

Original article

Pulmonary tuberculosis and main prevalent factors in a cohort of Latin American patients

Tuberculosis pulmonar y principales factores prevalentes en una cohorte de pacientes latinoamericanos

Tuberculose pulmonar e principais fatores prevalentes em uma coorte de pacientes latino-americanos

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This study aimed to conduct a descriptive study of the prevalence of the most common risk factors for pulmonary tuberculosis in a Latin American population. Basic sociodemographic factors and clinical characteristics of 103 patients were analyzed. The categorical variables were compared using the chi-square test and analyzed using logistic regression to evaluate their association. As a result, it was found that the study population had at least one non-communicable comorbidity. The most affected age group was 18-34 years (57 %). Forty-eight patients were HIV seropositive with a p-value of 0.019 and 0.023 with an odds ratio (OR) of 2.9 (2.5-3.3). Carbohydrate intolerance was present in four patients, OR 1.11 (1.0-1.35). Diabetes mellitus was present in four patients, OR 1.26 (1.13-1.65), and arterial hypertension was present in six patients, OR 1.28. Carbohydrate intolerance was present in four patients, OR 1.11 (1.0-1.35). Diabetes mellitus was present in four patients, OR 1.26 (1.13-1.65); and arterial hypertension in six patients, OR 1.28 (1.11-1.62) and an adjusted OR (ORa) of 1.18 (1.0-1.56). HIV infection, diabetes mellitus, as well as carbohydrate intolerance and arterial hypertension were commonly observed as proximate risk factors for tuberculosis. The conduction of studies of this nature is recommended in order to develop strategies to reduce its transmissibility.

Key words: *Mycobacterium tuberculosis*, epidemiology, sociodemographic factors, risk factors, latent tuberculosis infection.

Resumen

Esta investigación persiguió realizar un estudio descriptivo sobre la prevalencia de los factores de riesgo más frecuentes para tuberculosis pulmonar en una población latinoamericana. Se analizaron los factores sociodemográficos básicos y las características clínicas de 103 pacientes. Las variables categóricas se compararon mediante la prueba de chi-cuadrado; y analizaron mediante una regresión logística para evaluar su asociación. Como resultados, se identificó que la población de estudio tenía, al menos, una comorbilidad no transmisible. El grupo etario más afectado fue el de 18-34 años (57 %). Se diagnosticaron 48 pacientes seropositivos al VIH con un valor de 0.019 y 0.023 con R-R 2.9 (2.5-3.3). La intolerancia a los carbohidratos estuvo presente en cuatro pacientes, OR 1.11 (1.0-1.35). La diabetes mellitus se encontró en cuatro pacientes con OR 1.26 (1.13-1.65); y la hipertensión arterial en seis pacientes con OR 1.28 (1.11–1.62) y ORa de 1.18 (1.0-1.56). La infección por VIH, la diabetes mellitus, así como la intolerancia a los carbohidratos y la hipertensión arterial se observaron comúnmente como factores de riesgo próximos a la tuberculosis. Se recomienda la realización de estudios de esta índole con el fin de trazar estrategias para disminuir su transmisibilidad.

Palabras clave: *Mycobacterium tuberculosis*, epidemiología, factores sociodemográficos, factores de riesgo, infección tuberculosa latente.

Resumo

Esta pesquisa buscou realizar um estudo descritivo sobre a prevalência de fatores de risco mais frequentes para tuberculose pulmonar em uma população Latino Americana. Foram analisados fatores sociodemográficos básicos e características clínicas de 103 pacientes. As variáveis categóricas foram comparadas usando o teste de qui-quadrado; e analisados por meio de regressão logística para avaliar sua associação. Como resultados, identificou-se que a população do estudo possuía pelo menos uma comorbidade não transmissível. A faixa etária mais acometida foi de 18 a 34 anos (57 %). Foram diagnosticados 48 pacientes soropositivos para HIV com um valor de 0,019 e 0,023 com R-R 2,9 (2,5-3,3). A intolerância a carboidratos estava presente em quatro pacientes, OR 1,11 (1,0-1,35). Diabetes mellitus foi encontrado em

quatro pacientes com OR 1,26 (1,13-1,65); e hipertensão arterial em seis pacientes com OR 1,28 (1,11–1,62) e ORa de 1,18 (1,0-1,56). Infecção por HIV, diabetes mellitus, bem como intolerância a carboidratos e pressão alta foram comumente observados como fatores de risco próximos da tuberculose. Recomenda-se que estudos dessa natureza sejam realizados com o fim de traçar estratégias para reduzir sua transmissibilidade.

Palavras-chave: *Mycobacterium tuberculosis*, epidemiologia, fatores sociodemográficos, fatores de risco, infecção tuberculosa latente.

Introduction

Tuberculosis (TB) is a health issue that affects approximately 10 million people each year, according to the *Global Tuberculosis Report* (World Health Organization, 2021). Approximately 1.7 billion people have latent tuberculosis infection (LTBI), constituting 23% of the global population. The progression from LTBI to TB is estimated at a risk rate of 10% (Bagcchi, 2023). Furthermore, around 26% of the global population has been exposed to *Mycobacterium tuberculosis*, the bacteria responsible for this disease. The majority of these individuals have latent tuberculosis infection rather than active TB (World Health Organization, 2021).

On the other hand, diabetes mellitus (DM), a condition considered a risk factor for developing TB, affects about 537 million adults (International Diabetes Federation, 2021). Clinical and epidemiological studies have indicated that DM increases the risk of developing active TB. While the association between DM and active TB has been well-documented in other regions (Leung *et al.*, 2008), data clarifying the relationship between DM and latent TB are scarce. This is not the case for the role of HIV infection, which is well-characterized (Kumar *et al.*, 2017).

Another factor with a bidirectional relationship with TB is malnutrition, defined as a low body mass index (BMI). A low BMI increases the risk of developing active TB by 6 to 10 times. A quarter of the global TB burden is attributed to malnutrition, and this risk can be reduced by improving an individual's nutritional profile (Feleke *et al.*, 2019). The metabolic syndrome is diagnosed based on characterized alterations, which have been linked to the risk of developing

pulmonary mycobacterial infection. Such cases include obesity and arterial hypertension in adult patients (Pedditzi *et al.*, 2019). Epidemiological investigations conducted in young patients have failed to determine whether the presence of DM, obesity, and hypertension increases the risk of TB in this age group (Alberti *et al.*, 2009).

In view of the above, the main objective of this study was to conduct a descriptive study of the prevalence of the most common risk factors of TB in a Latin American community. The second objective was to determine whether these results could be extrapolated to other studies with similar characteristics.

Materials and methods

A descriptive study was conducted on the prevalence of proximate risk factors for active TB in the population diagnosed by smear microscopy, in a total of 103 patients in a hospital in Colombia. The study covered the period 2020-2022, through a quantitative assessment of multiple non-communicable morbidity focusing on DM, BMI, obesity and AHT as common risk factors for LTBI, progressing to active TB. The study was approved by the ethical boards of a hospital in northwestern Colombia, complying with ethical considerations and written informed consent.

HIV serology, anthropometric measurements (height, weight and waist circumference), biochemical parameters, glycosylated hemoglobin level (HbA1c) and blood pressure were obtained using standardized techniques. Individuals with symptoms or signs of active TB, history of previous TB, known cases of cancer, HIV or other immunosuppressive disease performed in the last 6 months prior to screening were considered in the exclusion criteria.

The primary outcomes of interest as *comorbidity* were DM or prediabetes mellitus (carbohydrate intolerance), defined on the basis of HbA1c percentages, according to *American Diabetes Association* criteria (DM > 6.4 %; carbohydrate intolerance, 5.7-6.4 %), and HbA1C kit (Beckman Coulter, Clare, Ireland) (Joshi *et al.*, 2011; Solá *et al.*, 2016).

The BMI was categorized based on the guidelines of the *American Heart Association / American College of Cardiology* ($\text{BMI} \leq 18.5 \text{ kg/m}^2$). Fasting serum albumin measurement $< 3.4 \text{ g/dl}$ (Beckman Coulter, Clare, Ireland) during fasting was used for assessment. Overweight ($\text{BMI} 23$ to 24.9 kg/m^2) and obesity ($\text{BMI} \geq 25.0 \text{ kg/m}^2$) were also defined. Arterial hypertension (AHT) was reported as systolic blood pressure $>130 \text{ mmHg}$, following the guidelines of the *American Heart Association* (Nyirenda *et al.*, 2023). Sociodemographic characteristics like age and gender were analyzed.

Trained personnel for the study used standardized and structured case notification forms on paper, along with electronic data capture methods for data collection. The clinical data management system Panacea® was employed for the secure management of patient identifiers, demographic data, laboratory results, and clinical information.

The statistical analysis was conducted to estimate the prevalence of the most frequently reported risk factors for TB in infected individuals, focusing on DM (Diabetes Mellitus), BMI (Body Mass Index), and AHT (Hypertension). Statistical results were based on two-sided tests, and a p-value ≤ 0.05 was considered statistically significant. A descriptive analysis of basic sociodemographic factors and clinical characteristics of individuals was performed. Categorical variables were compared using the chi-square test.

A logistic regression analysis was performed to assess the association between TB and potential covariates. A p-value ≤ 0.05 was considered statistically significant. A binomial test was conducted to determine the prevalence odds ratio (OR), adjusted odds ratio (ORa), and relative risk (RR) using the Clopper-Pearson exact test, with a 95% confidence interval (CI). Data were analyzed using IBM-SPSS version 20.0, following statistically validated standards (Harris *et al.*, 2009; Harris *et al.*, 2019).

Results

Sociodemographic and clinical characteristics

Table 1 represents the variables analyzed in the research. The average age of the adults infected with TB was 28 years (interquartile range 16-42).

Table 1

Sociodemographic and clinical characteristics of the reported population.

Variables	Total, n (%)	p-value
totals	103 (100)	
Socio-demographic characteristics-sex		
Female	21 (19)	-
Male	82 (81)	-
Age, years	Values	
18-34	49 (47 %)	0.0002
35-44	28 (27 %)	
45-54	17 (16 %)	
≥ 55	9 (10 %)	
IMC (kg/m²)	Values	
Normal (18.5-22.9)	57 (55.3 %)	0.89
Malnourished (≤ 18.5)	38 (36.9 %)	
Overweight (23.0-24.9)	4 (3.9 %)	
Obesity (≥ 25.0)	4 (3.9 %)	
HbA1c (%)	Values	
(≤ 5.7)	95 (95 %)	0.03
(>5.7 ≤ 6.4)	4 (3 %)	
DM (> 6.4)	4 (3 %)	
HTA (mm Hg)	Values	
Systolic pressure ≤ 130	97 (95 %)	0.41
Systolic pressure >130	6 (5 %)	
HIV infection	48 (48 %)	0.04

Men have an ORa of 1.49, 95% CI: 1.26–1.76 as higher odds of TB (Table 2). Age ≥55 years showed a significant association with LTB (Latent tuberculosis) odds ratio 1.46, 95% CI: 1.13-1.89 and ORa = 1.33, 95% CI: 1.1-1.76 (Table 2).

Table 2

Association of clinical comorbidities with CTB 2020-2022.

Variable	OR (95 % CI)	p-Value	ORa (95 % CI)
Socio-demographic characteristics-sex			
Female	Reference	0.001	Reference
Male	1.47 (1.25-1.74)		1.49 (1.26-1.76)

Variable	p-Value			
Years of age				
18-34	Reference	0.018	Reference	0.043
35-44	1.21 (0.98-1.49)		1.23 (0.99-1.52)	
45-54	1.25 (1.01-1.56)		1.24 (0.98-1.57)	
≥ 55	1.46 (1.13-1.89)		1.33 (1.1-1.76)	
IMC (kg/m²)				
Normal (18.5-22.9)	Reference	0.243	Reference	0.389
Malnourished (≤ 18.5)	1.07 (0.78-1.48)		1.15 (0.83-1.60)	
Overweight (23.0-24.9)	0.86 (0.67-1.09)		0.82 (0.64-1.05)	
Obesity (≥ 25.0)	0.85 (0.70-1.03)		0.84 (0.69-1.03)	
HbA1c (%)				
(≤ 5.7)	Reference	0.032	Reference	0.040
(> 5.7-<6.4)	1.11 (1.0-1.35)		1.10 (0.90-1.35)	
DM (> 6.4)	1.26 (1.13-1.65)		1.19 (1.10-1.58)	
HTA (mm Hg)				
Systolic pressure ≤ 130	Reference	0.028	Reference	0.043
Systolic pressure >130	1.28 (1.11-1.62)		1.18 (1.0-1.56)	
HIV infection	Reference	0.019	Reference	0.023
	2.9 (2.5-3.3)		2.7 (2.3-3.1)	

Note: CI, confidence interval.

Prevalence and Association of HIV with TB

The variable *HIV infection* was found in 48 patients (46.6%) with a p-value of 0.019 and 0.023, with an RR (Relative Risk) of 2.9 (2.5-3.3), and an OR (Odds Ratio) of 2.7 (2.3-3.1), as observed in Table 2. It's noteworthy that none of the patients were aware of their seroconversion status.

Prevalence and Association of DM and Carbohydrate Intolerance with TB

The median HbA1c levels among TB, DM, and carbohydrate intolerance were 6.9% (IQR 6.4-8.4) and 5.9% (IQR 5.8-6.1), respectively. There was a significant association between DM (OR = 1.26; 95% CI: 1.13-1.65) and carbohydrate intolerance (OR = 1.11; 95% CI: 1.0-1.35).

Prevalence and Association of BMI with TB

No association was observed between BMI and TB in both adjusted and unadjusted odds ratios (Table 2).

Prevalence and Association of AHT with TB

AHT showed a significant association with TB (OR = 1.28; 95% CI: 1.11-1.62).

Proximate Risk Factors for TB

The study population had at least one non-communicable comorbidity. Patients in the age group of 18-34 years were the most affected (57%), respectively. The most common comorbidity was HIV infection in 48 patients (48%) of them, with a p-value of 0.019 and 0.023, an RR of 2.9 (2.5-3.3), and an OR of 2.7 (2.3-3.1). Carbohydrate intolerance was present in 4 patients (3.88%), with an OR of 1.11 (1.0-1.35) and an adjusted OR (ORa) of 1.10 (0.90-1.35). DM was confirmed in 4 patients (3.88%), with an OR of 1.26 (1.13-1.65) and an ORa of 1.19 (1.10-1.58). Finally, arterial hypertension was found in a total of 6 patients (5.3%), with an OR of 1.28 (1.11-1.62) and an ORa of 1.18 (1.0-1.56). The association was determined by the inclusion of potential confounders in the regression models, adjusted for age, sex, BMI, DM, and AHT.

Discussion

Regarding the findings on the prevalence and association of multimorbid factors in individuals infected with TB, it can be said that household contacts are important representations of areas with severe *M. tuberculosis* transmission. However, the impact of such occurrences on the overall burden of the disease at the community level is still not fully understood.

The transmission of community-classified pulmonary TB accounts for over 80% of the cases, as observed in South Africa (Verver *et al.*, 2004). Less than 1% of households in a community are affected by TB at any given time. The likelihood of exposure of a tuberculous individual to their social network is substantial. In this context, it has been demonstrated that the fraction of household exposure attributed to the population was less than 20% (Martínez *et al.*, 2017).

The participants in this study, who are from a low socioeconomic stratum, have a high likelihood of exposure that could lead to disease transmission in the community. Non-communicable comorbidities such as DM, BMI, and AHT showed a strong association with the risk of

developing pulmonary TB. This study demonstrates that the prevalence of multimorbidity with the highest OR is significantly associated ($p < 0.001$) within the male gender.

A meta-analysis including 12 cross-sectional studies showed that DM is significantly associated as a risk factor for TB (Lee *et al.*, 2016; Hensel *et al.*, 2016; Lin *et al.*, 2019; Jackson *et al.*, 2019). Previous observational studies revealed that diabetics were 3.1 times more likely to have TB than non-diabetics (Jeon & Murray, 2008).

Likewise, Lee *et al.* (2016) demonstrated *age* as an associated factor with both DM and TB. The prevalence of DM and carbohydrate intolerance in the present study was observed to be 3 and 3.9 %, respectively, in individuals with TB. Furthermore, it reported that the crude OR (1.26; 95 % CI: 1.13-1.65) was substantially higher than the ORa (1.19; 95 % CI: 1.10- 1.58). Thus, it supports the existence of an increased risk of TB, although the magnitude of the risk cannot be numerically determined.

Among the many case reports and controlled studies, some have reported significant variations in the presence of HTN among TB patients and controls without TB (Marak *et al.*, 2016). However, AHT did not reveal a direct association or risk factor for the progression of active TB, except in the case of renal TB (Seegert *et al.*, 2017). It is suggested that AHT plays a subtle but significant role in the immune system, thereby increasing the risk of TB, as proposed by Caillon and Schiffrin (2016).

TB could also be indirectly related to AHT through DM, which, in turn, is strongly associated with the risk of cardiovascular disease, as suggested by Ferrannini and Cushman (2016). In this study, HTN showed a significant association with carbohydrate intolerance (ITL) in both unadjusted odds ratio analysis ($p < 0.041$) and adjusted odds ratio analysis ($p < 0.041$). There is a notable overlap between DM and HTN in terms of their etiology and disease mechanisms.

Landsberg and Molitch (2004) stated that in the U.S. population, the occurrence of AHT is 30% in individuals with type 1 DM and 50% to 80% in individuals with type 2 DM. A cohort study

documented that type 2 DM was 2.5 times more likely to develop in people with AHT (Gress *et al.*, 2000). The combination of HTN and DM results in the metabolic syndrome.

Though this study, AHT showed a significant association with DM in pulmonary TB (RR: 2.95; 95% CI: 2.26-4.12; $p < 0.0001$). The combined effect of HIV infection, DM, and AHT remains as predisposing factors, possibly requiring broader cohort studies that encompass different regions nationally and regionally. Therefore, lifestyle optimization remains the cornerstone in the prevention and treatment of DM and HTN, as well as timely implementation of antiretroviral therapy. This, in turn, could significantly help reduce the risk of TB.

The limitations of this study include limited sociodemographic data collection and the need for follow-up to identify individuals infected with TB, particularly contacts who may not always receive an adequate follow-up.

Conclusions

The research indicated a relatively high prevalence of TB burden. HIV infection, DM, as well as carbohydrate intolerance and AHT, were observed as proximate risk factors for TB. The existing trend calls for better management, lifestyle protection, and modification, as well as strengthening surveillance activities, especially in populations diagnosed with HIV-associated or co-infection. This is an imperative need in the ongoing fight to eradicate TB, which has faced setbacks in recent years due to various factors.

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Conflict of interest

The authors declare that they have no conflict of interest.

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