



Article/Artigo

Co-infection and risk factors of tuberculosis in a Mexican HIV⁺ population

Coinfecção e fatores de risco de tuberculose em uma população Mexicana com HIV⁺

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ABSTRACT

Introduction: The situation of tuberculosis (TB) is being modified by the human immunodeficiency virus (HIV), which is increasing the occurrence of new cases and the generation of drug resistant strains, affecting not only the people infected with HIV, but also their close contacts and the general population, conforming a serious public health concern. However, the magnitudes of the factors associated to this co-infection differ considerably in relation to the population groups and geographical areas. **Methods:** In order to evaluate the prevalence and risk factors for the co-infection of tuberculosis (TB) in a population with human immunodeficiency virus (HIV⁺) in the Southeast of Mexico, we made the analysis of clinical and epidemiological variables and the diagnosis of tuberculosis by isolation of mycobacteria from respiratory samples. **Results:** From the 147 HIV⁺ individuals analyzed, 12 were culture positive; this shows a prevalence of 8% for the co-infection. The only variable found with statistical significance for the co-infection was the number of CD4-T < 200 cells/mm³, OR 13 (95%, CI 2-106 vs 12-109). **Conclusions:** To our knowledge this is the first report describing the factors associated with tuberculosis co-infection with HIV in a population from Southern Mexico. The low number of CD4 T-cells was the only variable associated with the TB co-infection and the rest of the variables provide scenarios that require specific and particular interventions for this population group.

Keywords: Tuberculosis. HIV. Risk factors. Co-infection.

RESUMO

Introdução: A situação da tuberculose (TB) foi modificada pelo vírus da imunodeficiência humana (HIV). Com isso, aumentou-se a ocorrência de novos casos de TB e a geração de cepas resistentes à droga, afetando não só as pessoas infectadas com HIV, mas também seus contatos próximos e da população em geral, gerando um sério problema de saúde pública. No entanto, a magnitude dos fatores associados à esta coinfeção diferem consideravelmente em relação aos grupos populacionais e áreas geográficas. **Métodos:** Para avaliar a prevalência da comorbidade e fatores de risco da coinfeção de tuberculose (TB) em uma população com o vírus da imunodeficiência humana (VIH⁺) no sudeste do México, nós fizemos a análise das variáveis clínicas e epidemiológicas e de isolamento da micobactérias através de cultura de amostras respiratórias. **Resultados:** A partir de 147 indivíduos HIV⁺ analisados, 12 foram positivos na cultura, o que mostra uma prevalência de 8% para a coinfeção. A única variável com significância estatística encontrada para a coinfeção foi o número de células CD4-T < 200 células/mm³, OR 13 (95%, CI 2-106 vs 12-109). **Conclusões:** Ao nosso conhecimento este é o primeiro relatório que descreve os fatores associados à coinfeção de tuberculose com HIV em uma população do sudeste do México. O baixo número de células T CD4⁺ foi à única variável associada com a coinfeção por TB no resto das variáveis, proporcionando situações que exigem intervenções específicas e particulares para este grupo populacional.

Palavras-chaves: Tuberculose. HIV. Fatores de risco. Coinfeção.

INTRODUCTION

According to the World Health Organization (WHO) in 2007, out of a total of 9.3 million incident cases of tuberculosis (TB), 1.4 million cases and 480,000 deaths were related to HIV/AIDS coinfection¹. The epidemiology of TB is being modified by the human immunodeficiency virus (HIV), which is causing an increase in the occurrence of new cases and the generation of drug resistant strains, affecting not only individuals infected with HIV, but also their close contacts and the general population, a situation that poses a serious public health concern¹⁻⁴.

The epidemiological and clinical characteristics of TB in the HIV⁺ population are markedly different to those of TB alone³. The risk of acquiring TB increases by 10% and the speed of progression increases considerably. Malnutrition, domestic overcrowding and low number of CD4 T cells are factors frequently associated with the acquisition of TB in HIV⁺ individuals; however, the magnitude of individual factors varies considerably according to population groups and geographical areas³⁻⁶.

The annual incidence rates for TB and HIV in Mexico are 14 and 116 per 100,000 habitants, respectively. The State of Veracruz is located in southeastern Mexico, has 7 million habitants and annual incidences for TB and HIV of 23 and 162 per 100,000 habitants, respectively^{7,8}; however, the prevalence of TB in HIV⁺ individuals and the factors associated with coinfection are poorly understood. The aims of this study were to establish the prevalence of coinfection and to determine the risk factors for TB acquisition in an HIV⁺ population from Veracruz, Mexico.

METHODS

Population, diagnostic procedure and determination of risk factors

The study comprised a population of 240 individuals with a diagnosis of HIV confirmed by western blot. Only individuals older than 15 years of age and who consented to participation in the study

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were included. All the patients were receiving retroviral treatment and were registered at the Care Center for Patients with Sexually Transmitted Diseases and Acquired Immune Deficiency Syndrome (AIDS), from Xalapa, Veracruz, Mexico.

Sterile containers were given to each patient so that they could collect an early morning sputum sample at home for three consecutive days. When the patients returned to the clinic with their samples, a survey was conducted to identify the risk factors. Additional questions, regardless of knowledge of the main symptoms of TB, were put to the patients.

The samples were decontaminated by the modified Petroff's method⁹ and cultured in Lowenstein Jensen medium slants at 37°C. The slants were examined twice weekly for the first 2 weeks and once weekly thereafter. Cultures were considered negative when no growth was observed after 8 weeks.

Statistical analysis

The questionnaire and culture results for each patient were entered into a database and statistical analyses were performed using Epi-Info™ version 6 (CDC, USA) and SPSS 7.0 for Windows (SPSS, Inc., USA). Bivariate analyses were performed by using the Chi square (X^2) tests and estimation of *odds ratios* (OR) with 95% confidence intervals (95%CI). The results were considered to be significant when $p \leq 0.05$. Multivariate logistic regression models were constructed to identify the factors independently associated with TB infection among the HIV⁺ population. The dependent variable was TB infection and the covariables were: age ≤ 40 years-old, sex, salary, incidence of alcoholism and a cell count of < 200 CD4⁺ T cells/mm³. Adjusted OR with 95%CI for the independent variables was calculated for the final model.

Ethical considerations

Ethical considerations were strictly observed; all the information collected was confidential and written consent was obtained from each patient.

RESULTS

Between February and July 2007, questionnaire results and sputum clinical samples from 147 (61%) of the patients were collected. The remainder of the population, 93 (39%) individuals, declined to participate. Baseline information showed that 88 (60%) individuals were male and 59 (40%) were female. The mean age was 35 years-old and 104 (70%) were between 15-40 years-old. The mean number of years with a positive diagnosis of HIV was 2.4, with a standard deviation of 4 years. Ninety-seven (66%) individuals were single and 85 (57%) had received more than basic formal education (> 6 years of schooling). A monthly salary of more than US\$280 was reported by 105 (71%) individuals, 89 (69%) lived in an urban area, while 60 (40%) customarily slept with less than 3 people in the same room. Tobacco and alcohol consumption was observed in 30 (20%) and 37 (25%) individuals respectively. The CD4 T cell load of < 200 cells/mm³ was observed in 71 (48%) of individuals and a body mass index of ≤ 18.5 kg/m² was recorded in 66 (44%) individuals. Only 1 (0.6%) person reported previous TB diagnosis and prophylactic treatment. Contact with a person with TB in the preceding year was reported by 39 (26%) individuals, while 129 (87%) were able to recognize the main symptoms of TB.

Analysis of diagnosis by culture showed that only 12 patients were TB positive. Based on this information, TB prevalence in this HIV⁺ population group was 8%.

Despite the fact that no clinical signs of TB were observed in these TB-HIV⁺ individuals, they showed some common characteristics: 8 were male and single, all were less than 35 years-old, 9 slept in the same room with more than 3 people, 6 had low financial income, 11 presented a number of CD4 T cells < 200 cells/mm³ and 7 had a body mass index less than 18.5kg/m². Four individuals reported previous contact with a TB infected individual in the preceding year, while only two were unable to recognize the main symptoms of TB (**Table 1**).

TABLE 1 - Host-related variables for tuberculosis in HIV⁺ patients from Veracruz, México.

Variable	Patients diagnosed		Odds ratio	Confidence interval (95%)	P value*
	positive n = 12	negative n = 135			
Gender (male)	8	80	1.3	0.3-5.7	0.61
Marital status (single)	8	89	1.0	0.26-4.3	0.98
Education (≤ 6 years)	7	55	2.0	0.5-7.8	0.23
Domestic overcrowding (≥ 3 people sleeping in one room)	9	78	0.4	0.1-1.9	0.24
Rural residence	5	53	1.1	0.2-4.1	0.52
Alcohol consumption	4	33	1.5	0.3-6.1	0.49
Tobacco consumption	1	29	0.3	0.0-2.6	0.27
Monthly salary ≤ 280 US\$	6	36	2.7	0.7-10.4	0.08
Number of CD4-T cell ≤ 200 cells/mm ³	11	60	13.7	1.7-292	< 0.01
Body mass index ≤ 18.5 kg/m ²	7	59	1.8	0.4-6.9	0.32
Contact with a person with TB	4	35	1.4	0.3-5.6	0.62
No recognition of TB symptoms	2	16	1.4	0.0- 8.3	0.64

TB: tuberculosis, * χ^2 test, $p \leq 0.05$ for significance level.

TABLE 2 - Comparison of risk factors for tuberculosis, diagnosed by culture in an HIV+ population from Veracruz, Mexico.

Predictive factor	Unadjusted model			Adjusted model*		
	OR**	CI 95%	p	OR**	CI 95%	p
Age (< 40 year)	0.79	0.2 – 3.1	0.73	–	–	0.78
Gender (male)	1.0	0.3 – 4.2	0.90	–	–	0.76
Salary (≤US\$280)	2.9	0.8 – 11.0	0.11	–	–	0.14
Alcoholism	1.7	0.4 – 7.6	0.46	–	–	0.64
CD4-T+ < 200 cells/mm ³	13.0	2.0 – 106	0.02	13.0***	2-109	0.01

OR: *odds ratio*, CI 95%: confidence interval 95%, *Model was adjusted by forward conditional method, **odds ratio estimated by logistic regression, ***CD4-T was adjusted by age, gender, salary and alcoholism.

The only factor associated with TB infection was the number of lymphocyte CD4⁺ T cells < 200cells/mm³, OR = 13.7 (95%CI 1.7-292) (Table 1) and according to the multivariate analyses, this was the only significant risk factor for TB in the crude versus adjusted model OR = 13 vs OR = 13 (95%CI 2-106 vs 2-109) (Table 2).

DISCUSSION

Several of the variables identified in the HIV⁺ population in this study, such as the high number of patients below 40 years of age, low number of CD4⁺ T cells, body mass index and alcohol and tobacco consumption, were similar to those verified in studies from South Africa¹⁰, Brazil¹¹ and Kenya¹².

The prevalence for coinfection in this population was 8%, close to the 9% reported in South Africa¹⁰ and to the global estimate of 10% by the WHO^{1,2}. This is higher compared to the national (5%) and Latin American (1.3%) prevalences^{7,8}, but lower compared to reports from other states from northern and central Mexico, such as Baja California (18%) and City of Mexico (13%)^{13,14}.

To our knowledge, this is the first study related to the prevalence and identification of risk factors for TB coinfection in a HIV⁺ population from southern Mexico. The results showed that a CD4⁺ T cell count < 200cells/mm³ was the only variable associated with the acquisition of TB. However, several of the characteristics analyzed in the HIV⁺ population, such as sex, marital status, education, domestic overcrowding and body mass index, highlight particular tendencies within this population and should be taken into account if further interventions against TB are to be conducted.

In addition to diagnosis by culture, acid fast staining by Ziel Nielsen (AFS-ZN) was applied to the respiratory samples and an in-house PCR procedure, developed by our group¹⁵. The results showed prevalences for TB-HIV⁺ coinfection of 36% for AFS-ZN and 50% for PCR; however, these results were confirmed by the culture test in only 5 (41%) and 11 (90%) individuals, respectively. This over-diagnosis by the AFS-ZN diagnostic test is a phenomenon commonly reported in the literature^{4,6}, when respiratory samples from HIV⁺ individuals with a low number of CD4-T cells are analyzed, and is associated with the presence of acid-alcohol resistant microorganisms, such as *Actinomyces* or *Nocardia*¹⁶.

Nonclinical signs of TB were observed in the TB-HIV⁺ population studied, an aspect generally explained in terms of alterations in the normal host immune response that, among other things, markedly reduce the formation of cavitations in the lung and decrease the transference of bacilli into respiratory secretions,

affecting the presentation of clinical signs of the disease and therefore the sensitivity and specificity of traditional probes^{2,4,6}. This reveals the possibility of the existence of more TB cases, which may have gone undiagnosed by the culture procedure. The main limitations of the present study were that the experimental design did not consider the clinical follow-up of the patients with a negative diagnosis by culture and examination for other coinfections in the positive cases. Such information could help to confirm or invalidate the TB prevalences determined by AFS-ZN and the in-house PCR.

In conclusion, within the HIV⁺ population analyzed in the present study, the prevalence of TB comorbidity was 8% and a CD4⁺ T cell count < 200cells/mm³ was the only associated risk factor. More attention needs to be given to these individuals in order to increase the number of CD4 T cells and to improve the immune response against TB. It is also necessary to include more rapid, specific and sensitive diagnostic procedures¹⁷, in order to detect reactivation or new tuberculosis infections in the early stages of disease. This action will have important implications on the surveillance of HIV positivity in individuals from countries like Mexico, where TB is endemic.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

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