pagepress

Tailored treatment for tuberculosis in transgender individuals: a call for a patient-centered approach from a large Italian cohort

Niccolò Riccardi,[1,2] Roberta Maria Antonello,[1] Maurizio Ferrarese,[1,3] Alice Repossi,[1,3] Laura Saderi,[1,4] Giovanni Fumagalli,[1,3,5] Giorgio Besozzi,[1] Giovanni Sotgiu,[1,4] Luigi Codecasa[1,3]

[1]StopTB Italia ODV, Milan; [2]Infectious Diseases Unit, Department of Clinical and Experimental Medicine, University of Pisa; [3]Regional TB Reference Center, Villa Marelli Institute, Niguarda Hospital, Milan; [4]Clinical Epidemiology and Medical Statistics Unit, Department of Medical, Surgical and Experimental Sciences, University of Sassari; [5]Pulmonology Unit Niguarda Hospital, University of Milan, Italy

Abstract

Tuberculosis (TB) diagnosis and management in special populations remain challenging. Data about TB and transgender individuals is scarce, and strategies aimed at reducing the TB burden in this at-risk group are needed. We conducted an observational monocentric study from a national reference center for TB, including transgender individuals with active TB in a low-TB burden country (Italy), over 34 years (1990-2023).

A total of 66 transgender males and 2 transgender females (median age 30 years, interquartile range 26-38 years, 65 migrants) were included. Most patients (38/66, 57.6%) lived in poor social conditions. 65.2% (43/66) of patients were people living with HIV. Multidrug- and rifampicin-resistant TB and isoniazid-resistant TB were diagnosed in 5 (7.6%) and 3 (4.5%) patients, respectively. The overall treatment success rate was 72.7% (48/66 patients), with differences observed according to social conditions. Our study highlights the need for a tailored approach to increase treatment success in this at-risk population.

Correspondence: Roberta Maria Antonello, StopTB Italia ODV, Viale Zara 81, Milano 20159, Italy.
E-mail: rma.roby@gmail.com

Key words: tuberculosis, RR/MDR-TB, pre-XDR-TB, outcome.

Contributions: NR, RMA, MF, GB, LC, conceived the study; NR, RMA, GF, LC, collected data; NR, RMA, LS, GS, performed statistical analysis; NR, RMA, wrote the first version of the manuscript and designed graphs and tables and equally contributed; all authors reviewed the draft and approved the final version of the manuscript.

Conflict of interest: the authors have no financial or non-financial conflicts of interest to declare.

Ethics approval and consent to participate: the study received ethical approval n. 578–112,018 from the ethical committee of ASST Niguarda Ca′ Granda in Milan (Italy) and it was conducted in agreement with the Declaration of Helsinki (1964) and its later amendments.

Patient consent for publication: not applicable. This retrospective study was performed with anonymized data from clinical records.

Availability of data and materials: full data set is available from the corresponding author upon reasonable request.

Funding: none.

Received: 19 November 2023.
Accepted: 12 December 2023.
Early view: 11 January 2024.

Publisher's note: all claims expressed in this article are solely those of the authors and do not necessarily represent those of their affiliated organizations, or those of the publisher, the editors and the reviewers. Any product that may be evaluated in this article or claim that may be made by its manufacturer is not guaranteed or endorsed by the publisher.

Monaldi Archives for Chest Disease 2025; 95:2852
doi: 10.4081/monaldi.2024.2852

Introduction

With estimates of a quarter of the world population living with *Mycobacterium tuberculosis* and 10.6 million people diagnosed with active tuberculosis (TB) in 2021, disparities in diagnosis, access to care, and management are still experienced worldwide [1]. Management is particularly difficult in high TB burden low-income countries due to logistic difficulties and economic limitations. Likewise, in low TB burden high-income countries, some difficulties are met in reaching, testing, and treating special populations, such as migrants, incarcerated people, and people experiencing homelessness or sheltered housing conditions [2,3].

TB treatment and diagnosis are also challenging in transgender individuals due to difficulties both in screening and follow-up connected with social stigmatization [4]. In high-income countries, many transgender individuals resettle from high TB burden countries, resulting at higher risk of TB reactivation within 2 years from migration as well as with a higher probability of rifampicin-resistant (RR)/multidrug-resistant (MDR)-TB compared to natives of the destination countries [5].

Data on epidemiology, management, and treatment outcomes are extremely limited in transgender individuals, especially in low TB burden countries.

Materials and Methods

We conducted an observational, retrospective monocentric study including transgender individuals diagnosed with active TB at the Villa Marelli reference center for TB diagnosis and management in the metropolitan area of Milan (Italy), between 1/1/1990 and 30/06/2023.

The primary objective of the study was to describe the epidemi-

ological features of the study cohort. Secondary objectives were the evaluation of resistance patterns and clinical outcomes. Patients with TB infection and no signs of active disease were excluded. No age limits were set. The patients' nations of origin were classified according to the World Health Organization (WHO) region classification.

TB diagnosis was made when a subject met clinical/radiological and/or microbiological criteria. Clinical and radiological criteria included signs, symptoms, and/or imaging findings consistent with active TB in any site or the clinician's decision to treat the patient with anti-TB regimens [6].

Microbiological criteria included positive microscopy for acid-fast bacilli and/or culture, and detection of *M. tuberculosis* complex nucleic acid in a clinical specimen with GeneXpert® (after its clinical introduction in 2010) [6]. Miliary TB and cases involving both lungs and other sites were classified as pulmonary TB (PTB) due to lung involvement.

For each patient, we collected the following data: gender, age, WHO region of origin, more or less than 2-year stay in Italy, social background, legal status of regularity, first diagnosis or recurrence/re-treatment, PTB or extrapulmonary TB (EPTB) and site of EPTB, inpatient or outpatient management, pattern of *M. tuberculosis* resistance and treatment outcome. We reported whether the patients arrived in Italy 2 or fewer years prior to presentation, as this is generally considered a cut-off for a higher risk of TB reactivation [7]. Treatment outcomes were classified according to the WHO definitions [8].

The study received ethical approval n. 578-112,018 from the ethical committee of ASST Niguarda Ca' Granda in Milan (Italy), and it was conducted in agreement with the Declaration of Helsinki (1964) and its later amendments.

All data collected remained anonymous and it was not possible to link any patients to the collected data. Strengthening the Reporting of Observational Studies in Epidemiology recommendations were followed. The study received no internal or external funding, nor did the investigators receive payments for the research.

Results

A total of 66 transgender males and 2 transgender females (median age 30 years, interquartile range 26-38 years, 65 migrants) were included: 63 (95.5%) from the WHO region of Americas, 1 (1.5%) from the western Pacific region, 1 from the south-east Asian region, and 1 from the European region. Despite the population size not allowing the identification of a stable trend line, an overall rising trend was observed over the years up until the COVID-19 pandemic (Figure 1).

Almost half of the patients (30/66; 45.5%) had transferred to Italy ≤2 years before presentation. A total of 38 (57.6%) patients lived in poor social conditions (they did not have their own home nor a job), 24 (36.3%) had intermediate social conditions (they lived at home but did not have a job, or *vice versa*), and 4 (6.1%) reported excellent social conditions.

Most patients (54/66, 81.8%) did not have a regular resident permit. A total of 43 (65.2%) patients were people living with HIV; 55 (83.3%) patients had PTB or disseminated TB, while 11 (16.7%) had EPTB. Localization of EPTB was as follows: head-neck lymph nodes (4 patients), other extra-thoracic lymph nodes (2 patients), pleura (3 patients), central nervous system (1 patient), heart (1 patient), abdomen (1 patient).

Sputum culture was positive in 46/66 (69.7%) of patients (compared to 54.5% of sputum microscopy and 62.1% of molecular test). Most cases (57/66, 86.4%) were first diagnosed, while 9 patients (13.6%) were recurrence of TB. With regards to antimicrobial susceptibility test, 5 (7.6%) RR/MDR-TB and 3 (4.5%) isoniazid-resistant TB were diagnosed. Other patterns of resistance included 1 case of rifampin and streptomycin resistance and 3 cases of streptomycin monoresistance.

Overall treatment success rate was 72.7% (48/66 patients), with differences observed according to social conditions (Figure 2). Among patients with RR/MDR-TB, 4/5 (80%) successfully completed treatment. A full description of the study cohort is provided in Table 1.

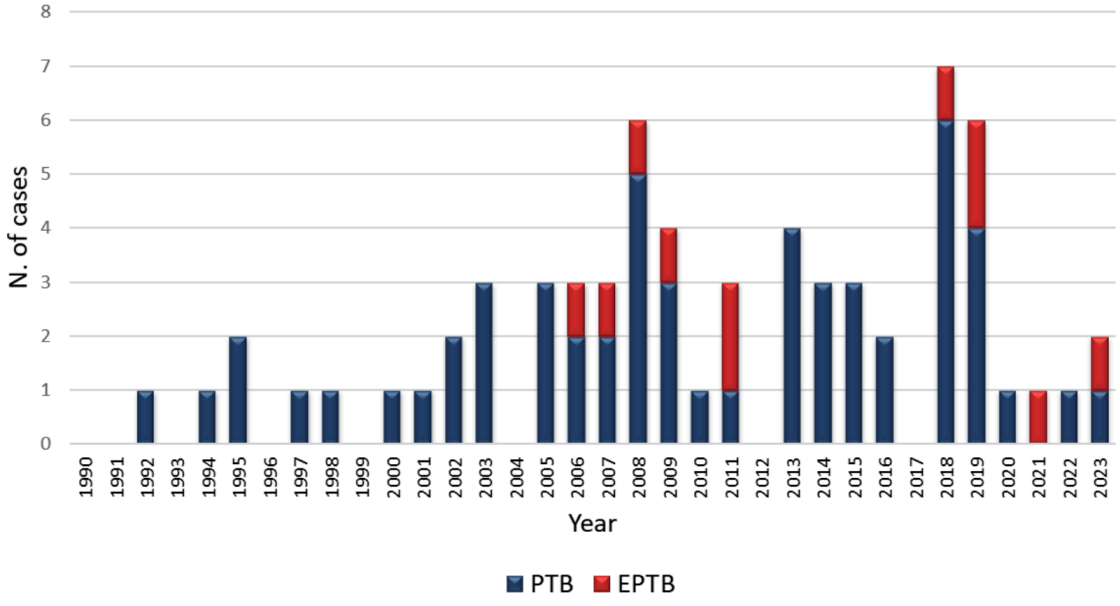

Figure 1. Notified cases of pulmonary tuberculosis (blue) and extrapulmonary tuberculosis (red) per year in the study population. PTB, pulmonary tuberculosis; EPTB, extrapulmonary tuberculosis.

Discussion

Our study describes one of the largest European cohorts of transgender individuals with TB, offering some insights.

First, an overall increasing trend of newly diagnosed cases of TB in transgender individuals was observed; however, since the beginning of the COVID-19 pandemic, the number of new cases of TB per year has significantly decreased, suggesting a possible gap in diagnosis and the need for effective efforts to recover the missed cases [9,10].

Second, most patients were from high TB burden countries, and high resistance rates (12.1% of patients with isoniazid-resistant or MDR-TB) were detected. This underlines the extreme need for active surveillance reaching special populations also in terms

Table 1. Descriptive analysis of the study population.

Variables		Total (n=66)
Year of diagnosis, n (%)	1990-1994	2
	1995-1999	4
	2000-2004	7
	2005-2009	19
	2010-2014	11
	2015-2019	18
	2020-2023	5
Median (IQR) age, years		30 (26-38)
Transgender males, n (%)		64 (97.0)
WHO Region of origin, n (%)	European region	1 (1.5)
	African region	-
	region of Americas	63 (95.5)
	Eastern Mediterranean	-
	South-east Asian region	1 (1.5)
	Western Pacific region	1 (1.5)
Stay in Italy, n (%)	Italian	1 (1.5)
	Transferred ≤ 2 years	30 (45.5)
	Transferred > 2 years	35 (53.0)
TB form, n (%)	New case	57 (86.4)
	Recurrence	9 (13.6)
Site of infection, n (%)	PTB or PTB + EPTB	55 (83.3)
	EPTB	11 (16.7)
Sputum microscopy, n (%)	NA	11 (16.7)
	Positive	36 (54.5)
	Negative	19 (28.8)
Sputum culture, n (%)	NA	15 (22.7)
	Positive	46 (69.7)
	Negative	5 (7.6)
Molecular test, n (%)	NA	19 (28.8)
	Positive	41 (62.1)
	Negative	6 (9.1)
Resistance, n (%)	Susceptible	54 (81.8)
	Rifampin monoresistance	-
	Isoniazid monoresistance	3 (4.5)
	MDR-TB	5 (7.6)
	Other pattern of resistance	4 (6.1)
HIV coinfection, n (%)		43 (65.2)
Therapy setting, n (%)	Outpatient therapy only	15 (22.7)
	Started as inpatient and continued as outpatient	51 (77.3)
Social conditions, n (%)	Excellent	4 (6.1)
	Intermediate	24 (36.4)
	Poor	38 (57.6)
Resident permit, n (%)	NA	2 (3)
	Yes	10 (15.2)
	No	54 (81.8)
Treatment outcome, n (%)	Treatment success	48 (72.7)
	Loss to follow-up	17 (25.8)
	Death	1 (1.5)

EPTB, extrapulmonary tuberculosis; HIV, human immunodeficiency virus; IQR, interquartile range; MDR-TB, multidrug-resistant tuberculosis; NA, not available; PTB, pulmonary tuberculosis; TB, tuberculosis; WHO, World Health Organization.

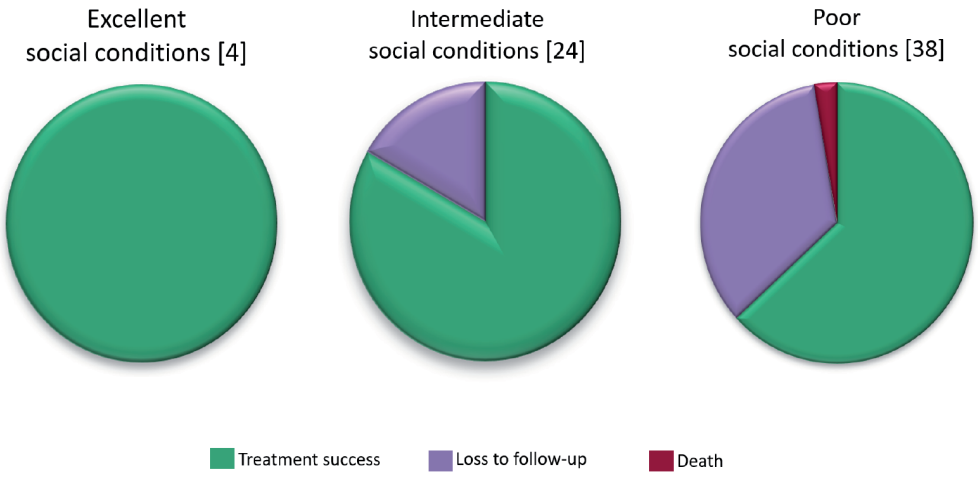

Figure 2. Clinical outcomes. Numbers in square brackets refer to the number of cases.

of public health, as treatment success rates are much lower in patients with RR/MDR-TB and pre-extensively drug-resistant-TB, with less than half of the patients completing treatment [1]. In our cohort, all except one patient with MDR-TB successfully completed treatment, but the overall treatment success rate was lower than the target set by the WHO in the End TB Strategy.

Third, economic conditions and social factors play a key role in TB management, and significant disparities in treatment outcomes were observed among different social condition groups, highlighting the need for an integrated medical and social approach in at-risk populations.

The main strength of our study is the description of a large cohort of transgender individuals diagnosed with TB and treated in a referral Italian center for TB over a long study period. Among limitations, due to the retrospective design of the study, some data were missing, and the study population, despite being one of the largest described, was too limited to make general assumptions.

Conclusions

A tailored patient-centered approach taking into account social and economic aspects, as well as health education actions aiming at stigma reduction, is crucial to optimize screening, management, and follow-up and to obtain high retention in care in transgender individuals with TB.

References

1. World Health Organization. Global tuberculosis report 2022. Available from: https://iris.who.int/bitstream/handle/10665/363752/9789240061729-eng.pdf?sequence=1.
2. Matucci T, Riccardi N, Occhineri S, et al. Treatment of latent tuberculosis infection in incarcerated people: a systematic review. Clin Microbiol Infect 2023;29:714-21.
3. Riccardi N, Antonello RM, Ferrarese M, et al. Tuberculosis in migrants: epidemiology, resistance and outcome in Milan, Italy. Infect Dis 2023;55:543-50.
4. Shah SA, Qayyum S, Baig S, et al. Results of community-based TB and HIV screening among transgender women and male sex workers in Pakistan. PLOS Glob Public Health 2023;3:e0000913.
5. Pareek M, Greenaway C, Noori T, et al. The impact of migration on tuberculosis epidemiology and control in high-income countries: a review. BMC Med 2016;14:48.
6. Commission of the European Communities. Commission decision of 28 April 2008 amending decision 2002/253/EC laying down case definitions for reporting communicable diseases to the Community network under decision no 2119/98/EC of the European Parliament and of the Council. In: Official Journal, L159/46, 18/06/2008.