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Prevalence and the Risk Factors Associated with HIV-TB co-infection in Kermanshah Province, Iran: Trends between 2005 and 2021

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ABSTRACT

Introduction: The problem of TB has been found to be worsened by HIV/AIDS, as people with HIV have a much higher risk of developing active TB. HIV and TB co-infection has been introduced as a fatal combination, as each disease speeds up the other's progress. Surveys in various countries have indicated that the HIV prevalence among TB patients is much higher than that observed in the general population. This study was designed to assess prevalence of TB/HIV co-infection and to determine its factors.

Material and Methods: This cross-sectional study was conducted in Kermanshah Province, in the west of Iran, from March 2005 to December 2021. The study population included all TB-positive patients who had healthcare records in the Tuberculosis and Lung Disease Center of the province. TB was routinely diagnosed by the positive sputum smear (Ziehel-Neelsen) and confirmed by taking GeneXpert as the reference investigation. Primary HIV infection was diagnosed by the enzyme linked immunosorbent assay (ELISA). Plus, positive ELISA results were then confirmed by real-time polymerase chain reaction (RT-PCR).

Results: Of 2569 TB patients, 366 were reported HIV–TB co-infection, which indicates 14.2% prevalence in this sample. It can be seen that there is a 13.6 ratio for the male-to-female. The risk of HIV infection for male was 2.84 times more than that in female. There was a statistically significant increase in risk of HIV infection for those who had pulmonary TB (OR = 2.29, 95% CI [1.46-2.94]). Patient with age between 0–15 years old (OR = 0.17, 95% CI [0.05-0.21]), 45–60 years old (OR = 0.14, 95% CI [0.04-0.19]), and ≥ 60 years old (OR = 0.09, 95% CI [0.01-0.13]) were all statistically significant for lower risk of HIV infection. Urban cases (OR = 2.48, 95% CI [1.89-3.73]) share a higher risk in HIV infection.

Conclusion: TB/HIV control programs that educate people on the prevalence and focus on these subgroups are likely to decrease the joint burden of TB and HIV.

Introduction

Mycobacterium tuberculosis (TB) is endemic in many parts of the world, including developing countries. It is usually present as latent TB infection (LTBI) and

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sometimes active TB disease (ATBD)(1). However, its incidence and prevalence has increased during recent years as a result of increased immunosuppressed states in the community. TB is most common among patients with cell-mediated immune deficiency, including those undergoing chemotherapy, immunosuppressive therapy for transplant or individuals who are infected with human immunodeficiency virus (HIV)(2-4); among these high risk groups, HIV-infected patients are at the highest risk of developing active TB infection. More than one-third of the HIV-infected world population are involved with tuberculosis(5). The significance of HIV-TB co-infection is the altered features of TB infection in the settings of HIV infection especially in advanced stages, which poses significant diagnostic and therapeutic challenges; TB may present with atypical or unusual manifestations in HIV positive individuals, especially in the late stage of HIV infection; non-cavitary pulmonary involvement, lung lower lobe infiltrates, pleural effusion and hilar lymphadenopathy are more common in HIV-associated pulmonary TB compared with non-HIV associated one(6, 7). Moreover, HIV-infected patients, particularly those in the acquired immunodeficiency syndrome (AIDS) phase, are more prone to develop extra pulmonary tuberculosis, compared with the general population (8-10). On the other hand, the risk of LTBI progression to ATBD is highly increased in HIV-infected patients, particularly those with advanced immunosuppression. Furthermore, both HIV and TB infections are important health threats for the general population especially those in the underdeveloped and developing nations, added to the fact that HIV and TB potentiate each other leading to increased morbidity and mortality(11, 12). Immune reconstitution inflammatory syndrome (IRIS) is another important issue that should be contemplated in HIV-TB co-infected patients who are candidates for antiretroviral therapy (ART) (13).

Being aware of the incidence and prevalence of HIV-TB co-infection in the community and the associated features and also understanding the predictors of HIV-TB co-infections can help us in planning programs in order to early detect and manage the co-infected patients and, more importantly, prevent this situation. Hence, the aim of this study was to investigate the epidemiological and demographic characteristics and clinical manifestations of patients with HIV-TB co-infection in Kermanshah, Iran.

Methods

Setting and Study design

This cross-sectional study was conducted in Kermanshah Province, in the west of Iran, from March 2005 to December 2021. The study population included all TB-positive patients who had healthcare records in the Tuberculosis and Lung Disease Center of the province. Kermanshah province, as a Kurdish region, includes 14 cities and a population of 1,997,864 people. In this province, there are 87 health centers (61 in rural and 26 in urban areas) and 631 health houses. During the 12-year study period, 2569 TB-positive patients reported. The cases were from the different parts of the province in both urban and rural areas.

Diagnosis of TB and HIV infections

TB was routinely diagnosed by the positive sputum smear (Ziehel-Neelsen) and confirmed by taking GeneXpert as the reference investigation. Primary HIV infection was diagnosed by the enzyme linked immunosorbent assay (ELISA). Plus, positive ELISA results were then confirmed by real-time polymerase chain reaction (RT-PCR).

Instrument used for data collection

Data were extracted from primary healthcare records available at the province health center. Moreover, data was collected using a researcher-developed questionnaire by a general physician. The questionnaire included data on age, gender, residence, type of TB, and etc.

Data Analysis

Data analysis was performed using the

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statistical package for social sciences (SPSS), version 26. Normally distributed variables (e.g., age and gestational age) were described using mean ± standard deviation (μ±SD). Otherwise, qualitative variables were reported as frequencies and percentages.

Ethics

The Research Ethics Committee at Deputy of Research of the Kermanshah University of Medical Sciences (KUMS) had approved the study protocol and had monitored the research process (ethics code IR.KUMS.REC.1401. 528). Further, individual personal information was kept confidential.

Results

Baseline demographic characteristics of TB stratified by time categories are presented in Table 1. The number of male was more than that of female in any given year. A significant share of TB infections happened among adults≥60 (29.4%) and those between 30-45 years old (around 31.3%) respectively. Urban region accounted for 88.5% of total TB cases, and rural region accounted for 11.5%.

Table 2 showed demographic characteristics of TB/HIV co-infection cases in Kermanshah province from 2005 to 2021. Of 2569 TB patients, 366 were reported HIV–TB co-infection, which indicates 14.2% prevalence in this sample. It can be seen that there is a 13.6 ratio for the male-to-female. The 366 TB/HIV co-infection cases were composed of 153 (41.8%) in 2005 to 2009, 123 (33.6%) in 2010 to 2014 and 90 (24.6%) in 2015 to 2021. 3 cases (0.8%) were aged 0–15 years old, 41 (11.2%) 15-30 years old, 256 (69.9%) 30–45 years old, 62 (16.9%) 45-60 years old and 4 (1.1%) over 65 years old. The number of rural region cases (5.5%) was always less than that of urban region cases (94.5%) in any given year.

Table 1. the characteristics of TB epidemic in Kermanshah province, Iran from 2005 to 2021.

Characteristics		Total (n=2569)	2005-2009 (n= 919)	2010-2014 (n= 904)	2015-2021 (n= 746)
Gender	Male	1490(58.0)	572(62.2)	494(54.7)	424(56.8)
	Female	1079(42.0)	347(37.8)	410(45.3)	322(43.2)
Age	0-15	71(2.8)	29(3.2)	27(3.0)	15(2.1)
	15-30	394(15.3)	182(19.8)	143(15.8)	69(9.2)
	30-45	803(31.3)	316(34.4)	310(34.3)	177(23.7)
	45-60	546(21.2)	167(18.2)	181(20.0)	198(26.5)
	60≤	755(29.4)	225(24.5)	243(26.9)	287(38.5)
Prison History	Yes	103(4.0)	60(60.5)	31(3.4)	12(1.6)
	No	2466(96.0)	859(93.5)	873(96.6)	734(98.4)
Region	Rural	295(11.5)	105(11.4)	106(11.7)	83(11.1)
	Urban	2274(88.5)	814(88.6)	798(88.3)	663(88.9)
Type of TB	Pulmonary	1750(68.1)	627(68.2)	583(64.5)	540(72.4)
	Extra Pulmonary	819(31.9)	292(31.8)	321(35.5)	206(27.6)

Table 2. the characteristics of TB/HIV co-Infection epidemic in Kermanshah province, Iran from 2005 to 2021.

Characteristics		Total (n=366)	2005-2009 (n=153)	2010-2014 (n=123)	2015-2021 (n=90)
Gender	Male	341(93.2)	149(97.4)	114(92.7)	78(86.7)
	Female	25(6.8)	4(2.6)	9(7.3)	12(13.3)
Age	0-15	3(0.8)	1(0.7)	0(0)	2(2.2)
	15-30	41(11.2)	28(13.3)	9(7.3)	4(4.4)
	30-45	256(69.9)	107(69.9)	99(80.5)	50(55.6)
	45-60	62(16.9)	16(10.5)	14(11.4)	32(35.6)
	60≤	4(1.1)	1(0.6)	1(0.8)	2(2.2)
Prison History	Yes	34(9.3)	18(11.8)	12(9.8)	4(4.4)
	No	332(90.7)	135(88.2)	111(90.2)	86(95.6)
Region	Rural	20(5.5)	6(3.9)	6(4.9)	8(8.9)
	Urban	346(94.5)	147(96.1)	117(95.1)	82(91.1)
Type of TB	Pulmonary	278(76.0)	119(77.8)	86(69.9)	73(81.1)
	Extra Pulmonary	88(24.0)	34(22.2)	37(30.1)	17(18.9)

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Table 3 illustrated the possible risk factors for HIV in HIV/TB co-infected patients. The risk of HIV infection for male was 2.84 times more than that in female. There was a statistically significant increase in risk of HIV infection for those who had pulmonary TB (OR = 2.29, 95% CI [1.46-2.94]). Patient with age between 0–15 years old (OR = 0.17, 95% CI [0.05-0.21]), 45–60 years old (OR = 0.14, 95% CI [0.04-0.19]), and ≥ 60 years old (OR = 0.09, 95% CI [0.01-0.13]) were all statistically significant for lower risk of HIV infection. Urban cases (OR = 2.48, 95% CI [1.89-3.73]) share a higher risk in HIV infection.

Table 3. regression analysis of possible risk factors for HIV in HIV/TB co-infected patients.

Characteristics		OR(95% CI)	P-value
Gender	Male	2.84(1.65-3.81)	0.001
	Female	1	-
Age	0-15	0.17 (0.05-0.21)	0.001
	15-30	1.24(0.92-1.86)	0.187
	30-45	1	-
	45-60	0.14(0.04-0.19)	0.001
	60≤	0.09(0.01-0.13)	0.001
Prison History	Yes	1.08(0.39-1.54)	0.503
	No	1	-
Region	Rural	1	-
	Urban	2.48(1.89-3.73)	0.001
Type of TB	Pulmonary	2.29(1.46-2.94)	0.002
	Extra Pulmonary	1	-

Discussion

Globally, the problem of TB has been found to be worsened by HIV/AIDS, as people with HIV have a much higher risk of developing active TB. HIV and TB co-infection has been introduced as a fatal combination, as each disease speeds up the other's progress. Surveys in various countries have indicated that the HIV prevalence among TB patients is much higher than that observed in the general population (14). This study aimed at drawing out the profile of individuals with dual infection of HIV–TB. A total 2569 TB patients reported in the Kermanshah province, between 2005 and 2021. Of them, 366 were reported HIV–TB co-infection, which indicates 14.2% prevalence in this sample. Our findings are similar to those reported by Sebastião et al. in Angola (12%) (15), Chen et al. (13.7%) in China (16), and Bjerrum et al. (13%) in Ghana (17). Ugwu et al. from Nigeria illustrated that the prevalence of HIV among the TB patients was 20.3% (18). Besides, the pooled prevalence of TB / HIV co-infection in studies conducted in China, India and Brazil was 23.5%, 18.9% and 19%, respectively (19-21). A study conducted by Dirie et al. reported that the prevalence of HIV infection among the TB cases in Somalia was 1.5% (22). A cross-sectional survey which was done in Zambia found that 23.8% of TB patients were HIV positive (23). In Eastern India, a cross-sectional study showed that the HIV prevalence among TB patients was reaching up to 12.3% in a 10-year period (24). The possible reasons for variation in TB/HIV co-infection prevalence across the world may be due to difference in study settings, sample size, diagnosis facility, HIV infection rate, study area and study time.

There was a decreasing trend in HIV–TB co-infection prevalence from 41.8% in 2005 to 2009 to 24.6% in 2015 to 2021. This change might be the result of improvements in public awareness and better treatment regimes, moreover indicates that governments have paid more attention to this issue.

Our finding demonstrated that the prevalence of co-infection has been reported to be higher among males than females. Moreover, the most affected age group in this study comprised patients aged 30–45 years. This may be due to that people in 30–45 years would be sexually active comparing with

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other age group, increasing the chances of an individual's risky sexual behavior. Manjareeka et al. have found significantly higher numbers of male with HIV–TB co-infection than females and also they showed the most affected age group was 30–45 years (24). Moreover, Wei et al., Peierdun MIJITI et al. (25), Li WG et al. (26), and Zhang Y et al. (27) illustrated that TB patients aged 30–45 had higher risk of HIV infection than other age groups, which is in accord with the our conclusion. In a study conducted by Kumar P et al., they had reported a very high male to female ratio of 9:1 for TB/HIV co- infection (28). Conversely, Idowu et al. reported that more females than males had been infected with TB/HIV co- infection (29).

Our results indicate that HIV prevalence present more prominently in patients with pulmonary TB. In line with our findings, Jain et al. (30), Ahmad et al. (31), and Susheel et al. (32) reported that HIV prevalence was more common in patients with pulmonary TB. Tiewsoh et al. (33), Kamath et al. (20) and even Shastri et al. (34) had reported that majority of TB/HIV co-infected were diagnosed with pulmonary TB. In contrast, Manjareeka et al. (24), Patel et al. (35), and Sharma et al. (36) have observed that HIV prevalence is more prominent in extra pulmonary TB patients. They believed that as HIV-related immune-suppression increases, the clinical pattern of TB changes, with an increasing number of extra pulmonary TB cases.

Our results demonstrated that male (OR: 2.84, p=0.001), those suffering from pulmonary TB (OR: 2.29, p=0.002), and living in urbanized areas (OR: 2.48, p=0.001) had a higher risk of HIV/TB co-infection. Plus, patient with age between 0–15 years old (OR = 0.17, p=0.001), 45–60 years old (OR = 0.14, p=0.001), and ≥ 60 years old (OR = 0.09, p=0.001) were all significantly at lower risk of HIV/TB co-infection. Sebastião et al. found that patients over 30 years of age (OR: 4.13, p=0.072), female (OR: 1.08, p=0.898), and living in urbanized areas (OR: 1.90, p=0.578) had a higher risk of HIV/TB co-infection (15). Datiko et al. from Ethiopia, indicated that TB patients over 35 years of age (OR: 7.10, p=0.001) and living in urbanized areas (OR: 1.77, p=0.001) also had a higher risk of co-infection (37). In contrast, Chen et al. (16) and Sebastião et al. (15) found no difference in the rate of HIV infection between the different types of TB.

Our results have some limitations that must be considered. Firstly, the stage of HIV infection, viral load, and/or CD4/CD8 cell count was not described. Secondly, the impact of HIV/TB co-infection on clinical outcome was not presented. Finally, the nature of the study design (cross-sectional) did not allow further evaluation of any apparent associations over time.

Conclusion

In this study the prevalence of TB/HIV co-infection was high (14.2%). The risk of TB/HIV occurrence was found to be high among male, those aged between 15-45 years, who had pulmonary TB and urban residence. TB/HIV control programs that educate people on the prevalence and focus on these subgroups are likely to decrease the joint burden of TB and HIV.

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Conflicts of interest

The authors declare no conflict of interest.

Authors' contributions

All authors were involved in the conception and design, analysis and interpretation of the data, drafting of the manuscript and revising it critically for intellectual content, approved the final version for submission, and agreed to be accountable for all aspects of the work.

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