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Prevalence of HIV among newly diagnosed tuberculosis patients in Erbil Governorate, Iraq

Zakarea Abdullah Yaseen Al-khayat[1]*, Nabaz Fisal Shakir Agha[2], Pshtiwan Dhahir Majeed[3], Kawthar Ibrahim Fatah Alharmni[4], Derin Nabaz Fisal Agha[5]

[1] Department of Microbiology, College of Medicine, Hawler Medical University, Erbil, Iraq.
[2] Department of Anesthesia, Erbil polytechnic university, Erbil Medical Technical Institute, Iraq.
[3] Department of Nursing, Erbil polytechnic university, Erbil Medical Technical Institute, Iraq.
[4] Department of Anatomy & Histology, College of Medicine, Hawler Medical University, Erbil, Iraq.
[5] Department of Pharmacology, Erbil polytechnic university, Erbil Medical Technical Institute, Iraq.
*Correspondence to: Zakarea Abdullah Yaseen Al-khayat (E-mail: dr_zakarea@yahoo.co.uk)
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Abstract

Objective This study was accomplished with a purpose to determine the sociodemographic profile and the prevalence of HIV among tuberculosis (TB) patients.

Methods This prospective study was carried out in the Department of Microbiology at the Chest and Respiratory Disease Specialized Centre in Erbil City (In collaboration with the Specialist physician) through a period from January 2017 to December 2019. New TB patients were interviewed on a predesigned questionnaire. Collected samples were processed in a special laboratory in TB center. The samples were subjected to microscopy with Ziehl–Neelsen staining and inoculated on solid medium; the third sputum sample was tested directly by GeneXpert test. HIV testing was done using screening test and if the screening result was positive, the diagnosis was confirmed by Western Blot.

Results A total of 397 approved new TB patients underwent HIV testing. Among them, 41 cases (10.3%) were found to be positive on ELISA screening, and subsequently they were all confirmed by the Western Blot test. The highest prevalence of HIV positivity according to gender, age range, and occupation, were as follows: male (29; 70.7%), 30–42 years (21; 51.2%), laborers (13; 31.7%) respectively. The male to female ration is 2.7 statistically, the differences of distribution of the HIV positivity concerning the above-mentioned demography were as follows: gender: significant ($P \leq 0.05$), age range: not significant, occupation: not significant. The highest prevalence of HIV positivity was among pulmonary TB (25; 61%). Rifampicin resistant prevalence was higher among HIV positive in comparison to HIV negative TB case (23; 56.1%) (134; 37.4%), respectively. Statistically, the differences of distribution of the HIV positivity in relation to both TB pattern & rifampicin monodrug resistant were significant ($P \leq 0.05$).

Conclusions The prevalence of HIV infection in TB patients in current study was 10.3%. If HIV testing was done for all TB patients, then routine reporting of HIV status for all TB patients would provide even better information which may provide a base to future planning.

Keywords HIV prevalence, Tuberculosis, Erbil, Sociodemographic determinants, Rifampicin resistance.

Introduction

Tuberculosis (TB) is a paramount reason of morbidity and is amongst the peak 10 causes of death universally, standing over HIV as a sole infectious cause of death.[1] Based on speculation from 2017, there were 10 million TB cases and 1.6 million TB-linked deaths worldwide, despite of a 2% incline in incidence proportion per annum in recent years.[1] According to the World Health Organization (WHO), in 2019, 770,000 persons had passed away from HIV. An estimated third of these deaths were pertained to TB.[2] HIV and TB are well known as a syndemic which is clarified as "the concourse of two or more diseases that perform in an interactive pattern to aggrandize the encumbrance of disease".[3]

Al-Salihy[4] concluded that Iraq had been classified as a low-prevalence HIV epidemic, with a low number of formally reported cases (0.1% of the total population). The first case was announced in 1986 among hemophilic patients who had received contaminated blood products. Furthermore, the cumulative number of HIV/AIDS registered cases from 1986 up to 2011 was 306. Among the registered cases, 85% were male and the most common mode of transmission (66%) was via imported blood products, 17% by heterosexual route, and 5% by vertical transmission from infected mother. No cases of transmission due to homosexual or drug addicts were reported. Since 2003, the transmission mode shifted towards the heterosexual route, as the government adopted strict measures to ensure blood safety.

Today, TB continues to be the main infectious reason of death in people with HIV, who are probably 15–22 times more likely to be infected with TB than people without.[5] Presently, the Center for Disease Control and Prevention (CDC) advises that all patients with active or latent TB be checked for HIV because HIV is a quite-recognized stimulator of hidden TB.[6] Nearly one-quarter of the universal inhabitance is appraised to be latently infected with *Mycobacterium tuberculosis* (Mtb) also referred to as latent tuberculosis (LTBI).[7] A person with LTBI has an Mtb infection, but the bacteria continues to be recumbent and ineffectual within the host's body with no clinical markers.[8] In HIV negative patients, a latent TB infection has a 10% chance of proceeding into an active infection throughout a lifetime. However, this jeopardy is considerably boosted in HIV positive patients and it progressively magnifies as immune function descends.[9] Individuals with HIV and TB also have the potency to impact the health of HIV negative individuals because the brisk of LTBI makes Mtb highly infectious.[10] Awareness about the predominance of HIV-positive infection in active TB patients is mandatory, as

it is increasingly being realized that such facts would motivate arranging and may also be pivotal for setting the convenient treatment regime.[11] The significance of HIV monitoring in TB patients is increasingly being recognized as the HIV epidemic keeps on to uphold the global TB epidemic.[10] In numerous territories, the HIV dispersal in TB patients is a critical signal of the propagation of HIV into the overall inhabitance. Information about the HIV prevalence in TB patients is indispensable for supplying overall HIV/AIDS attention and assistance, encompassing antiretroviral therapy (ART) to HIV-positive patients.[11,12]

Thus, the objectives of this study were to explore the feasibility of HIV screening among TB patients registered for treatment in a selected TB treatment center in Erbil governorate and to depict the prevalence of HIV amongst TB patients in the research district. In addition, the study also describes various clinical presentations among these co-infected cases.

Materials and methods

Study protocol

This prospective study was carried out in the Department of Microbiology at the Chest and Respiratory Disease Specialized Centre in Erbil City (In collaboration with the Specialist physician) through a period from January 2017 to December 2019. This study was achieved with the cooperation of Prevention Health Department, Erbil Medical Technical Institute, Erbil Polytechnic University, with Departments of: Microbiology, Anatomy & Histology, College of Medicine, Hawler Medical University, Erbil, Iraq.

Moral considerations

This study was confirmed by: the Ethics Committee of Hawler Medical University, Erbil; the Committee of Erbil Medical Technical Institute, Erbil Polytechnic University, Iraq; Health Directorate of Erbil. Acquainted endorsement was possessed from each patient. The patients were aware of study's goals and they could regress thereof if they wished so to do.

Study population

In the current study, all newly approved cases of TB (18 years of age and above) who were inhabitants of Erbil governorate were embroiled during the study period. All TB patients who conferred agreement for HIV testing (after pretest counseling) in the in- and outpatient wards of the Department of Medicine were involved in the study. Using a structured, pre-tested questionnaire including all personal information, such as age, gender, socioeconomic background, education level, profession, sexual preferences and promiscuity, history of past surgery, or blood transfusion were collected by patient interview. Patients receiving or who received anti-TB treatment in the previous month and non-consenting patients were excluded from this study. In addition, cases on ART who were attending the hospital for follow-up were also excluded.

Sample and diagnostic procedures

Suspected TB patients for collecting specimens were allocated in this study on the basis of presenting symptoms and chest radiography findings. Pulmonary specimens were taken from the sputum. Patients meeting the clinical eligibility criteria were asked to provide three sputum specimens: two spot samples and one obtained in the morning. Extra-pulmonary specimens were taken from pleural fluid, lymph node biopsy, gastrointestinal, cerebrospinal fluid, skin, and genitourinary.

AFB and culture

Collected samples were processed in a special laboratory in TB center, then two of the three samples were randomly selected and processed with *N*-acetylcysteine and sodium hydroxide followed by centrifugation.[13] The samples were resuspended in 1.5 mL of sample buffer and underwent microscopy analysis with Ziehl–Neelsen staining and cultured on solid medium (Löwenstein–Jensen, bioMerieux, France). The third sputum sample was tested directly by GeneXpert test. Solid cultures were considered negative after 42 days of incubation without isolation of any Mycobacteria.[14]

Non-respiratory specimens from closed and normally sterile sites were not decontaminated prior to smear preparation and culture but were concentrated by centrifugation at 3,000*g* for 20 min. Processed specimens from non-sterile sites and centrifuged specimens from sterile sites were directly cultured.[13,14]

GeneXpert assay

The GeneXpert assay was used as previously used.[15] Briefly, the provided buffer was added at a 3:1 ratio to clinical samples. The tubes were mixed manually twice in 15-min period at room temperature before 2 mL of the inactivated material was transferred to the test cartridge. The cartridge was then inserted into the test platform, and the hand on work ended. Then, the machine automatically filtered, washed, and ultrasonically lyzed to release DNA. Real-time PCR amplification and detection were performed in an integrated reaction tube. Primers used for this assay were forward: (CGTGGAGGCGATCACACCGCAGAC) and reverse: (AGCTCCAGCCCGGCACGCTCACGT) (Applied Biosystems). The results were finally read after 1 h 45 min, in which fluorescent signal was measured automatically. Negative or positive and defined susceptible or resistant to rifampin depending on the detection of mutations in *rpoB* gene (MTB-RIF Instructions). The patient confirmed to be infected with TB disease when: bacteriologically or microscopically confirmed pulmonary TB (PTB), i.e., positive culture and/or at least one sputum sample with a positive acid-fast bacillus (AFB) test; AFB positive smear which was a Fluorochrome-stained smear with at least one acid fast bacilli in 40 fields (or Xpert MTB/RIF positive).[7,8]

HIV test

HIV testing was done using KHB (Shanghi Kehua Bioengineering, Ltd, Shanghai, China) as a screening test. If the screening result was positive, the diagnosis was confirmed by Western Blot test (HIVBLOT 2.2, Genelabs Diagnostics, Singapore).

Statistical analysis

The data analysis was performed using descriptive statistics, including frequency, and frequency percentage. Comparisons were made using chi^2 test by using standard equations. The results were announced with $p \leq 0.05$ or $p \leq 0.01$ as the acceptable level of significance.

Results

A total of 1436 TB patients were registered for treatment during the study period. Of the total TB patients, 397 had met the present study criteria mentioned above. The total 397 approved TB patients underwent HIV testing. Among them, 41 cases (10.3%) were found to be positive on ELISA screening, and subsequently they were all confirmed by the Western Blot test. The remaining 356 TB cases were HIV negative.

Table 1 delineates the prevalence of HIV infection among new tuberculosis patients according to age, gender and occupation.

The highest prevalence of HIV positivity according to gender, age range and occupation, were as follows: male (29; 70.7%), 30–42 years (21; 51.2%), laborers (13; 31.7%) respectively. The male to female ration is 2.7. Statistically, the differences of distribution of the HIV positivity concerning the above-mentioned demography were as follows: gender: significant ($P \leq 0.05$), age range: non-significant, occupation: non-significant

Table 2 illustrates TB pattern i.e.: pulmonary and extra pulmonary, and the rifampicin drug resistant among HIV seropositive and seronegative cases. The highest prevalence of HIV positivity was among pulmonary TB (25; 61%). Rifampicin resistant prevalence was higher among HIV positive in comparison to HIV negative TB case (23; 56.1%) (134; 37.4%) respectively. Statistically, the differences of distribution of the HIV positivity in relation to both TB pattern and rifampicin monodrug resistant were significant ($p \leq 0.05$).

Table 1. **Prevalence of HIV infection among new tuberculosis patients in relation to age, gender, occupation.**

Parameters	N	HIV+	(%)	HIV-	(%)
Gender					
Male	223	29	(70.7)	194	(54.5)
Female	174	12	(29.3)	162	(45.5)
Total	397	41	(100)	356	(100)
		$\chi^2 = 3.9373$ df=1, Significant ($P \leq 0.05$)			
Age					
18-30	116	11	(26.8)	105	(29.5)
30-42	177	21	(51.2)	156	(43.8)
>42	104	9	(22)	95	(26.7)
Total	397	41	(100)	356	(100)
		df = 2 NS			
Occupation					
Farmer	71	6	(14.6)	65	(18.3)
Service	83	7	(17.1)	76	(21.3) (clerk/ tailor)
Drivers	79	10	(24.4)	69	(19.4)
Housewives	66	5	(12.2)	61	(17.1)
Laborers	98	13	(31.7)	85	(23.9)
Total	397	41	(100)	356	(100)
		df = 4 NS			

Table 2. **Tuberculosis pattern and Rifampicin status among HIV seropositive & seronegative patients.**

Type of TB	HIV positive	(N)%	HIV negative	(N)%	Total
Pulmonary	25	(61)	269	(75.6)	294
Extra pulmonary	16	(39)	87	(24.4)	103
Total	41	(100)	356	(100)	397
		$\chi^2 = 4.0712$ df = 1, Significant ($P \leq 0.05$)			
Rifampicin					
Sensitive	18	(43.9)	222	(62.4)	240
Resistant	23	(56.1)	134	(37.4)	157
Total	41	(100)	356	(100)	397
		$\chi^2 = 5.2389$ df = 1, Significant ($P \leq 0.05$)			

Discussion

To the best of our knowledge, no published data are available on the prevalence of HIV among newly diagnosed TB patients in Erbil governorate, hence this study can be considered the first study of such quality to deal with and investigate the prevalence, correlated risk factors, and impact of such an infection among these patients. According to the CDC recommendation, HIV screening to be accomplished for all TB patients comprising persons with TB disease, latent TB disease, and persons suspected of having TB and contact to TB patients. Thus, the current study was achieved to define the prevalence of HIV among diagnosed TB patients in Erbil. This study expounds that HIV seroprevalence among TB patients attending the Chest and Respiratory Disease Specialized Centre in Erbil City in Erbil in 2017–2019 was 10.3%. Prevalence rates of HIV TB patients vary internationally.[16] The present prevalence of HIV among TB patients was found to be less than 12%, WHO's estimate of HIV among the world TB patients.[17] The prevalence of TB/ HIV co-infection in India,[18] and Ethiopia[19] were 18.9% and 28.6%, respectively, and were higher than our rates.

In a study carried by van der Werf *et al.* (20), the highest co-infection rates were recorded from Latvia (19.5%), Malta (17.1%), Portugal (14.7%), and Estonia (10.1%). Gao et al[21] performed a systematic review and meta-analysis to determine the prevalence of TB/HIV co-infection by recognizing 47 studies comprising 272,466 persons except China. Their prime findings were that, a high prevalence of TB/HIV co-infection and they deduced that TB/HIV co-infection dispersal was higher among TB patients than among HIV/AIDS patients, but which were not significantly different.

Studies from Sub-Saharan Africa had enrolled those HIV seroprevalence rates of 50–70% in patients with tuberculosis.[16]

Hospital-based HIV seroprevalence studies amongst TB patients from various territories of India had exhibited

a considerable divergences in the prevalence which varied from 0.4% to 28.1% have been reported.[22] Studies performed in various provinces of Brazil had manifested that the prevalence of HIV infection in individuals with tuberculosis varies immensely, i.e., from 0.8% to 30%, pertaining to the location studied and the technique applied.[23] Furthermore, a research by Thanh et al[24] determined fundamental geographical distinctions in HIV prevalence among TB patients.

These enormous diversities in the co-infection rates of TB/HIV across the planet, as declared, can partially be attributed to: under-recording, diagnostic procedures used, discrepancies in TB diagnosis, epidemiology of TB in different nations, and study methodology utilized.[20,23,24]

Table 2 explicates the prevalence of HIV seropositivity in regarding to gender, age, and occupational status.

Like other studies in different developing countries,[17,18,25] the present study declared more prevalence of HIV co-infection amongst male TB patients.

Excepting a few nations in Africa (Sub-Saharan Africa), the prevalence of co-infection has been proclaimed to be higher among males than females.[25–28] The prevalence of HIV is known to be higher among women than men in sub-Saharan Africa as a consequence of several reactions to socio-demographic risk factors, sexual attitude, and HIV/AIDS knowledge. Also, women are renowned to have a higher predisposition to HIV infection and are usually subjected to sexual behaviors earlier than men at most due to economic circumstances.[27,28]

Sentinel observational study accomplished in Delhi by Jain et al.[29] in 1997–98 proposed a higher jeopardy of HIV co-infection existing among males complaining from TB which is in harmony with the present study. In the current study, HIV/TB patients were found to have a male-to-female ratio of 2.4. Others have found that the male/female ratio of HIV-associated TB in Africa was 0.83,[28] although in other territories such as the Western Pacific, that ratio was 3.1.[32] The ration of the current study is akin to the ratio of 2.7 revealed in 16 WHO European countries in 2005 and signaled that both infectious diseases are more widespread in the male population.[30,31]

With regard to the gender structure, it had been presumed that women with TB are not announced owing to a numerous of sociocultural issues, or diversified affairs affined with access in the health-care system and health services.[16] Therefore, in spite of the biological elucidations, there are sturdy evidences that corroborate such a liaison between female under proclamation rates in the context of specific cultural factors which perform an important role in developing and transitional societies.[25] Studies have been suggested that higher rate of TB infection in men may be due to the more vulnerability of males to pulmonary TB, difficulty in diagnosing TB in women, women with pulmonary TB have different symptoms from men and may not test positive on microscopic examination of the sputum, or that TB lung lesions might not be as severe in women as in men, resulting in women not being accurately diagnosed.[18,22,32]

In spite of the non-significant differences, the current study illustrate that HIV sero-positivity was higher among TB patients of age range 30–42 years and in laborer: 21 (51.2%); 13 (31.7%), respectively.

Studies had deduced that seroprevalence rates were highest among males in the age group between 31 and 40 years.[19,22,27] HIV infection among TB patients continue to be astonishing, as it has been declared that more than 1 in 6 TB patients aged 25–44 year infected with HIV.[25]

The TB/HIV encumbrance was also had been observed to be higher within the age group that is mostly affected by TB.[28] A study notified that the greatest leverage of the embarkation in TB extent had been on people between 25 and 45 years of age, since this is the age group mainly affected by HIV.[29] This age prevalence of HIV co-infection among TB patients likely point out the age-specific prevalence of HIV in the community. This may be related to patients' being in a sexually active age group in which both TB and HIV dominate most.[29,33] The other possible elucidation for this may be their increased family, organizational, and societal responsibilities as people in this age group involve themselves in various peculiar and distinctive daily activities in order to win the socioeconomic tribulation which increases the frequency of their contact with other patients in their society.[28,34]

The aforementioned outcomes of this study support this fact as the majority of the TB-HIV co-infected patients were in the productive age group 31–40 years, mostly illiterate and lack of skills. All these factors in linking with unsafe sexual practice were found to be the major cause of HIV transmission.[16,22,24]

TB is a disease of destitution. It is excessively realized that poorer community, the greater the probability of being infected with TB. Insufficiency of basic health services, poor nourishment and inappropriate living circumstances, all participate in the propagation of TB and its influence upon the society.[16,24,27]

In India, a study had determined that 76% of TB/HIV cases were in the age group of 21–40 years and also the occupational profile of their patients disclosed that a majority of them were farmers and laborers followed by transport drivers.[18] Channa et al.[16] announced that 36.8% of TB/HIV patients were working as manual laborers while Thanh et al.[24] found majority (55.6%) of patients were working as farmers. Manjareeka[22] had detected seropositivity proportion was elevated among those who were jobless (40%) followed by the laborers (35%).

The percentage of the professions is thus noted to alter in various studies, hugely due to the divergences in the occupational style and the origin from where the patients were picked.[22] Some studies pointed out a strong interconnection of seropositivity with socioeconomic factor, whilst other studies linked knowledge and educational level.[22,24]

The current study revealed that the highest prevalence of HIV positivity was among pulmonary TB (25; 61%). This result is consistent with findings reported by Chandra et al,[35] Kamath et al,[18] and Olowe et al[36] where higher seropositivity of HIV were detected in cases of pulmonary TB. In addition, a study by Jha et al[37] from eastern Nepal showed that 71.4% of the TB/HIV co-infected cases were suffering more commonly from pulmonary TB than with extra-pulmonary TB (28.6%). The pulmonary TB (85.7%) was more common than extra-pulmonary TB (14.3%) was also reported by the study done in Western Nepal.[38] Contrasting results have been found in studies conducted by Dahiya et al,[39] Mitku et al[25], and Kavya et al[40] with higher incidence of extra-pulmonary TB than pulmonary TB among HIV-TB co-infected patients.

Globally, the TB-associated HIV mortality in co-infected patients is three times higher than mortality among TB patients.[3] There are a number of possible explanations that

have been proposed for the increased mortality among co-infected patients.[16,19] The location and the extent of TB are influenced by the degree of immunosuppression, often increasing the difficulty of diagnosis and hence delaying treatment initiation, which may result in higher mortality.[9,11]

With the scarcity of checking studies for EPTB and the deprivation of an appropriate diagnostic equipment, it is strenuous to estimate the actual spread of the disease or precisely evaluate the anatomical distribution of disease.[20, 22, 24]

Enormous retrospective explorations have been incapable to denote an appropriate matching amidst characteristics of EPTB because of the fickle appearance of the disease.[16] A study in Brazil found similar non-specific symptoms in their patients with EPTB.[23] The differential diagnosis for the existence of these fundamental symptoms is spacious, but stay as a substantial hint for the diagnosis of TB in a high TB/HIV load situation. Whilst symptoms and signs are beneficial in guidance; moreover, checking to confirm the location of disease, there is a shortage of data on distinguishing clinical findings that may be utilized to assist the diagnosis of TB over other pathologies at these sites. The clinical presentation of EPTB is protean, and establishing the diagnosis presents significant challenges in resource-limited settings.[41,42]

The deficiency of diagnostic devices take part to a diagnostic predicament, and future evolution in molecular established technology may ameliorate our capability to diagnose the disease adequately. The application of obtainable technologies demand better guide-based direction. Due to the reliance on non-microbiological diagnostic tests for EPTB, diagnostic certainty remains elusive.[22,42]

The complex relationship, however, between patient demographic characteristics, behavioral risk factors, clinical characteristics and comorbidities, and EPTB remains poorly understood.[42]

Studies revealed that newly diagnosed TB/HIV infected have greater risk of MDR-TB than those negative to HIV.[43,44]

While most studies in North America showed an association between HIV infection and MDR-TB, not a single study from Africa demonstrated such association, and results from other regions were conflicting. Individual studies varied widely in study design and sample size, and results were rarely adjusted for potential confounding.[44] These restrictions and the noted diversity imped a comprehensive deductions considering the inclusive linking between HIV infection and MDR-TB. When stratified by type of MDR-TB, the analysis suggests that primary, but not acquired, MDR-TB is associated with HIV infection.[45]

Different biological mechanisms relating drug-resistant TB to HIV infection have been proposed. Drug malabsorption in HIV-infected patients, particularly rifampin and ethambutol, can produce drug resistance leading to treatment failure.[46]

The linkage between HIV infection and MDR-TB may be discomposed by risk factors such as injection drug use, imprisonment, socioeconomic status, alcohol use, and hospitalization which are shared between both. HIV-infected patients and MDR-TB patients are more likely to be hospitalized compared to those who are HIV negative.[47] HIV-infected patients may thus be more likely to be exposed to patients with drug-resistant isolates, and thus be infected or re-infected with a resistant isolate as the associations between MDRTB and HIV infection observed in many North American studies, which included in part patients involved in institutional outbreaks in New York City, support this possibility.[46,47] It is of worthy to mention that Albujeer[48] had concluded in their study in Iraq that preventing the spread of HIV in conservative communities such as Middle Eastern communities requires a comprehensive strategy that includes effective, continued health education and health promotion programs at both community and health professional levels.

Conclusions

The prevalence of HIV infection among TB patients in this study was 10.3%. Greater focus of health intervention should be required on reproductive age group and in area in which high immigration and overcrowding present. Even with unavoidable restrictions, we can still determine that the HIV prevalence among TB patients was high. Involvement planes aiming sociodemographic and behavioral factors linking with higher risk of TB-HIV co-infection are imperatively needed for.

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Conflicts of interest

There are no conflicts of interest.

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