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A comparison of HTLV-1 Infection Frequency in Patients with or without Tuberculosis

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ABSTRACT

Introduction: To recognize the predisposing factors in tuberculosis as an endemic infection in Northeast province of Iran, this study was aimed to evaluate whether HumanT-lymphocyte type 1 (HTLV-I) as an immunosuppressive factor increases the risk of tuberculosis.

Materials and Methods: A Case-control study was conducted in 278 tuberculosis patients from 2007 to 2010, in Mashhad, Iran. Tuberculosis has been diagnosed by gold standard tests like sputum culture, bronchoalveolar lavage (BAL) culture or cytology. For detection of HTLV-I antibody, Enzyme Linked Immunosorbant Assay method and western Blot as the confirming test were performed. Then 276 healthy cases were matched for gender and age.

Results: The mean age of tuberculosis patients was 49.67±21.36 years and for control cases was 48.36±20.74. In patients group, 114 (41.6%) were male, 160 (58.4%) were female and in controls 123 (44.6%) were male and 153 (55.4%) were female. Pulmonary tuberculosis was presented in 84.2% of the patients. The frequency of HTLV-1 was 2.9% and 3.3% in patients and controls, respectively. HTLV-I frequency was higher in male patients and it increased by age.

Conclusion: Regarding to this study, HTLV-I infection is not stand-alone sufficient for increasing the risk of tuberculosis.

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Introduction

The human T cell lymphotropic virus type 1 (HTLV-I) has a world-wide distribution, with higher prevalence in some areas including Central and South America, Central Africa, south west of Japan, and Iran (1). HTLV-I from retrovirus transforms genes and causes immunosuppression (2, 3). This virus is the known etiological agent of adult T-cell leukemia (a hematological malignancy of CD4+) (4), adult T- cell Leukemia - Lymphoma (ATLL), and

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progressive HTLV-I associated Myelopathy or HTLV-associated myelopathy and Tropical spastic paraparesis (HAM/TSP) (5-7). There are evidences that confirmed HTLV-I infection increases the severity and susceptibility to pulmonary cryptococcosis, strongyloidiasis, community-acquired pneumonia, and tuberculosis (8-13).

It is known that immune system has an important role protecting the body against major infections such as tuberculosis (2, 3). Previous studies have reported the pulmonary involvement in the patients infected with HTLV-I (12, 14). However this finding was confirmed by a radiological study among HTLV-I virus carriers and non-infected individuals (15). Disease prevention by identifying the risk factors due to contaminative nature and high mortality rate (before treatment) of the disease is the mechanism of action to supress the infection in the area. HTLV-I infects the CD4 +T cells that might impair the body deference against Mycobacterium Tuberculosis.

HTLV1 infection will reduce the delayed hypersensitivity reaction to the infection. Reduced Tuberculosis skin test (PPD) response is a marker of cell mediated immunity deficit which associates with presence of higher active Tuberculosis (5-7). In this study the relationship between these two common infections was investigated.

Materials and Methods

Studied patients

This study was performed between 2007-2010 in health provider centers of Mashhad, Emam Reza and Ghaem hospitals. 278 patients with tuberculosis that their diagnosis were confirmed by gold standard tests such as sputum culture, tissue sample or bronchoalveolar lavage (BAL) cultures were recruited in study. Our studied inclusion criteria were positive history of tuberculosis and ages greater than or equal to 15 years. The patients who were IV drugs abusers or other immunosuppressive conditions such as lymphoma or systemic steroids therapy, were excluded. We also selected 276 healthy control participants from healthy, gender and age matched persons among our studied community. They did not have past history of tuberculosis disease and no symptoms or signs of disease in visits. They were selected from different cluster groups in Mashhad population. All the patients and the controls informed about the study procedure and they signed the consent form. Then the demographic information including age, gender, the infected organ, and results of the gold standard confirmatory tests were collected by check list.

Laboratory methods

Ten milliliter of blood were withdrawn from antecubital vein of all the patients and undergone for assessing HTLV-I infection. The first step was ELIZA test for HTLV1 which was done for all cases. In case of positive tests the confirmatory test including Western blot and HTLV-I PCR were performed.

Statistical Analysis:

All data such as demographic, laboratory and clinical information were analyzed by using the statistical package for social sciences (SPSS 11.5 Inc., Chicago, IL, USA). The variables presented as percentages and means ± standard deviations. All data were checked for normality by Kolmogorov–Smirnov test (K–S test). Descriptive statistics were used to summarize the demographic characteristics of the case and the control groups. For continuous and categorical variables, independent student's t-tests and chi-square tests were used to evaluate the statistical significance of any difference or relationship between the study parameters respectively. Pearson and Spearman correlation coefficients were calculated. *P*-values less than 0.05 were considered significant. Acceptable study power was agreed a priori to be > or = 80% (type-I error of < or =0.20) and this was used for sample size calculation as well.

Results

In this study, 551 individuals were enrolled from 2007 to 2010. There were recruited 278 patients and 276 healthy control subjects. The mean age was 49.67 years in patients (ranged 11 to 90 years old). Also 114 individuals (41.6%) were male and 160 (58.4%) were female in patients. The control participants were included 123 males (44.6%) and 153 females (55.4%). Involvement of different organs in tuberculosis patients is presented in Table 1. As this table shows, pulmonary involvement, pleural tuberculosis and tuberculosis (TB) lymphadenitis had the most frequencies among tuberculosis patients.

There were 13 HTLV-I infected persons in

Table 1. Different involved organs in Tuberculosis patients

Involved organ	Number	Percentages
Lung	234	84.2
Pleural	14	5.1
Lyphadenopathy	11	4
Musculoskletal	7	2.5
Pritoneal	3	1.1
Kidney	3	1.1
Miliary	2	0.7
Central nervous system	1	0.4
Other sites	2	0.7
Total	277	100

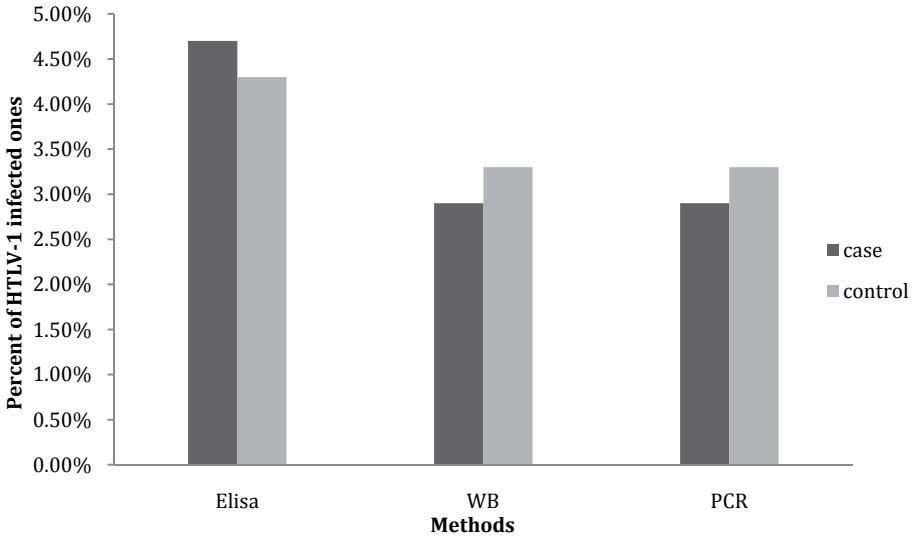

Figure 1. Percent of HTLV-1 infected individuals between three methods Elisa, WB (Western Blot) and PCR among case and control groups

Table 2. Comparison of HTLV1 percent in cases and controls by ELIZA test

ELIZA	Cases (%)	Controls (%)
positive	13 (4.7)	12 (4.3)
negative	265 (95.3)	264 (95.7)

patient group and 12 cases in controls that were confirmed by ELIZA test (Table 2). There was no statistically significant difference between HTLV-I- infected persons in cases and controls (*P*=0.852). Western blot tests were conducted as confirmatory test for positive ELIZA subjects and it revealed eight positive ones in case and nine in control group. There were no significant difference between the two groups (*P*=0.806) and western blot test approved the same result like HTLV-I- PCR (Figure 1).

Discussion

Tuberculosis and HTLV-I infections are both endemic in our study area. In this study we found that prevalence of HTLV-I in our TB patients was 2.9 percent that was approved by HTLV-I PCR and western blot test. Norrgren *et al* investigated the prevalence of HTLV-I among hospitalized adult pulmonary tuberculosis patients (16). They reported that in the TB group, a total of 32 (11.4%) of 280 patients were positive for HTLV-I. This was significantly higher compared with the population-based group in which 74 (3.5%) of 2117 were HTLV-I positive.

In the cross-sectional study with De Lourdes Bastos and colleagues at the pulmonary disease hospital, they evaluate 607 patients, 360 (59.3%) had current or past history of tuberculosis and 50 (8.2%) had HTLV-I infection; 39 (6.4%) had both.

The prevalence of HTLV-I infection in patients with tuberculosis and in controls of endemic areas for HTLV-I infection were reported in Verdonck *et al* study (18) in Peru; 5.8% with 1.3% and in Brazil by Marinho *et al* (12); 4.27% with 1.3% respectively. The prevalence has been reported 0.77% in 2003 by Abbaszadegan *et al* (7). In our study the prevalence of HTLV-I among 1389 blood donor was 2.3% and in age and gender matched control group was 3.3%.The studies on HTLV-I and Tuberculosis relationship have many different and inconclusive results, but previous studies had not compared tuberculosis infected patients with healthy control participants (16,17,18).

For the first time, Matsuzaki *et al* (19) and Verdonck *et al* (18) have authorized the increased risk of tuberculosis among HTLV-I positive cases versus HTLV-I negative subjects. But Mutsuzaki *et al* (19) did not focused on HIV status while Verdonck *et al* (18) has assessed HIV in only 23 subjects between 1305 patients, as well. Marinho's *et al* (12) in a case-control study has reported the increased HTLV-I positive cases in pulmonary and lymph node tuberculosis in HIV negative patients, but they ignored some confounding factors. Norrgren *et al* (16) did not report any statistical significant of increased risk of HTLV-I infection in tuberculosis/HIV negative patients, but in coincident HIV and tuberculosis there were significant increase of HTLV-I. In this study, we could not find any statistical significant for increased risk of HTLV-I among tuberculosis group versus healthy age and gender matched control group (*P*=0.81). This might be due to insufficient effect of HTLV-I on immune system which does not increase the risk of tuberculosis in endemic area.

Limitations of the study

One of the limitations of our study is minority of the HTLV-I positive cases, so it was not possible to assess the association of the

severity of the disease and HTLV-I. Also we did not analyze the detail of symptoms, disease onset and involved organs in Tuberculosis patients in our assessment.

Conflict of Interest

The authors declare no conflict of interest.

References

1. Proietti FA, Carneiro-Proietti AB, Catalan-Soares BC, Murphy EL. Global epidemiology of HTLV-I infection and associated diseases. Oncogene. 2005; 24:6058–68.
2. Jacobson S. Immunopathogenesis of human T cell lymphotropic virus type Iassociated neurologic disease. J Infect Dis. 2002, 186(Suppl 2):S187–S92.
3. Longo D, Fauci A. The Human Retroviruses. In: Fauci A, Braunwald E, Kasper D, Hauser S, Longo D, Jameson JL, et al. Harrison' S Principles of Internal Medicine. 14th ed. New York: McGrow Hill; 2008. p.1132-37.
4. Lairmore M, Franchini G. Human T cell leukemia virus Types 1 and 2. In: Knipe D, Howley P, Griffin D, lamb R, martin M, Roizman B, et al. Fields virology. 5th ed. Philadelphia: Lippincott Williams and wilkins,a Wolters Kwwer Business; 2007.vol3. p.2072-92.
5. Santos SB, Porto AF, Muniz AL, de Jesus AR, Magalhaes E, Melo A, et al. An exacerbated inflammatory cellular immune response characteristic of HAM/TSP is observed in a large proportion of HTLV-I asymptomatic carriers. BMC Infect Dis. 2004, 4(1):7.
6. Marsh BJ. Infectious complications of Human T cell leukemia/lymphoma virus type1 infection.Clin Infect Dis. 1996; 23:138-45.
7. Abbaszadegan M, Gholamin M, Tabatabai A, Houshmand M, Abbaszadegan Mo. Prevalence of Human T-lymphotropic Virus Type 1among blood donors from Mashad, Iran. J Clin Microbiol. 2003; 41:2593-5.
8. Marinho J, Galvao-castro B, Rodrigues Lc, Barreto Ml. Increased risk of tuberculosis with human T-lymphotropic virus-1 infection: A case control study. J Acquir Immune Defic Syndr. 2005; 40:625-8.
9. Brites C, Weyll M, Pedroso C, Badaro R. Severe and Norwegian scabies are strongly associated with retroviral (HIV-1/HTLV-I) infection in Bahia, Brazil. Aids. 2002; 16:1292–3.
10. Neva FA, Murphy EL, Gam A, Hanchard B, Figueroa JP, Blattner WA. Antibodies to Strongyloides stercoralis in healthy Jamaican carriers of HTLV-I. N Engl J Med. 1989; 320:252–3.
11. Pedral-Sampaio DB, Martins Netto E, Pedrosa C, Brites C, Duarte M, Harrington W Jr. Co-Infection of Tuberculosis and HIV/HTLV Retroviruses: Frequency and Prognosis Among Patients Admitted in a Brazilian Hospital. Braz J Infect Dis. 1997; 1:31–5.
12. Marinho J, Galvao-Castro B, Rodrigues LC, Barreto ML. Increased risk of tuberculosis with human T-lymphotropic virus-1 infection: A case-control study. J Acquir Immune Defic Syndr. 2005; 40: 625–8.
13. Porto AF, Santos SB, Muniz AL, Basilio V, Rodrigues W Jr, Neva FA, et al. Helminthic infection down-regulates type 1 immune responses in human T cell lymphotropic virus type 1 (HTLV-I) carriers and is more prevalent in HTLV-I carriers than in patients with HTLV-I-associated myelopathy/tropical spastic paraparesis. J Infect Dis. 2005; 191:612–8.
14. Atsumi E, Yara S, Higa F, Hirata T, Haranaga S, Tateyama M, et al. Influence of human T lymphotropic virus type I infection on the etiology of community-acquired pneumonia. Intern Med. 2008; 48:959-65.
15. Kimura I, Tsubota T, Tada S, Sogawa J. Presence of antibodies against adult T cell leukemia antigen in the patients with chronic respiratory diseases. Acta Med Okayama. 1986; 40:281-284.
16. Norrgren HR, Bamba S, Larsen O, Da silva Z, Aaby P, Koivula T, et al. Increased prevalence of HTLV-I in patients with pulmonary tuberculosis coinfected with HIV, but not in HIV-negat patients with tuberculosis. J Acquir Immune Defic syndr. 2008; 48:607-10.
17. Porto AF, Santos SB, Alcantara L, Guerreiro JB, Passos J, Gonzalez T, et al. HTLV-I modifies the clinical and immunological response to schistosomiasis. Clin Exp Immunol. 2004; 137: 424-9.
18. Verdonck K, Gonzalez E, Henostroza G, Nabeta P, Lanos F. HTLV-I infection is frequent among out patients with pulmonary tuberculosis in Northern Lima, Peru. Int J Tuberc Lung Dis. 2007; 11: 1066-72.
19. Matsuzaki T, Otose H, Hashimoto K, Shibata Y, Arimura K, Osame M. Diseases among men living in human T-lymphotropic virus type1 endemic areas in Japan. Intern Med. 1993;32:623-8.