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Predictors of Tuberculosis in HIV/AIDS Patients Referred to Behavioral Diseases Consultation Center: A Registry-Based Study in Abadan, Southwest of Iran

Salman Khazaei,[1] Leila Molaeipoor,[2] Shahab Rezaeian,[3] Erfan Ayubi,[4,5] Mehran Yari,[6,*] Ali Asghar Valipour,[6] and Somayeh Khazaei[7]

[1]Department of Epidemiology, School of Public Health, Hamadan University of Medical Sciences, Hamadan, Iran
[2]Department of Epidemiology, Pasteur Institute of Iran, Tehran, Iran
[3]Social Determinant of Health Research Center, Kurdistan University of Medical Sciences, Sanandaj, Iran
[4]Department of Epidemiology, School of Public Health, Shahid Beheshti University of Medical Sciences, Tehran, Iran
[5]Department of Epidemiology and Biostatistics, School of Public Health, Tehran University of Medical Sciences, Tehran, Iran
[6]Student Research Committee, Abadan School of Medical Sciences, Abadan, Iran
[7]Department of Operating Room, Rafsanjan University of Medical Sciences, Rafsanjan, IR Iran

[*]*Corresponding author*: Mehran Yari, Student Research Committee, Abadan School of Medical Sciences, Abadan, Iran. Tel: +98-9379849441, E-mail: yari.mehran2020@gmail.com

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Abstract

Background: In the world, it is estimated that 36.9 million people are living with HIV (PLHIV). Tuberculosis (TB) remains as the leading cause of death among PLHIV. This study aimed to determine the predictors of TB among HIV positive patients.
Methods: This cross-sectional study was based on the data from 366 patients with HIV/AIDS acquired from 2010 to 2013 in Abadan and Khorramshahr cities, southwest of Iran. Demographic and clinical data were obtained from patients' medical records in Abadan and Khorramshahr triangular clinics. Univariate and multivariable binary logistic regression models were used to identify TB predictors among HIV/AIDS patients.
Results: The prevalence of TB patients was 21.9% among HIV patients. About 57.4% of the patients were below 35 years of age, and most of them (85.5%) were male. Univariate logistic regression showed a statistically significant association between the occurrence of TB and explanatory variables including sex, imprisonment history, HCV and HBV status, addiction, stage of disease, CD4 cell and TLC (Total lymphocyte count) count. In multivariate analysis, being addicted (adjusted OR = 7.03, 95% CI: 1.28, 38.66) and positive HBV (adjusted OR = 4.28, 95% CI: 1.53, 12.00) were associated with incidence of TB after adjusting for age, sex, phase at diagnosis, addiction and HBV status.
Conclusions: Addiction and HBV infection can be considered as predictors of incidence of TB in HIV/AIDS patients then early diagnosis of TB especially in higher-risk groups, such as those with addiction and HBV infection is recommended.

Keywords: Predictors, Tuberculosis, HIV/AIDS, Cross-Sectional Study, Iran

1. Background

In 2014, it was estimated that 36.9 million people are living with HIV (PLHIV) in the world (1). In some part of the world, the prevalence of PLHIV continues to increase as result of availability of anti-retroviral drugs (1). The statistics showed that nearly 2 million people were newly infected with HIV and 1.2 million people died due to AIDS-related diseases annually (1).

In 2014, 9.6 million new cases of tuberculosis (TB) were estimated globally, whereas 1.2 million of them were occurred among PLHIV (2). It is estimated that the risk of developing TB is 26 to 31 times higher in PLHIVs than people without HIV infection (2). TB remains the leading cause of death among PLHIVs, so that around one in three AIDS-related deaths attributed to TB (3). In contrast, HIV infection is also a main risk factor for TB, by promoting of latent infections of TB and increasing the rate of recurrence of TB. The interaction between TB and HIV has become a public health challenge worldwide (4). In many countries with low healthcare resources, the rate of TB has increased 5 to 10 fold after identification of HIV, also the prevalence of HIV infection among newly diagnosed TB patients is more than 80% (5). HIV epidemic in the Sub-Saharan African countries is known as a cause for inefficiency of TB programs (6).

The risk of developing active TB in HIV patients increases from 5 to 15% annually due to reactivation of latent infection (7). Based on the results from previous studies, risk of TB acquisition is two times higher at the time of HIV seroconversion so that, it have a positive association with declining CD4+ cell count (8). In contrast, the risk of TB decreases during effective anti-retroviral therapy (HAART) but it never reached to the level of risk in general population (9).

2. Objectives

Limited studies investigated the risk factors of HIV/TB co-infected patients in Iran. Therefore, we conducted this study to determine possible predictors of developing TB in PLHIVs.

3. Methods

This cross-sectional study was conducted in Abadan and Khorramshahr, the south west of Iran, from 2010 to 2013 with enrolling 366 patients with HIV/AIDS. The study subjects are restricted to those who are living in Abadan and Khorramshahr cities. Demographic and clinical data were obtained from patients' medical records in Abadan and Khorramshahr triangular clinics.

According to the national protocol, a case of HIV considered a patient by two sequential enzyme-linked immunosorbent assay (ELISA) tests positive for HIV antibody and confirmation by a Western blot test (10). A case of AIDS was defined as a presumptive or definitive diagnosis of stage 3 or stage 4 condition and/or CD4 count < 200 per mm^3 of blood in an HIV-infected subject (11). TB diagnosis was based on the national protocols for the diagnosis of TB (12).

Data collectionform was a checklist including demographic information (sex, location area, age, marital status, prison history and job), mode of HIV transmission (injection drug users (IDUs), sexual, mother to child, unknown), and the clinical features (first CD4 cell and TLC count, AIDS stage based on what was proposed by the world health organization (WHO) staging system (13), from stages 1 to 3 are considered as non AIDS and stage 4 as AIDS, reason of death (if any) and receiving highly active anti-retroviral therapy (HAART), co-infection with TB (extra- and pulmonary TB cases), status of HBV and HCV morbidity.

Chi-square test was used to assess the association between the HIV only infected patients and those with TB/HIV co-infected and categorical explanatory variables. Univariate and multivariable binary logistic regression models were used to identify TB predictors among HIV/AIDS patients.

Data were analyzed at 0.05 significance levels using the statistical software, Stata 11 (StataCorp, College Station, TX, USA).

4. Results

A total of 366 HIV/AIDS positive patients with medical records were enrolled in the study. The number (%) of TB among HIV/AIDS patients was 80 (21.9%). All of TB/HIV co-infected patients had received anti-TB treatment. 57.4% of the patients were under 35 years of age, and 85.5% were male. Co-morbidity of HCV and HBV infection among TB/HIV were 36.51% and 55%, respectively. In addition, the percentage of addicted people in TB/HIV patients was 26.44%. Other demographic and clinical characteristics in patients with HIV alone and TB/HIV co-infected are shown in details in Table 1.

Table 2 presents the determinants of TB among HIV/AIDS positive patients. In univariate logistic regression, there was a statistically significant association between sex, imprisonment history, HCV and HBV status, addiction, stage of disease, CD4 cell and TLC count and TB among the patients ($P < 0.05$). In multivariate analysis, being addicted (adjusted OR = 7.03, 95% CI: 1.28, 38.66) and positive HBV (adjusted OR = 4.28, 95% CI: 1.53, 12.00) were associated with incident of TB after adjusting for age, sex, phase at diagnosis, addiction and HBV status.

5. Discussion

In this study, the role of several important predictors of TB in HIV positive patients was examined. Totally, the prevalence of TB patients in the study population was 21.9 percent. Our findings showed that co-infection with hepatitis B and drug abuse can dramatically increases the risk of TB in HIV/AIDS patients. In univariate model, male gender, history of imprisonment, co-morbidity with hepatitis C, stage of disease, CD4 cell count and TLC were statistically significant and associated with the incident of TB while in multivariable analysis the significant association was found for addiction and HBV infection after adjusting for confounder variables.

WHO have declared that drug abuse is an important factor associated with an increased risk of TB among HIV positive patients (14). On the other hand, previous studies have shown that patients with TB that had a history of drug use compared to non-addicts people were more likely prone to acquire AIDS (15, 16). Multivariate regression analysis in this study revealed that drug abuse can be an important risk factor for incidence of TB in HIV positive patients.

The odds of acquiring TB infection was 3.48 and 4.9 times higher for co-infected HCV/HIV and HBV/HIV patients

Table 1. Demographic and Clinical Characteristics Distribution Among HIV and TB/HIV Co-Infected Patients in Abadan and Khorramshahr cities, Iran (2010 - 2013)

Variable	Total	HIV		TB/HIV Co-Infected		P Value
		Number (286)	Percent (78.1)	Number (80)	Percent (21.9)	
Gender						0.002[a]
Male	313	236	75.40	77	24.60	
Female	53	50	94.34	3	5.66	
Age group, y						0.370
0 - 14	3	3	100.00	0	0.00	
15 - 34	207	167	80.68	40	19.32	
35 - 54	150	112	74.67	38	25.33	
55+	6	4	66.67	2	33.33	
Marital status						0.608
Single	168	128	76.19	40	23.81	
Married	110	84	76.36	26	23.64	
Divorce	70	58	82.86	12	17.14	
Widow	18	16	88.89	2	11.11	
Way of transmission						0.015[a]
IDUs[b]	269	202	75.09	67	24.91	
Illegal sexual	62	49	79.03	13	20.97	
From husband	33	33	100.00	0	0.00	
Occupational exposure	2	2	100	0	00.00	
Addiction status						< 0.001[a]
Yes	295	217	73.56	78	26.44	
No	71	69	97.18	2	2.82	
Imprisonment history						0.001[a]
Yes	250	183	73.20	67	26.80	
No	116	103	88.79	13	11.21	
HCV[c] status						< 0.001[a]
Yes	126	80	63.49	46	36.51	
No	240	206	85.83	34	14.17	
HBV[d] status						< 0.001[a]
Yes	20	9	45.00	11	55.00	
No	346	277	80.06	69	19.94	
Stage of disease						< 0.001[a]
HIV	225	203	90.22	22	9.78	
AIDS	141	83	58.87	58	41.38	
Type of TB						
Extra-pulmonary	17	-	-	17	21.3	-
Pulmonary	63	-	-	63	78.7	

[a] $P < 0.05$.
[b] Injecting drug users.
[c] Hepatitis C virus.
[d] Hepatitis B virus.

Table 2. Prognostic Factors of Tuberculosis Among HIV/AIDS Positive Patients in Abadan and Khorramshahr cities, Iran (2010 - 2013)

Variable	Unadjusted OR	95% CI	P Value	Adjusted OR[a]	95% CI	P Value
Gender						
Female	References			References		
Male	5.43	1.65, 17.9	0.005[b]	1.53	0.26, 8.88	0.637
Addiction status						
No	References			References		
Yes	12.4	2.96, 51.7	0.001[b]	7.03	1.28, 38.66	0.025[b]
Imprisonment history						
No	References			References		
Yes	2.9	1.53, 5.5	0.001[b]	NM[c]		
HCV status						
No	References			References		
Yes	3.48	2.08, 5.81	< 0.001[b]	NM		
HBV status						
No	References			References		
Yes	4.9	1.96, 12.3	0.001[b]	4.28	1.53, 12.00	0.006[b]
Stage of disease						
HIV	References			References		
AIDS	6.44	3.7, 11.21	< 0.001[b]	NM		
CD4 cell count (per 10 unit)	0.96	0.94, 099	0.007[b]	1.01	0.99, 1.03	0.270
TLC[d] (per 100 unit)	0.96	0.93, 0.99	0.046[b]	NM		

[a] Adjusted for age, sex, phase at diagnosis, addiction and HBV status.
[b] The bold indicates P < 0.05.
[c] NM: not measured due to colinearity with other variables.
[d] Total lymphocyte count.

respectively compared to those with HIV alone. Hepatitis B and C are two common and routine infections among HIV positive patients (17). Viral infections are an important cause of morbidity and mortality among IDUs (18). An HCV and HBV infection affects various aspects of natural history of HIV, for example it is suggested that serious infection of the liver can reduce ability to tolerate anti-retroviral drugs (ART) in patients with AIDS (19-21). Therefore, suppression of immune system can provide susceptibility for opportunistic infections such as TB.

The present study in line with previous studies showed that the high number of CD4 cells can reduce the chances of TB infection in HIV positive patients (22-24). There is no specific cut off point for CD4 cells in the literatures. However there is a clear inverse correlation between the number of CD4 cells and the risk of opportunistic infections and death (25, 26). In a study by Crump et al., the patients with lower CD4 count were at risk for TB infection (27).

There is inconsistent evidence regarding the association between gender and incidence of TB among HIV positive patients so that some studies were endorsed this association (22, 23, 28), while this association was not found in other studies (24). In Nakiyingi et al. study (29), male gender had increased odds of mycobacteremia among HIV-infected and sputum smear-negative patients after controlling for other variables (Adjusted OR = 3.4). Gender disparity in occurrence of TB (30) and other health related indicators (31) has been reported, one reason for this disparity may be because men have the poorer health seeking behavior than women.

Prisoners are often neglected populations and both of TB and HIV is frequent among them because appropriate preventive and treatment interventions in prisons are less available. Inadequate health services could lead to increase of drug-resistance in TB patients, TB/HIV co-infection, HIV virus and other sexually transmitted diseases. High prevalence of high-risk behavior, intravenous drug abuse, population density, long and close contact, malnutrition, poor sanitation and lack of access to appropriate healthcare in prisons are predisposing factors for morbidity and the spread of TB/HIV coinfection (32-34). More than one quarter of the people with history of imprisonment in this study were co-infected with TB and HIV, while the prevalence of co-morbidity in patients without history of imprisonment was 11.21 percent. Also results of univariate logistic regression showed that people with a history of imprisonment approximately are at risk of TB three times higher than others.

Like other observational studies, some limitations should be considered when interpreting the finding. The obtained data was based on recorded information in the medical records of patients who were referred to behavioral diseases consultation center. So accuracy of the findings of this study depends on the accuracy of the registered information. Therefore, information bias may be occurred in the registered data. Moreover, the result can be accompanied with degree of reporting bias.

5.1. Conclusion

Addiction and HBV infection can be considered as important predictors among HIV/AIDS patients. Further longitudinal studies with efficient sample size are recommended to clarify the validity of predictors of TB among HIV/AIDS patients.

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Footnote

Authors' Contribution: All authors contributed equally and participated in the analysis and interpretation. All authors critically reviewed, refined and approved the manuscript.

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