeloproliferative disease. Mann et al. 1999 and Starkebaum et al. 1987, reported a case of HTLV-1 and B-cell chronic lymphocytic leukemia and a case of HTLV-1 and large granular lymphocyte leukemia respectively. We conclude that there is a relationship between HTLV-1 and Myeloid malignancies in Iran and this relationship is consistent with the findings of other studies; however, the association of Hodgkin disease that we see in these cases and its relationship with HTLV-1 needs other studies.

References

Altafulla, M., De Bernal, J., Espino, H., Rios, B., 1989. Human T-cell Leukemia Virus-/and Hematologic Malignancies in Panama. Canc., 63, 2186-91.

Andrada-Serpa, M.J., Tosswill, J., Schor, D., Linhares, D., Dobbin, J., Pereira, M.S., 1989. Seroepidemiologic survey for antibodies to human retroviruses in human and non-human primates in Brazil. Int. J. Canc., 44(3), 389-93.

- Araújo, A.P., Fontenelle, L.M., Pádua, P.A., Maia, Filho, H.S., De, Q.C., Araújo, A., 2002. Juvenile human T lymphotropic virus type 1-associated myelopathy. Clin. Infect. Dis., 35(2), 201-4.
- Bartman, M.T., Kaidarova, Z., Hirschkorn, D., Sacher, R.A., Fridey, J., Garratty, G., 2008. Long-term increases in lymphocytes and platelets in human T-lymphotropic virus type II infection. Blood., 112(10), 3995-4002.
- Beilke, M.A., Theall, K.P., Clayton, J.L., Benjamin, S.M., Winsor, E.L., Kissinger, P.J., 2004. Clinical outcomes and disease progression among patients coinfected with HIV and human T lymphotropic virus types 1 and 2. Clin. Infect. Dis., 39(2), 256-63.
- Clark, J.W., Robert-Guroff, M., Ikehara, O., Henzan, E., Blattner, W.A., 1985. Human T-cell leukemia-lymphoma virus type 1 and adult T-cell leukemia-lymphoma in Okinawa. Canc. Res., 45(6), 2849-52.
- Delacrétaz, F., Perey, L., Schmidt, P.M., Chave, J.P., Costa, J., 1987. Histopathology of bone marrow in human immunodeficiency virus infection. Virchows Archiv A., 411(6), 543-51.
- Edlich, R., Hill, L.G., Williams, F.M., 2003. Global epidemic of human T-cell lymphotrophic virus type-I (HTLV-I): an update. J. long. Term. Eff. Med. Implants., 13(2).
- Einsiedel, L., Fernandes, L., Spelman, T., Steinfort, D., Gotuzzo, E., 2011. Bronchiectasis is associated with human Tlymphotropic virus 1 infection in an Indigenous Australian population. Clin. Infect. Dis., 766.
- Garlet, G.P., Giozza, S.P., Silveira, E.M., Claudino, M., Santos, S.B., Avila-Campos, M.J., 2010. Association of human T lymphotropic virus 1 amplification of periodontitis severity with altered cytokine expression in response to a standard periodontopathogen infection. Clin. Infect. Dis., 50(3), e11-e8.
- Hayashi, S., Fine, R., Chou, T-C., Currens, M., Broder, S., Mitsuya, H., 1990. In vitro inhibition of the infectivity and replication of human immunodeficiency virus type 1 by combination of antiretroviral 2',3'-dideoxynucleosides and virus-binding inhibitors. Antimicrobial agents and chemotherapy., 34(1), 82-8.
- Henry, L., Carillo, S., Jourdan, E., Arnaud, A., Brun, S., Lavabre-Bertrand, T., 2007. Association of essential thrombocythemia and chronic lymphocytic leukemia: absence of the V617F JAK2 mutation in the lymphoid compartment. Am. J. Hematol., 82(6), 500-1.
- Laurian, Y., Le Bras, P., Ellrodt, A., Alvin, P., 1986. Immune Thrombocytopenia Gammaglobulin, and Seropositivity to the Human T-Lymphotropic Virus Type III. Ann. Inter. Med., 105(1), 145-6.
- Manns, A., Hisada, M., La Grenade, L., 1999. Human T-lymphotropic virus type I infection. The Lancet., 353(9168), 1951-8.
- Mori, N., Yamada, Y., Ikeda, S., Yamasaki, Y., Tsukasaki, K., Tanaka, Y., 2002. Bay 11-7082 inhibits transcription factor NF-κB and induces apoptosis of HTLV-I–infected T-cell lines and primary adult T-cell leukemia cells. Blood., 100(5), 1828-34.
- Olière, S., Douville, R., Sze, A., Belgnaoui, S.M., Hiscott, J., 2011. Modulation of innate immune responses during human T-cell leukemia virus (HTLV-1) pathogenesis. Cytokine & growth factor reviews., 22(4), 197-210.
- Sarvi, F., Momenian, S., Khodadost, M., Pahlavanzadeh, B., Nasehi, M., Sekhavati, E., 2016. The examination of relationship between socioeconomic factors and number of tuberculosis using quantile regression model for count data in Iran 2010-2011. Med J Islam Repub Iran. Vol. 30:399.
- Schuurman, H., Krone, W., Broekhuizen, R., Van Baarlen, J., Van Veen, P., Golstein, A., 1989. The thymus in acquired immune deficiency syndrome. Comparison with other types of immunodeficiency diseases, and presence of components of human immunodeficiency virus type 1. Am. J. Pathol., 134(6), 1329.
- Scoazec, J., Marche, C., Girard, P., Houtmann, J., Durand-Schneider, A., Saimot, A., 1988. Peliosis hepatis and sinusoidal dilation during infection by the human immunodeficiency virus (HIV). An ultrastructural study. Am. J. Pathol., 131(1), 38.
- Sharief, M.K., Hentges, R., 1991. Association between tumor necrosis factor-α and disease progression in patients with multiple sclerosis. New England. J. Med., 325(7), 467-72.
- Stahl-Hennig, C., Eisenblätter, M., Jasny, E., Rzehak, T., Tenner-Racz, K., Trumpfheller, C., 2009. Synthetic doublestranded RNAs are adjuvants for the induction of T helper 1 and humoral immune responses to human papillomavirus in rhesus macaques. PLoS Pathog., 5(4), e1000373.
- Starkebaum, G., Kalyanaraman, V., Kidd, P., Loughran, T., Kadin, M., Singer, J., 1987. Serum reactivity to human Tcell leukaemia/lymphoma virus type I proteins in patients with large granular lymphocytic leukaemia. The Lancet., 329(8533), 596-9.
- Tang, S.W., Ducroux, A., Jeang, K.T., Neuveut, C., 2012. Impact of cellular autophagy on viruses: Insights from hepatitis B virus and human retroviruses. J. Biomed. Sci., 19(92), 10.1186.

- Zeeb, H., Blettner, M., 1998. Adult leukaemia: what is the role of currently known risk factors? Radiation and environmental biophysics. 36(4), 217-28.
- Zhang, Y., Nakata, K., Weiden, M., Rom, W.N., 1995. Mycobacterium tuberculosis enhances human immunodeficiency virus-1 replication by transcriptional activation at the long terminal repeat. J. Clin. Investig., 95(5), 2324.

How to cite this article: Ayoubi, S., Hashemzadeh, M.S., Lakzaie Azar, O., Naeimpour, F., Padasht, N., Mirtajani, B., Aghajani, J., Tat, M., Sharti, M., Dorostkar, R., 2016. Relationship between the human T- lymphotropic virus and myeloid leukemia, mycobacterium tuberculosis. International journal of Advanced Biological and Biomedical Research, 4(2), 152-157.	Submit your next manuscript to CASRP Central and take full advantage of: • Convenient online submission • Thorough peer review • No space constraints or color figure charges • Inmediate publication on acceptance • Inclusion in Google Scholar • Research which is freely available for redistribution Submit your manuscript at www.casrp.co.uk/journals
--	--