

Nontuberculous mycobacteria in patients registered in a tuberculosis control program in Southwestern Colombia

Micobacterias no-tuberculosa en pacientes registrados en un programa de control de tuberculosis en el suroccidente de Colombia

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Received: 30 January 2019

Accepted: 13 May 2019

Published: 30 June 2019

Keywords: Nontuberculous mycobacteria, pulmonary disease, *Mycobacterium* spp, tuberculosis treatment

Palabras clave: mycobacteria no tuberculosa, enfermedad pulmonar, *Mycobacterium* spp., tratamiento tuberculosis

Citación: Delgado LE, Escobar DR, Hoyos DM, Luna L, Pacheco R, Ferro BE. Nontuberculous mycobacteria in patients registered in a tuberculosis control program in Southwestern Colombia. *ijep*. 2019; 2(1): e-017. Doi: 10.18041/2665-427X/ijep.1.5449.

Abstract

Introduction: Pulmonary disease produced by nontuberculous mycobacteria and pulmonary tuberculosis can share clinical signs and symptoms. It is important to discern one from the other in order to provide the proper treatment and programmatic management.

Objective: To describe the frequency of nontuberculous mycobacteria isolated from patients registered in the tuberculosis control program in Cali.

Methods: We conducted a descriptive study to know what extent of the pulmonary tuberculosis load in Cali-Colombia corresponds to nontuberculous mycobacteria, in a four-year period, 2014-2017. Demographic (sex, age, health insurance), clinical (diagnosis dates, laboratory data, comorbidities) and programmatic data (tuberculosis treatment initiation and duration) was collected for statistical analysis.

Results: Of 3,651 patients registered in the local tuberculosis program with an initial diagnosis of pulmonary tuberculosis, 2,904 had sputum culture and among them 1.5% (43/2904) had nontuberculous mycobacteria isolation rather than *Mycobacterium tuberculosis*. Most of the nontuberculous mycobacteria isolates were not identified at the species level; *M. fortuitum* and *M. abscessus* were the most common species identified. 86% of patients initiated unnecessary tuberculosis treatment.

Conclusion: Nontuberculous mycobacteria isolation from pulmonary samples could be frequent in patients registered in the tuberculosis program in Cali, Colombia. The lack of clinical suspicion, the limited laboratory infrastructure, and the absence of a reporting system could be contributing factors to underestimate the importance of nontuberculous mycobacteria in this setting. We recommend that nontuberculous mycobacteria identification should be considered for public health intervention.

Resumen

Introducción: La enfermedad pulmonar producida por micobacterias no tuberculosas y la tuberculosis pulmonar pueden compartir signos y síntomas. Es importante discernir entre estas dos enfermedades para poder proveer un tratamiento y manejo adecuado para cada una.

Objetivo: Describir la frecuencia de micobacterias no tuberculosas aisladas de pacientes registrados en el programa de control en la ciudad de Cali.

Métodos: se realizó un estudio descriptivo para conocer la carga de micobacterias no tuberculosas con respecto a la tuberculosis pulmonar en Cali, Colombia, en un periodo de cuatro años (2004-2017). Datos demográficos (sexo, edad, aseguramiento en salud), clínicos (diagnóstico, de laboratorio y comorbilidades) y datos del programa (iniciación y duración del tratamiento) fueron recolectados para los análisis.

Resultados: del registro de 3,651 pacientes en el programa de tuberculosis con un diagnóstico inicial de tuberculosis pulmonar, 2,904 se les realizó un cultivo de esputo y entre estos, 1.5% (43/2,904) se les aisló micobacteria no tuberculosa en lugar de *Mycobacterium tuberculosis*. La mayoría de las micobacterias no tuberculosas no se identificaron hasta el nivel de especie. *M. fortuitum* y *M. abscessus* fueron las más frecuentemente identificadas. El 86% de estos pacientes iniciaron un tratamiento innecesario contra la tuberculosis.

Conclusiones: Fueron identificadas Micobacterias no tuberculosas aisladas de esputo en pacientes del programa de control de tuberculosis. La falta de sospecha clínica, la infraestructura limitada de los laboratorios y la ausencia de un sistema de información podría contribuir a subestimar la importancia de micobacterias no tuberculosas. Nosotros recomendamos que la identificación de estas bacterias debe considerarse en una intervención de salud pública.

Key Study Facts

Objective	To describe the frequency of nontuberculous mycobacteria (NTM) isolated from patients registered in the tuberculosis control program in Cali, during the years 2014-2017
Study design	Descriptive study of a historical cohort of patients
Source of data	Registries of the tuberculosis control program of Cali, Colombia, between 2014 and 2017
Population / sample statistical analysis	43 patients presented a NTM isolation rather than <i>Mycobacterium tuberculosis</i> . We used SPSS version 24 for statistical analysis; numerical variables are summarized with median (IQR), qualitative variables are presented as proportions. NTM isolation from pulmonary samples could be frequent in patients registered in the TB program in Cali, Colombia. In a four-year period, from 2014 to 2017, 1.5% of patients diagnosed with pulmonary tuberculosis were infected with NTM and not <i>M. tuberculosis</i> . The lack of clinical suspicion, the limited laboratory infrastructure, and the absence of a reporting system could be contributing factors to underestimate the importance of NTM in this setting
Main finding	



ISSN: 2665-427X

Introduction

Pulmonary disease produced by nontuberculous mycobacteria and pulmonary tuberculosis can share clinical signs and symptoms. Due to similarities in their clinical presentation it is challenging to achieve a correct diagnosis; without the appropriate laboratory studies, many cases of pulmonary disease produced by nontuberculous mycobacteria can be misdiagnosed as pulmonary tuberculosis. It is important to discern one from the other in order to provide the proper treatment and programmatic management: there is no standard pharmacological treatment for pulmonary disease produced by nontuberculous mycobacteria in Colombia and nontuberculous mycobacteria does not respond effectively to most of the current anti-tuberculosis agents (1). Due to this lack of response, some cases may be erroneously classified as resistant or multidrug-resistant pulmonary tuberculosis; it is important to suspect pulmonary disease produced by nontuberculous mycobacteria in patients diagnosed with pulmonary tuberculosis when the standard treatment does not led to the expected outcome (2).

Globally, there is increased identification of nontuberculous mycobacteria from pulmonary samples as etiologic agents of pulmonary disease produced by nontuberculous mycobacteria. However, it is not mandatory to report pulmonary disease produced by nontuberculous mycobacteria cases (3) and in countries with high tuberculosis incidence, there is not enough awareness about nontuberculous mycobacteria and the preparation to deal with the potential problem they can represent is deficient. There is a gap of information on the prevalence and incidence of pulmonary disease produced by nontuberculous mycobacteria in Colombia, however, few studies available evidence an increase in the presentation of nontuberculous mycobacteria infections (4,5). In Cali, the third largest city of Colombia, where tuberculosis incidence is one of the highest in the country (44 cases per 100,000 inhabitants) (6), it is important to know how many of the pulmonary tuberculosis cases can correspond to pulmonary disease produced by nontuberculous mycobacteria. Here we describe the frequency of nontuberculous mycobacteria isolated from patients registered in the tuberculosis program in Cali, during the years 2014-2017.

Methods

We conducted a descriptive study of a historical cohort of patients registered in the tuberculosis program of Cali, Colombia, between 2014 and 2017. The study population was the registries of symptomatic respiratory patients with an initial diagnosis of pulmonary tuberculosis by direct sputum smear microscopy and culture, provided by local health authorities. Demographic (sex, age, health insurance), clinical (diagnosis dates, laboratory data, comorbidities) and programmatic data (tuberculosis treatment initiation and duration) was collected. According to registries, Lowenstein-Jensen media was used for Mycobacterial isolation and identification, when available, was performed with commercial molecular probes.

We used SPSS version 24 for statistical analysis; numerical variables are summarized with median (IQR), qualitative variables are presented as proportions.

Universidad Icesi Institutional Review Board Ethical provided approval (#238/2017).

Results

Of 3,651 patients registered in the local tuberculosis program with an initial diagnosis of pulmonary tuberculosis during 2014-2017, 2,904 had sputum culture and among them 1.5% (43/2904) presented a nontuberculous mycobacteria isolation rather than *Mycobacterium tuberculosis*. The number of effective nontuberculous mycobacteria identifications was variable through these years and depended on local laboratory capacity. Most of the isolates were not identified at the species level; from 12 nontuberculous mycobacteria isolates identified, *M. fortuitum* and *M. abscessus* were the most common species, both being rapidly growing mycobacteria (Figure 1). Four patients had more than one specimen with nontuberculous mycobacteria isolation.

Almost half of the patients were women (51.2%), the median age was 55 years (IQR 46-71) and the most common health

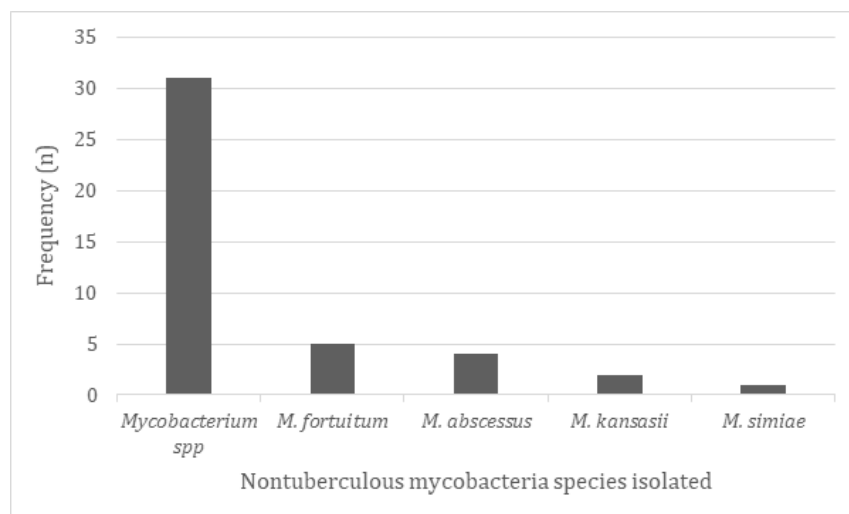


Figure 1. Frequency of nontuberculous mycobacteria in pulmonary samples of patients registered in the tuberculosis program of Cali, Colombia, 2014-2017.

insurance was the public subsidized (58.1%). History of previous tuberculosis was present in 14% of patients (6/43). The most frequent comorbidity was diabetes (9/43), followed by HIV co-infection (4/43) and cardiovascular disease (4/43) (Table 1).

Pulmonary tuberculosis treatment was wrongly initiated to 86% (37/43) of patients with nontuberculous mycobacteria isolates, out of those 54.1% (20/37) completed the entire regimen; a median permanency time in the tuberculosis program was 138 days. No radiological findings were available for the patients with NTM isolation. Two patients had died at the time we conducted this study, but causes were unknown.

Discussion

There is a global increased attention on nontuberculous mycobacteria as the causative agents of disease in humans. Which is demonstrated by the emergence of reports from different regions and countries (3,7-11). Several studies on the epidemiology of nontuberculous mycobacteria-related diseases in low and middle-income countries support this trend (5). Brazil reported increasing from 2007 to 2013 number of pulmonary disease cases produced by nontuberculous mycobacteria. This is partly explained by a higher awareness of nontuberculous mycobacteria in the health community and/or better laboratory capacity (7,8).

This is the first report showing the presence of nontuberculous mycobacteria isolates in patients originally diagnosed with pulmonary tuberculosis in Colombia. Our study provides a baseline information that will help to make visible nontuberculous mycobacteria within tuberculosis control programs in the country, where some patients can be misclassified as having resistant or multidrug-resistant tuberculosis (2,10). Although, 1.5% of the cultures presented a nontuberculous mycobacteria isolation, sputum culture was not available for all the cases in this study and initial tuberculosis diagnosis relied on direct smear; this could have led to a sub-registry of nontuberculous mycobacteria.

In this study, an important proportion of nontuberculous mycobacteria isolates remained unidentified at the species level.

Nevertheless, it should be noted that rapidly growing mycobacteria were more frequently isolated in contrast to the global trend of nontuberculous mycobacteria distribution that shows slowly growing mycobacteria and particularly *Mycobacterium avium* complex (MAC) as the most frequent species (7-11). In order to obtain a better picture of distribution of nontuberculous mycobacteria in Colombia and to conduct future studies on the clinical significance of circulating species producing pulmonary disease, it is necessary to strengthen laboratory capacity for the isolation and identification of nontuberculous mycobacteria through currently recommended methods like PCR and partial sequencing of genes like *rpoB* and *hsp65* (10).

The likelihood of nontuberculous mycobacteria to cause lung disease increases with previous tuberculosis infection and HIV (5,8,9). In one study in Brazil, common comorbidities of patients diagnosed with nontuberculous mycobacteria infection were bronchiectasis, chronic obstructive pulmonary disease, cardiovascular disease, and HIV. Surprisingly, 85% of the patients received tuberculosis treatment (8). In our study, diabetes and previous tuberculosis were common, and HIV coinfection was detected in 9.3% of patients. Unfortunately, we were not able to establish pulmonary disease produced by nontuberculous mycobacteria according to American Thoracic Society/Infectious Diseases Society of America criteria (12) due to the lack of imaging and incomplete microbiological information. For a better description of the local epidemiology of nontuberculous mycobacteria-related diseases in Cali, Colombia, personnel from the local Secretary of Health is being sensitized towards the importance of visiting patients infected with nontuberculous mycobacteria and collecting clinical, radiological and microbiologic information.

Conclusion

Nontuberculous mycobacteria isolation from pulmonary samples could be frequent in patients registered in the tuberculosis program in Cali, Colombia. In a four-year period, from 2014 to 2017, 1.5% of patients diagnosed with pulmonary tuberculosis were infected with nontuberculous mycobacteria and did not have *M. tuberculosis*. The lack of clinical suspicion, the limited

Clinical and demographic characteristics		n (%)
Age: Median (IQR)		55 (46-71)
Sex	Female	22 (51.2)
Health insurance	Public subsidized	25 (58.1)
	Private	18 (41.9)
Comorbidities*	Diabetes	9 (20.9)
	HIV	4 (9.3)
	Cardiovascular disease	4 (9.3)
	Smoking-Alcoholism	3 (7.0)
	Malnutrition	3 (7.0)
	None	22 (51.2)
TB program permanency: Median in days (IQR)	138 (37-229)	

*Some patients have multiple comorbidities

laboratory infrastructure, and the absence of a reporting system could be contributing factors to underestimate the importance of nontuberculous mycobacteria in this setting. Under the current circumstances, nontuberculous mycobacteria findings are occasional, but an active search will allow a better understanding of the nontuberculous mycobacteria load among patients presumptively diagnosed with tuberculosis in Cali and other similar settings. Additionally, patients misdiagnosed with tuberculosis, but actually infected with nontuberculous mycobacteria often suffer, partly because they are confused due to misdiagnosis, erroneous treatment or poor follow up due to the complex health system, therefore we recommend that nontuberculous mycobacteria identification should be considered for public health intervention.

Conflict of interest

Authors declare no conflict of interests.

Acknowledgements

We would like to thank Sustainable Sciences Institute for the valuable review of manuscript drafts, and to Liliana Forero, Fernanda Ortiz and Yesenia Niño for kindly provide preliminary information on programmatic reports.

Founding:

Universidad Icesi supported this study (COL0099642-837).

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