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

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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). Sixty-six transgender males and two 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 tuberculosis and isoniazid-resistant TB were diagnosed in five (7.6%) and three (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.

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

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 challenging also 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 burden TB countries, resulting at higher risk of TB reactivation within two years from migration as well as with an higher probability of RR/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 epidemiological 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 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 (AFB) 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 two or less years prior to presentation as this is generally considered a cut-off for 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 (STROBE) recommendations were followed. The study received no internal or external fundings, nor did the investigators receive payments for the research.

Results

Sixty-six transgender males and two transgender females (median age 30 years, IQR 26 - 38 years, 65 migrants) were included: 63 (95.5%) from the WHO Region of Americas, one (1.5%) from the Western Pacific Region, one from the South-East Asian Region, and one from the European Region. Despite the population size not allowing to identify a stable trend line, an overall rising trend was observed over years up until COVID-19 pandemic (Figure 1).

Almost half of patients (30/66; 45.5%) had transferred to Italy ≤ 2 years prior to presentation. Thirty-eight (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. Forty-three (65.2%) patients were people living with HIV (PLWHI). Fifty-five (83.3%) patients had pulmonary or disseminated TB (PTB), while 11 (16.7%) had EPTB. Localization of EPTB was as follows: head-neck lymph nodes (four patients), other extra-thoracic lymph nodes (two

patients), pleura (three patients), central nervous system (one patient), heart (one patient), abdomen (one 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 nine patients (13.6%) were recurrence of TB. With regards to antimicrobial susceptibility test (AST), five (7.6%) RR/MDR-TB and three (4.5%) isoniazid-resistant TB were diagnosed. Other patterns of resistance included one case of rifampin and streptomycin resistance and three 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. Full description of the study cohort is provided in Table 1.

Discussion

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

First, an overall increasing trend of new diagnosed cases of TB in transgender individuals was observed; however, since the beginning of SARS-CoV-2 pandemic, the number of new cases of TB per year 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 of public health, as treatment success rates are much lower in patients with RR/MDR- and pre-XDR-TB, with less than half patients completing treatment [1]. In our cohort, all except one patient with MDR-TB successfully completed treatment, but 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 outcome 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.
7. Getahun H, Matteelli A, Chaisson RE, Raviglione M. Latent mycobacterium tuberculosis infection. *N Engl J Med* 2015;372:2127-35.
8. World Health Organization. WHO consolidated guidelines on tuberculosis. Module

4: treatment - drug-resistant tuberculosis treatment, 2022 update. Available from: <https://iris.who.int/bitstream/handle/10665/365308/9789240063129-eng.pdf?sequence=1>.

9. Canetti D, Antonello RM, Saderi L, et al. Impact of SARS-CoV-2 infection on tuberculosis outcome and follow-up in Italy during the first COVID-19 pandemic wave: a nationwide online survey. *Infez Med* 2022;30:418-26.

10. Morrison H, Perrin F, Dediccoat M, et al. Impact of COVID-19 on NHS tuberculosis services: Results of a UK-wide survey. *J Infect* 2023;87:59-61.

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 \leq 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 ad 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, multidrug-resistant; NA, not available; PTB, pulmonary tuberculosis; WHO, World Health Organization.

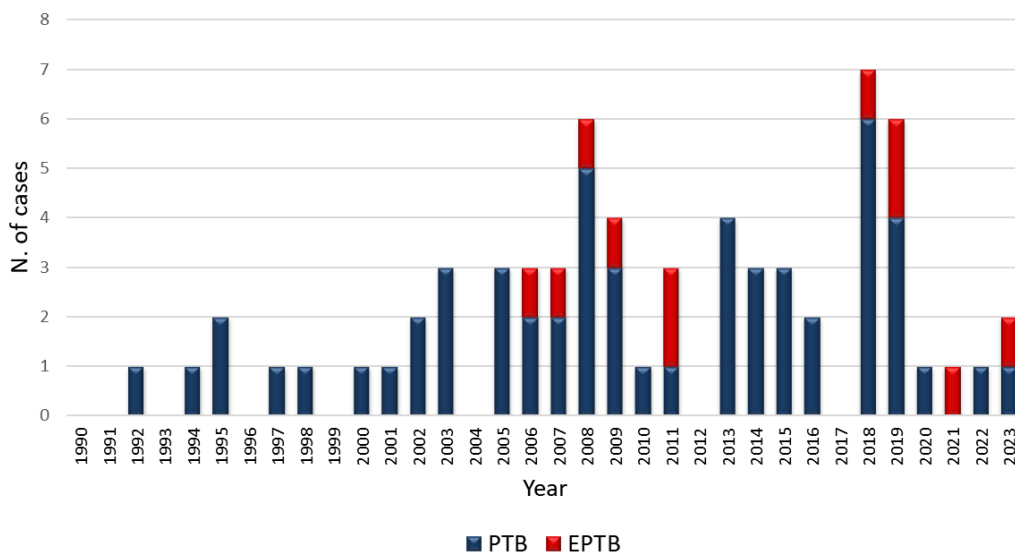


Figure 1. Notified cases of pulmonary tuberculosis (blue) and extrapulmonary tuberculosis (red) per year in the study population.

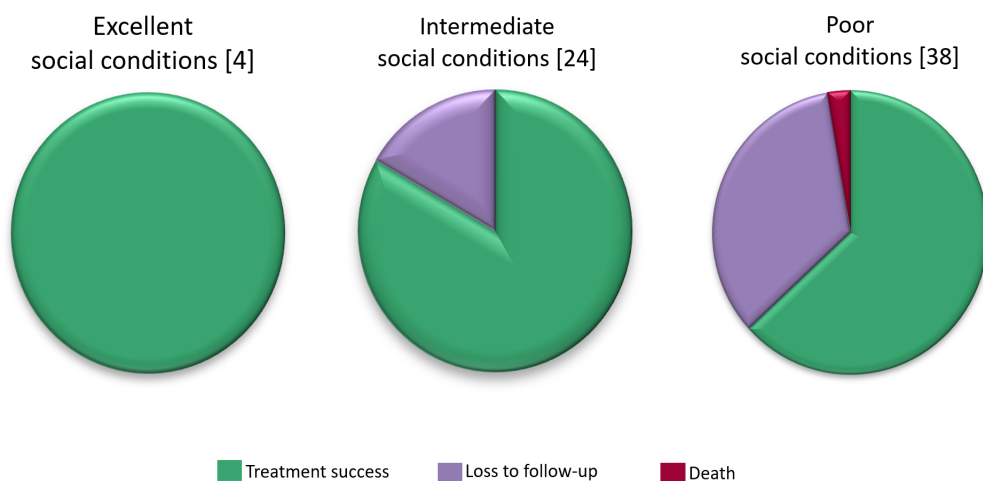


Figure 2. Clinical outcomes. Numbers in square brackets refer to the number of cases.