Latent Tuberculosis Infection Prevalence and Characteristics in the HIV disease population in Two Major Medical Centers in Tegucigalpa, Honduras

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Research Article

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Abstract

Background

In Honduras, thirteen percent of patients with tuberculosis are coinfected with HIV, but the prevalence of latent tuberculosis infection among people with HIV infection is unknown. The goal of this study is to determine the prevalence and characteristics of latent tuberculosis infection among HIV diagnosed patients.

Methods

A cross-sectional study was conducted from June 2015 to December 2015 in two major clinical centers in Tegucigalpa, Honduras. This study used an adapted questionnaire-based clinical algorithm from the World Health Organization, procedures described by the Pan American Health Organization, and the Honduran National Norms for Tuberculosis Control included in the supplement material. There were two hundred ten individuals interviewed. Laboratory testing included tuberculin skin testing with absolute CD4 counts.

Results

There was a statistically significant higher risk of latent tuberculosis infection with HIV disease in the subgroups with a lower level of education ($p = 0.002$) and prior history of tuberculosis ($p < 0.001$).

Conclusion

The prevalence of latent tuberculosis infection is lower than in high-prevalence regions in different countries. The tuberculin skin test continues to identify patients with latent tuberculosis with HIV disease and intervene with concurrent antiretroviral therapy and tuberculosis chemoprophylaxis. A low education level is probably related to low socioeconomic status and access to healthcare. The findings of this study represent an opportunity to reach underserved areas, test the HIV population with the tuberculin skin test, and administer chemoprophylaxis.

Introduction

Tuberculosis and human immunodeficiency virus infection (HIV) tend to coexist. When they do, they are associated with high morbidity and mortality in underdeveloped countries. Tuberculosis and human immunodeficiency virus are among the leading causes of mortality in the underdeveloped world.[1,2] In 2014 alone, 9.6 million new cases of tuberculosis were reported worldwide, reaching 1.5 million deaths yearly. Twelve percent of patients with tuberculosis have HIV coinfection.[3] Moreover, the World Health

Organization (WHO) reported that 1.6 million individuals with HIV died from a myriad of opportunistic infections; Of these, tuberculosis was found to be the fourth leading cause of death.[2]

The natural history of tuberculosis begins with a quiescent asymptomatic state to a clinically evident active disease. The quiescent state of tuberculosis, what we know as latent tuberculosis infection, may be silent for decades or go unnoticed in a lifetime; much depends on the T-cell integrity of the individual. The diagnosis of this condition is not easy and depends on a combination of risk factors, lung imaging, and either a positive reaction to the tuberculin skin test (TST) or a positive interferon-gamma release assay.[4–6] Many clinical situations can disrupt the equilibrium of the tightly regulated memory T-cells, thus allowing for the progression to active tuberculosis. Examples of high-risk groups are HIV infection, diabetes mellitus, end-stage renal disease, silicosis, head and neck cancer, tumor necrosis factor inhibitors, glucocorticoids or immunosuppressive therapies for organ transplantation.

Tuberculosis and HIV are highly prevalent in countries with high poverty levels. Evidence suggests that the age group most affected is the economically active young adult.[1–3, 7] Honduras has the second-highest incidence rate of tuberculosis in Central America.[5] Furthermore, the calculated annual risk of an HIV-positive patient acquiring and eventually dying from tuberculosis is ten percent, hence the importance of identifying this specific group. The chemoprophylaxis regimens include isoniazid, rifampin, or a combination to prevent the progression to clinically active disease. Heretofore, there is insufficient data of this patient population in Honduras.[1,4–6]

In order to determine the frequency of latent tuberculosis infection among people living with HIV, a cross-sectional study was performed at the Integral Healthcare Center for HIV at the following medical centers: The Hospital Escuela Universitario (University School Hospital) and the Instituto Nacional Cardiopulmonar (National Cardiopulmonary Institute).

Materials And Methods

Geographic Areas

The Hospital Escuela Universitario and Instituto Nacional Cardiopulmonar are part of an urban academic primary and tertiary care medical system at the cities of Tegucigalpa, Francisco Morazán in Honduras. The Integral Healthcare Center for HIV of the Public Health area follow individuals with an established diagnosis of HIV infection as outpatients. These two centers comprised an estimated population of 1,600 patients.

Study Protocol

The Committee of Ethics in Biomedical Research of the Scientific Research Unit of the Universidad Nacional Autónoma de Honduras approved this study. A descriptive cross-sectional study, following the STROBE statement Guidelines for cross-sectional studies, was performed between June 2015 and December 2015. Selected individuals had an established diagnosis of HIV infection who regularly visit

outpatient clinics. The patients received educational lectures on the transmission of tuberculosis, symptoms, and latent tuberculosis infection utilizing WHO/PAHO (Pan American Health Organization) educational materials. An adapted clinical questionnaire using clinical algorithms from WHO/PAHO to identify active tuberculosis cases was used. The patients received information on the laboratory tests required to participate in this study. The patients signed a written informed consent approved by the Bioethics Committee, to be eligible to participate in the study.

The inclusion criteria were as follows: subjects over 18 years old, HIV positive serology, and outpatient enrollment in outpatient clinics between June 2015 to December 2015. The exclusion criteria were as follows: individuals under 18 years old, unwillingness to participate, pregnancy or suspicion of pregnancy, forearm injury at the targeted skin site for TST, clinically active tuberculosis or mental disability.

Data Collection

A uniform data collection form recorded the demographic and clinical information, history of comorbidities, risk factors associated with TB infection, and history of immunosuppressive drugs. The TST was performed by injecting 0.1 mL of purified protein derivative in the left arm using the Mantoux technique. The TST was considered positive in those with induration of equal or more than 5 mm within the first 72 hours of the test.

Statistical Analysis

Data documentation and statistical analysis on clinical data were performed using Epi Info 7.1.5.2 (Centers for Disease Control and Prevention, Atlanta, Georgia, USA). Sampling was calculated using StatCalc Epi Info, which gave an expected frequency of coinfection of 30% with a statistical power of 80% and in a sample result of 220 patients.

Results

This study included 210 interviews, of the original 410 interviews from June to December 2015 at the two health facilities. The details of the clinical data are in Table.1 and 2.

Both tables are a cross-tabulation that compares patients' characteristics (social-demographical, comorbidities, risk factors, and CD4-count) in relationship with the TST result. Women had a higher representation (62.3% of the patients), without a significant statistical difference between the gender and TST result ($p = 0.5$). Eight percent of the patients had a positive TST result. There was a nonstatistical difference based upon age; most patients were in the middle adult age group ($p = 0.6$). Illiterate patients, combined with those who only completed elementary school, had a higher percentage of a positive TST ($p < 0.002$). A prior history of having tuberculosis was the only variable of statistical significance in the comorbidities and risk factors category ($p < 0.001$). The CD4 count and body-mass index did not show a significant difference. ($p = 0.2$ and $p = 0.1$ respectively).

Discussion

Tuberculosis is among the leading causes of death in the HIV population in low-income economies. When a patient is co-infected, each disease speeds up the progress of the other. In the authors' opinion, this is a comprehensive study to search for the frequency of latent tuberculosis infection among HIV-infected patients in Honduras. The estimated global burden of latent tuberculosis infection is twenty-three percent worldwide. The HIV-infected population has a ten percent lifetime risk of developing active tuberculosis as well as high associated mortality. [9,16]

A low level of education correlated significantly between HIV and LTBI coinfection. There were seven participants with a prior history of tuberculosis with the completion of therapy. They had a positive TST reaction as expected. On the other side, seventeen participants with a prior history of tuberculosis who underwent treatment completion had a negative TST reaction. Probably this finding is related to immunosuppression. Most of the patients had recently initiated antiretroviral therapy. There was no significant correlation between the CD4, body-mass index, and age between the groups. HIV disease population is among the most vulnerable to acquiring tuberculosis infection.[11,12]

The WHO and PAHO have created strategies and clinical guidelines to prevent and manage tuberculosis-HIV coinfection based on studies performed in sub-Saharan Africa population.[1,7,13–15] These guidelines recommend the use of a clinical algorithm to determine whether HIV-positive patients should receive prophylaxis to prevent clinical disease.[1] The government of Honduras adopted this recommendation.[13] Based on this algorithm, this study indicates that the prevalence of latent tuberculosis infection in Honduran HIV population is 8.1%, which is lower than in sub-Saharan Africa.

When compared with other high prevalence countries, Honduras has lower rates of tuberculosis. The disease occurs among young adults living in urban areas and with a low level of education, which is a different scenario compared with African countries.[13,15] There is an opportunity to validate and utilize this clinical algorithm in low-income underdeveloped countries.

A limitation of this study is the use of a clinical-algorithm questionnaire created on data from different epidemiological characteristics from Honduras population. Additionally, the lack of a reference standard for the diagnosis of latent tuberculosis infection could present a problem. TST have only modest predictive value and low sensitivity. It could be relevant to evaluate the possibility of a prospective cohort study to compare the use of interferon-gamma release assay with the TST in diagnosing latent tuberculosis infection in the HIV population, especially in patients with a prior history of tuberculosis.

Conclusion

The prevalence of latent tuberculosis infection is lower than in high-prevalence regions in different countries. The tuberculin skin test continues to identify patients with latent tuberculosis with HIV disease and intervene with concurrent antiretroviral therapy and tuberculosis chemoprophylaxis. A low education level is probably related to low socioeconomic status and access to healthcare. The findings of this study

represent an opportunity to reach underserved areas, test the HIV population with the tuberculin skin test, and administer chemoprophylaxis.

Declarations

Ethical approval and consent to participate

The patients gave a written inform consent to participate. Ethics committee in Honduras need for approval was waived.

Consent for publication

The study participants and the authors consented for publication in written.

Availability of data and materials

All the supporting data generated of analyzed during this study are in included in the supplementary information files.

Competing interests

There are no competing interests in this study.

Funding

The study is unfunded, not applicable.

Authors' contributions

Miriams T Castro-Lainez: Manuscript writing, tables construction, organizing material, design of the work and concept, review version for approval, intellectual content.

Cecilia Varela-Martinez: Data concept design, acquisition, analysis, interpretation of data, drafted the article, intellectual content.

Rebeca Rivera: Manuscript review, concept design, acquisition, analysis, interpretation of data, drafted the article, intellectual content.

Jose A. Diaz-Romero: concept design, acquisition, analysis, interpretation of data, drafted the article, revision for intellectual content.

Leticia N. Solorzano-Flores: Data concept design, acquisition, analysis, interpretation of data, drafted the article, intellectual content.

Alan Howell: Data interpretation, analysis, intellectual component, editions, critical revisions.

Miguel Sierra-Hoffman: Data concept design, acquisition, analysis, interpretation of data, drafted the article, intellectual content, work design

Mark L. Stevens: Data analysis and interpretation, organization of manuscript, intellectual component.

Elsa Palou-Garcia: Data concept design, research model and design of work, acquisition, analysis, interpretation of data, drafted the article, intellectual content, work design.

Rafael J. Deliz: Analysis, interpretation of data, drafted the article, critical revision for important intellectual content, corresponding author responsibilities.

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Tables

Table 1
Socio-demographic characteristics and comorbidities according to the TST results of the Honduran population living with HIV and receiving treatment at Integral Healthcare Center for HIV at the Hospital Escuela Universitario and the Instituto Nacional Cardiopulmonar in Tegucigalpa, Honduras, from June 2015 to December 2015.

	Tuberculin Skin Test				
Characteristics					
Gender	Positive	Negative	Indeterminate	SD	P value
Female	11 (8.4%)	110 (84.0%)	0 (0.0%)	10 (7.6%)	0.5
Male	6 (7.6%)	63 (79.7%)	1 (1.3%)	9 (11.4%)	
Age					
18–30	0 (0.0%)	26 (96.3%)	0 (0.0%)	1 (3.7%)	0.6
31–45	9 (10.0%)	71 (78.9%)	1 (1.1%)	9 (10.0%)	
46–59	8 (10.3%)	63 (80.8%)	0 (0.0%)	7 (9.0%)	
60+	0 (0.0%)	13 (86.7%)	0 (0.0%)	2 (13.3%)	
Education Level					
Illiterate or Elementary School	13 (12.7%)	86 (84.3%)	0 (0.0%)	3 (2.9%)	0.002
More than Elementary School	4 (3.7%)	87 (80.6%)	1 (0.9%)	16 (14.8%)	
Place of origin					
Tegucigalpa	14 (8.6%)	135 (82.8%)	1 (0.6%)	13 (8.0%)	0.1
Francisco Morazán	2 (6.7%)	27 (90.0%)	0 (0.0%)	1 (3.3%)	
Other	1 (5.9%)	11 (64.7%)	0 (0.0%)	5 (29.4%)	
Comorbidities					
Alcoholism					
Yes	0 (0.0%)	6 (85.7%)	1 (14.3%)	0 (0.0%)	< 0.001
No	17 (8.4%)	167 (82.3%)	0 (0.0%)	19 (9.4%)	
Hepatitis					
Yes	1 (12.5%)	7 (87.5%)	0 (0.0%)	0 (0.0%)	0.7
No	16 (7.9%)	166 (82.2%)	1 (0.5%)	19 (9.4%)	
Liver Cirrhosis					
Yes	0 (0.0%)	1 (100.0%)	0 (0.0%)	0 (0.0%)	0.9

	Tuberculin Skin Test				
No	17 (8.1%)	172 (82.3%)	1 (0.5%)	19 (9.1%)	
Diabetes Mellitus					
Yes	2 (18.2%)	7 (63.6%)	0 (0.0%)	2 (18.2%)	0.3
No	15 (7.5%)	166 (83.4%)	1 (0.5%)	17 (8.5%)	

Table 2
TST results according to the predisposing risk factors for TB of the Honduran population living with HIV and receiving treatment treatment at Integral Healthcare Center for HIV at the Hospital Escuela Universitario and the Instituto Nacional Cardiopulmonar in Tegucigalpa, Honduras, from june 2015 to December 2015.

	Tuberculin skin test result				
	Positive	**Negative**	**Indeterminate**	**SD**	**P value**
Risk Factors					
Prior History of TB					
Yes	7 (31.8%)	13 (59.1%)	0 (0.0%)	2 (9.1%)	< 0.001
No	10 (5.3%)	160 (85.1%)	1 (0.5%)	17 (9.0%)	
Living with a person with TB					
Yes	2 (5.3%)	32 (84.2%)	0 (0.0%)	4 (10.5%)	0.8
No	15 (8.7%)	141 (82.0%)	1 (0.6%)	15 (8.7%)	
Imprisonment history					
Yes	2 (16.7%)	7 (58.3%)	0 (0.0%)	3 (25.0%)	0.1
No	15 (7.6%)	166 (83.8%)	1 (0.5%)	16 (8.1%)	
Smoking history					
Yes	5 (15.6%)	24 (75.0%)	0 (0.0%)	3 (9.4%)	0.4
No	12 (6.7%)	149 (83.7%)	1 (0.6%)	16 (9.0%)	
Living in a nursing home					
Yes	0 (0.0%)	2 (66.7%)	0 (0.0%)	1 (33.3%)	0.5
No	17 (8.2%)	171 (82.6%)	1 (0.5%)	18 (8.7%)	
Serving in the military					
Yes	0 (0.0%)	4 (80.0%)	0 (0.0%)	1 (20.0%)	0.7
No	17 (8.3%)	169 (82.4%)	1 (0.5%)	18 (8.8%)	
Working in health care					
Yes	1 (7.1%)	11 (78.6%)	0 (0.0%)	2 (14.3%)	0.9
No	16 (8.2%)	162 (82.7%)	1 (0.5%)	17	
Being a returned migrant					
Yes	0 (0.0%)	4 (80.0%)	0 (0.05)	1 (20.0%)	0.7

	Tuberculin skin test result				
No	17 (8.3%)	169 (82.4%)	1 (0.5%)	18 (8.8%)	
BCG vaccination					
Yes	16 (8.8%)	148 (81.3%)	1 (0.5%)	17 (9.3%)	0.7
No	1 (3.6%)	25 (89.3%)	0 (0.0%)	2 (7.1)	
CD4 count					
0-200	1 (2.5%)	35 (87.5%)	0 (0.0%)	4 (10.0%)	0.2
201–499	8 (7.1%)	92 (82.1%)	0 (0.0%)	12 (10.7%)	
500+	8 (13.8%)	46 (79.3%)	1 (1.7%)	3 (5.2%)	
Body Mass Index					
< 18	2 (33.3%)	4 (66.7%0	0 (0.0%)	0 (0.0%)	0.1
18–25	4 (3.6%)	96 (86.5%)	1 (0.9%)	10 (9.0%)	
26–30	7 (10.4%)	52 (77.6%)	0 (0.0%)	8 (11.9%)	
31+	4 (15.4%)	21 (80.8%)	0 (0.0%)	1 (3.8%)	

Supplementary Files

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- PrevalenceoflatenttuberculosisamongasymptomaticHIV.docx