

## **Original article**

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# Mycobacterium tuberculosis complex bacteremia among HIV and non-HIV patients in a Mexican tertiary care center



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#### ABSTRACT

*Objectives*: To determine the factors associated with Mycobacterium tuberculosis complexpositive blood culture.

*Methods*: Case-control study. Sociodemographic, clinical and laboratory data were collected from 2000 to 2015.

Results: We reviewed medical records of 533 patients with culture-proven tuberculosis, of whom 27.2% (145/533) had blood culture available. Patients with mycobacteremia presented more frequently with abdominal tuberculosis, body mass index <18 kg/m<sup>2</sup>, and had lower hemoglobin and albumin levels. No differences were observed regarding HIV status.

Conclusions: Few studies have reported on the characteristics associated with Mycobacterium tuberculosis complex bacteremia, especially among Human Immunodeficiency Virus-negative patients. Out of 145 tuberculosis-infected patients with blood culture results available, 21 turned out positive. Anemia, hypoalbuminemia, and a body mass index < 18 kg/m<sup>2</sup> were associated with mycobacteremia.

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#### Introduction

Tuberculosis (TB) is still a major cause of mortality in most regions of the world. This highly transmisible infectious disease is caused by the Mycobacterium tuberculosis complex (MTBC), a closely related group of mycobacteria.<sup>1</sup> Since the majority of the cases are pulmonary, it is considered a respiratory infection; therefore, most TB cases are diagnosed through smear microscopy, mycobacterial culture, and more recently PCR mainly from respiratory samples. Nevertheless, extrapul-

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monary involvement co-exists in 20%–30% of the pulmonary TB cases, mainly due to lymphatic and, in some cases, hematogenous spread. Isolation of MTBC from blood cultures has been reported since the early 20th century from patients with miliary tuberculosis.<sup>2</sup> However, blood culture in mycobacterial infections was rarely requested before the HIV era,<sup>3</sup> but its use has been boosted by improvements in blood culture media, mainly for differential diagnosis with Mycobacterium avium-intracellulare complex or Histoplasma capsulatum. In most geographic regions, lytic blood cultures supporting mycobacteria and fungi growth (i.e., BACTEC Myco-F Lytic or Isolator) are rarely requested for HIV-negative patients suspected of TB.

Most of the data arise from high HIV and TB burden countries, where MTBC is one of the most frequent blood isolates. However, the diagnostic utility of performing lytic blood cultures in an intermediate TB (20-50 cases/1000000, according to the Global Tb report 2017)<sup>4</sup> and low HIV burden as Mexico (HIV prevalence in Mexico as of 2016, according to the Global Health Observatory Data Repository: 0.3%)<sup>5</sup> is unknown, as blood cultures are rarely requested. This is perhaps related to the high cost of cultures compared to other TB diagnostic techniques and the unpractical turnover time for clinical decision making. However, the immunocompromised HIV-negative population is growing, with many presenting high-risk for disseminated tuberculosis, defined by the recovery of MTBC from blood cultures which entails a poor prognosis.<sup>6</sup> In Latin America and the Caribbean, studies reporting blood culture positivity for Mycobacterium spp include mainly patients with advanced HIV infection, MAC isolates, and were mainly conducted in Brazil.<sup>7,8</sup>

Therefore, we aimed to determine the clinical presentation and factors associated with MTBC-positive blood culture in both HIV-infected and HIV-negative patients.

#### Methods

A retrospective analysis was conducted at a national reference center for TB in adult patients in Mexico City. We identified all patients with culture-proven TB for the period 2000–2015 in the clinical microbiology database of the hospital laboratory. The same database was used to identify those patients with available lytic blood culture obtained during the TB episode, with subsequent review of their medical records to obtain sociodemographic, clinical, and laboratory data, including the use of immunosuppressive drugs, and underlying conditions and HIV status. Those patients with blood cultures positive for non-tuberculous mycobacteria (i.e., *M. avium-intracellulare* complex) or fungi were excluded from the analysis.

#### Microbiological methods

The BACTEC MYCO/F LYTIC bottles were available at physician's request during the entire study period. Blood samples were cultured in BACTEC MYCO/F LYTIC medium bottles (Beckton Dickinson, Franklin Lakes New Jersey), following the manufacturer's instructions and incubated for 56 days in the BACTEC-9240<sup>9</sup> apparatus. When positive, bottles were retrieved for Ziehl-Nieelsen stain, and sub-cultured in MGIT tubes for mycobacterial recovery and identification.<sup>10</sup> Upon growth, mycobacteria were identified as MTBC using a DNA probe (Accuprobe, GEN-PROBE, San Diego, CA). Biochemical tests (niacin production, nitrate reduction, thiophen-2carboxylic acid anhydride susceptibility, and pyrazinamidase deamidation) were used for identification of *M. bovis*, confirmed by spoligotyping.

#### Statistical analysis

The characteristics of patients with positive and negative blood cultures were compared by univariate analysis using  $\chi^2$  test, Fisher's exact test, or Mann–Whitney U test, as appropriate. Statistical analyses were performed using STATA 11.0 software (StataCorp, College Station, TX).

#### Ethics

This study was reviewed and approved by the institutional review board (Comisión Institucional de Ética en Investigación REF 952 and 1547). Patient identification data was anonymized for the analysis.

#### Results

During the study period, 533 patients with culture-proven TB were identified and 27.2% (145/533) had an available result of mycobacterial blood culture requested at baseline. Of those, 44.1% (64/145) were HIV-infected, 48.2% (70/145) tested negative for HIV, and 7.5% (11/145) had unknown HIV status. The overall prevalence of MTBC-bacteremia was 14.4% (21/145; 95% CI: 9.1%-21.2%), 17.1% (11/64; 95% CI: 8.9%-28.6%) among HIV-infected and 12.8% (9/70; 95% CI: 6.0%-23.0%) among the HIV-negative patients (p=0.482). One patient with unknown HIV status had MTBC-bacteremia. The median time to positivity of lytic blood cultures for MTBC was eight days (IQR 7–21 days. Blood culture was the only positive culture leading to TB diagnosis in two HIV-infected and one HIV-negative patient.

Patients with MTBC-bacteremia presented more frequently with abdominal TB, underweight (BMI < 18 kg/m<sup>2</sup>), hemoglobin  $\leq$ 10 g/dL, and albumin  $\leq$ 2 g/dL. There was no difference regarding HIV status. In-hospital TB-related mortality rate was 19% (4/21) among MTBC-bacteremia patients and 4.8% (6/124) in those with no bacteremia (p = 0.017) (Table 1). Among patients with MTBC-bacteremia, the median age was 30 years (IQR 29-45) among the HIV-infected and 51 years (IQR 27-54) in HIV-negative patients (p = 0.567); 90% (10/11) of HIV-infected and 55.5% of the HIV-negative patients were male (p = 0.069). The proportion of patients with underweight was higher in the MTBC-bacteremia group (50% vs 14.8%, p = 0.003). Presenting symptoms, radiologic findings, and time to symptoms onset were not statistically different between groups. Positive bone marrow culture was more frequent in patients with MTBCbacteremia (50% vs 12%, p = 0.034). Regarding laboratory test results, hemoglobin level lower than 10 g/dL and albumin levels lower than 2 g/dL were more frequently seen in patients with MTBC-bacteremia.

Among the 10 HIV-negative patients presenting with MTBC-bacteremia, three had systemic lu pus erythematosus

CharacteristicPeritive bioloculture (n=2.1)Negative bioloculture (n=2.4)Peritive bioloculture (n=2.4)A g-, exr, makin (NZ)54 (3-5)64 (3-5)64 (3-5)Sex (mak)N16 (60)64 (3-5)64 (3-5)64 (3-5)C marcino (NZ)10/20 (5)58/8 (50, 2)64 (3-5)64 (3-5)C D cont funct (NZ)60 (7-15)57/4 (1-4)67/4 (1-4)64 (1-4)C D cont funct (NZ)60 (7-15)57/4 (1-4)67/4 (1-4)67/4 (1-4)D algobed with 20 days of TB0/21 (2-7)61/2 (1-4)67/4 (1-4)67/4 (1-4)D algobed with 20 days of TB7/21 (2-7)5/2 (1-4)6/2 (1-4)6/2 (1-4)D algobed with 20 days of TB2/21 (2-7)5/2 (1-4)6/2 (1-4)6/2 (1-4)D algobed with 20 days of TB7/21 (2-7)5/2 (1-4)6/2 (1-4)6/2 (1-4)D algobed with 20 days of TB2/21 (2-7)5/2 (1-4)6/2 (1-4)6/2 (1-4)D algobed with 20 days of TB7/21 (2-7)5/2 (1-4)6/2 (1-4)6/2 (1-4)D algobed with 20 days of TB1/21 (1-1)6/2 (1-4)6/2 (1-4)6/2 (1-4)D algobed with 20 days of TB1/21 (1-4)0/21 (1-4)0/21 (1-4)0/21 (1-4)D algobed with 20 days of TB1/21 (1-4)0/21 (1-4)0/21 (1-4)0/21 (1-4)D algobed with 20 days of TB1/21 (1-4)0/21 (1-4)0/21 (1-4)0/21 (1-4)0/21 (1-4)D algobed with 20 days of TB1/21 (1-4)1/21 (1-4)0/21 (1-4)0/21 (1-4)0/21 (1-4)0/21 (1-4) <th colspan="4">Table 1 – Characteristics of patients with Mycobacterium tuberculosis complex bacteremia.</th>	Table 1 – Characteristics of patients with Mycobacterium tuberculosis complex bacteremia.			
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Sex (male)15/21 (7.14)39/124 (66.9)0.68Underweight8/76 (50)15/08 (14.8)001BGC vaccination9/12 (75)58/85 (68.2)0.63HIV coinfection11/20 (55)35/44 (73.3)0.77CD4 count : 200 cells/mm³6/8 (75.0)35/44 (73.3)0.73Diagnosed within 30 days of TB8/11 (72.7)2/52 (50)0.66Diabetes mellitus2/21 (9.5)16/124 (12.9)0.66Connercive tissue disease3/21 (4.7)16/124 (12.9)0.68Solid or Hematologi malignarey12/21 (4.7)6/124 (4.8)0.988Charlson comorbidity index, median (10,8)76 (37-118)6/124 (4.8)0.892Symptoms76 (37-118)6/124 (4.8)0.6310.631Respiratory symptoms11/21 (4.9)0.612 (4.8)0.632Night sweats8/21 (8.1)6/124 (48.54)0.592Respiratory symptoms11/21 (54.3)6/124 (48.54)0.888Catoritestinal symptoms11/21 (4.5)6/124 (4.8)0.812Additional istes of MTBC isolation11/21 (54.3)6/124 (24.9)0.812Pulnonary14/21 (16.6)89/124 (71.7)0.630.625Central nervous system2/21 (9.5)18/124 (1.5)0.63Catoritestinal symptoms1/21 (4.3)2/124 (16.9)0.29Central nervous system2/21 (9.5)18/124 (1.7)0.63Catoritestinal symptoms1/21 (4.7)3/124 (2.4)0.99Catoritestinal symptoms1/21 (4.7)3/124 (2.	Age, years, median (IQR)	34 (38–54)	36 (28–51)	0.92 <sup>b</sup>
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BCC succination         912 (7)         58/85 (68.2)         0.63           HV colip(cin)         11/20 (55)         51/14 (46.4)         0.48           CD4 count ≤100 cells/mm <sup>3</sup> 60 (75.0)         35/4 (79.5)         0.37           CD4 count ≤100 cells/mm <sup>3</sup> 60 (75.0)         35/4 (79.5)         0.393           Dignosed units 00 days of TB         8/11 (72.7)         26/52 (50)         0.66           Diabetes mellitus         2/21 (4.2)         14/24 (11.2)         0.69           Solid or Hematologic malignancy         2/21 (4.7)         6/124 (4.2)         0.838           Charlson comorbidity index, median (1QN)         7 (67-118)         6/124 (4.5)         0.838           Symptoms         17/21 (00.9)         06/124 (85.4)         0.592           Weight loss         17/21 (00.9)         06/124 (85.4)         0.216           Night swasts         8/21 (38.1)         6/124 (56.1)         0.266           Symptoms         11/21 (64.3)         6/124 (5.1)         0.818           Casto intensities of MTBC isolation         11/21 (65.0)         0.214         0.59           Use of inmunosuppressive drugs         4/21 (33.3)         21/24 (16.9)         0.214           Shin, joint, bone, and soft tissue         0/21 (0.3)         21	Underweight	8/16 (50)	16/108 (14.8)	0.001
IIV conjection11/20 (c5)53/14 (46,4)0.48CD4 court ::00 cells/mP6/8 (75.0)37.5 (21.94.5)0.73CD4 court ::00 cells/mP6/17(2.7)26/52 (50)0.16Diagnosed uithin 30 days of TB8/11 (7.7)26/52 (50)0.66Connective tissue disease3/21 (4.7)14/124 (1.2)0.69Connective tissue disease1/21 (4.7)1/24 (4.8)0.888Charlson comorbidity index, median (UQN)5 (1-6)3.5 (0-6)0.685Symptomssymptoms onset, days, median (UQN)76 (37-118)0.67124 (6.54)0.592Symptoms onset, days, median (UQN)76 (37-118)0.69123 (56.1)0.126Rever1/21 (4.5)1/21 (4.5)0.126Night sweats8/21 (38.1)69/123 (56.1)0.126Night sweats8/21 (19.0)21/24 (15.9)0.631Additional sites of MTBC isolation1/21 (4.7)21/24 (15.9)0.631Additional sites of MTBC isolation21/12 (19.0)21/124 (16.9)0.025Central nervous system2/21 (19.3)21/124 (12.9)0.631Addominal5/21 (19.1)1/21 (4.7)0.324 (2.4)0.924Central nervous system2/21 (19.1)21/124 (1.9)0.251Central nervous system2/21 (19.1)3/124 (2.4)0.324Charlangaphy pattern1/21 (4.7)3/124 (2.4)0.331Normal3/19 (15.7)16/122 (12.1)0.33Sin, joint, bone, and soft tissue3/19 (10.1)3/124 (2.4)0.331Lipwi	BGC vaccination	9/12 (75)	58/85 (68.2)	0.63
CD4 court = 100 cells/mm <sup>2</sup> 6/7 5/0         35/44 (79.5)         0.77           CD4 court menu (DQ)         60 (7-185 5)         35 (21-94.5)         0.393           Diagnosed within 90 days of TB         8/11 (72.7)         26/52 (50)         0.16           Diabets mellitus         2/21 (14.2)         14/124 (11.2)         0.66           Concretive tissue disease         3/21 (14.2)         6/124 (4.1)         0.988           Solid or Hematologic malignancy         1/21 (4.7)         6/124 (4.8)         0.685           Symptoms         5 (1-6)         30 (6-6)         0.685           Symptoms onset, days, median (tQR)         7.6 (37-118)         6/124 (85.4)         0.592           Weight loss         1/21 (0.9)         06/124 (85.4)         0.592           Weight loss         1/21 (0.9)         06/124 (85.4)         0.592           Weight loss         1/21 (14.5)         0.712 (5.5)         0.266           Respiratory symptoms         1/21 (24.3)         0.7124 (54)         0.888           Cattrait symptoms         4/21 (33.1)         2/124 (15.9)         0.81           Additional sites of MTBC isolation         1         1         0.54           Pulmonary         1/21 (66.5)         3/21 (42.1)         0.31	HIV coinfection	11/20 (55)	53/114 (46.4)	0.48
CD4 court mean (IQR)         607-185.5)         37.5 (21-94.5)         9.999           Diagnosed within 90 days of TB         8/11 (7.7)         26/22 (50)         0.16           Diabetes mellitus         2/21 (9.5)         16/124 (12.9)         0.66           Connective tissue disease         3/21 (14.2)         14/124 (11.2)         0.99           Solid or Hematologie malignany         1/21 (4.7)         61/214 (4.8)         0.988           Charlson comorbidity index, median (IQR)         5 (1-6)         0.631         0.631           Symptoms	CD4 count $\leq$ 100 cells/mm <sup>3</sup>	6/8 (75.0)	35/44 (79.5)	0.77
Diagnosed uithin 90 days of TB         V11 (72.7)         26/52 (50)         0.16           Diabetes mellitus         2/21 (9.5)         16/124 (12.9)         0.66           Connective tissue disease         3/21 (14.2)         14/124 (11.2)         0.69           Solid or Hematologic malignany         1/21 (4.7)         6/124 (4.8)         0.988           Charlson comorbidity index, median (IQR)         76 (37-118)         64 (29-131)         0.6131           Fever         1/22 (80.9)         106/124 (85.4)         0.552           Weight loss         14/21 (14.5)         71/23 (57.7)         0.441           Night sweats         8/21 (81.3)         69/123 (56.1)         0.166           Respiratory symptoms         1/22 (54.3)         0/124 (24.4)         0.888           Castrointestinal symptoms         1/21 (94.5)         0/124 (24.4)         0.888           Castrointestinal symptoms         1/21 (94.5)         0/124 (24.4)         0.888           Additional sites of MTBC isolation         1/21 (94.5)         0.812         0.214           Pulmonary         1/21 (21.5)         1/21/24 (14.5)         0.54         0.54           Adominal*         6/21 (9.1)         2/21 (24.4)         0.54         0.59         0.54           Jymph node<	CD4 count mean (IQR)	60 (7–185.5)	37.5 (21–94.5)	0.939
Diabetes mellitus         2/21 (9.5)         16/124 (1.9)         0.66           Connective tissue disease         3/21 (14.2)         14/124 (11.2)         0.69           Solid or Hernatologic malignancy         1/21 (14.7)         1/21 (4.8)         0.988           Charlson comorbidity index, median (IQR)         5 (1-5)         3.5 (0-5)         0.685           Symptoms         -         -         0.6121 (85.4)         0.531           Fever         17/21 (80.9)         106/124 (85.4)         0.532           Weight loss         14/21 (14.5)         17/123 (57.7)         0.441           Night sweats         8/21 (38.1)         6/9/123 (56.1)         0.126           Respiratory symptoms         1/22 (18.3)         2/1/24 (15.9)         0.81           Castrointestinal symptoms         2/21 (9.5)         2/1/24 (15.9)         0.63           Additional sites of MTBC isolation         2/12 (9.5)         18/124 (14.5)         0.54           Genitourinary of tissue         0/21 (9.5)         18/124 (2.4)         0.025           Contral nervous system         2/21 (9.5)         12/124 (2.4)         0.54           Genitourinary         12/12 (9.7)         12/12 (2.4)         0.54           Genitourinary onosonitist tissue         0/21 (9.7)	Diagnosed within 90 days of TB	8/11 (72.7)	26/52 (50)	0.16
Connective tissue disease         3/21 (14.2)         14/12 (1.1.2)         0.69           Solid or Hematologic malignary         1/21 (4.7)         6/124 (4.8)         0.988           Charlson connobidity index, median (IQR)         5 (1-6)         0.651           Symptoms onset, days, median (IQR)         7 (67.7-18)         64 (29-131)         0.631           Fever         17/21 (80.9)         106/124 (85.4)         0.592           Weight loss         8/21 (18.1)         67/123 (57.7)         0.441           Night sweats         8/21 (18.1)         67/123 (57.7)         0.488           Gastrontestinal symptoms         11/21 (54.3)         67/124 (54)         0.888           Gastrontestinal symptoms         11/21 (56.6)         89/124 (71.7)         0.631           Additional sites of MTBC isolation         12/124 (16.5)         0.54           Central nervous system         2/21 (9.5)         16/124 (20.9)         0.21           Skin, joint, bone, and soft tissue         0/21 (0         1/124 (24)         0.39*           Skin, joint, bone, and soft tissue         0/21 (0,1)         1/124 (24)         0.39*           Skin, joint, bone, and soft tissue         0/21 (0,1)         1/124 (24)         0.39*           Skin, joint, bone, and soft tissue         1/21 (4.7) <td>Diabetes mellitus</td> <td>2/21 (9.5)</td> <td>16/124 (12.9)</td> <td>0.66</td>	Diabetes mellitus	2/21 (9.5)	16/124 (12.9)	0.66
Solid or Hematologic malignancy         1/21 (4.7)         6/124 (4.8)         0.988           Charlson comorbidity index, median (IQR)         5 (1-6)         3.5 (0-6)         0.685           Symptoms onset, days, median (IQR)         76 (37-118)         64 (29-131)         0.631           Fever         17/21 (80.9)         106/124 (85.4)         0.592           Weight Loss         14/21 (14.5)         71/123 (57.7)         0.414           Night sweats         8/21 (18.3)         69/123 (56.1)         0.126           Respiratory symptoms         11/21 (54.3)         69/123 (56.1)         0.818           Castrointestinal symptoms         21/21 (19.0)         21/124 (16.9)         0.816           Additional sites of MTBC isolation	Connective tissue disease	3/21 (14.2)	14/124 (11.2)	0.69
Charlson comorbidity index, median (IQR)         5 (1–6)         3.5 (0–6)         0.685           Symptoms	Solid or Hematologic malignancy	1/21 (4.7)	6/124 (4.8)	0.988
Symptoms         Symptoms onset, days, median (IQR)         76 (37-18)         64 (29-13)         64 (29-13)         64 (29-13)           Fever         17/21 (80.9)         106/124 (85.4)         0.592           Weight loss         14/21 (14.5)         17/123 (57.7)         0.441           Night sweats         8/21 (38.1)         6/31 (35.1)         0.126           Respiratory symptoms         1/21 (54.3)         6/1124 (59)         0.88           Gastrointestinal symptoms         4/21 (19.0)         2/1124 (16.9)         0.81           Additional sites of MTBC isolation	Charlson comorbidity index, median (IQR)	5 (1-6)	3.5 (0–6)	0.685
Symptoms onset, days, median (IQR)         76 (37-118)         64 (29-131)         0.631           Fever         17/21 (80.9)         106/124 (85.4)         0.592           Weight loss         14/21 (84.3)         69/123 (57.7)         0.441           Night sweats         8/21 (38.1)         69/123 (56.1)         0.126           Respiratory symptoms         11/21 (54.3)         69/123 (56.1)         0.81           Gastrointestinal symptoms         Use of immunosuppressive drugs         4/21 (19.0)         21/124 (16.9)         0.81           Additional sites of MTBC isolation          14/21 (66.6)         89/124 (7.7)         0.63           Abdominal*         8/21 (38.1)         21/124 (16.9)         0.225         0.214           Central nervous system         2/21 (9.5)         18/124 (14.5)         0.54           Genitourinary         7/21 (33.3)         26/124 (20.9)         0.21           Skin, joint, bone, and soft tissue         0/21 (0)         3/124 (2.4)         0.54           Bone marrow positive TB culture         3/19 (15.7)         16/112 (14.2)         0.36           Milary         3/19 (14.7)         3/124 (2.4)         0.34           Cavitary         0/19 (0)         3/112 (12.1)         0.33           Cavitary	Symptoms			
Fever         17/21 (80.9)         10/6124 (85.4)         0.552           Weight loss         14/21 (14.5)         71/123 (57.7)         0.441           Night sweats         8/21 (38.1)         65/123 (56.1)         0.226           Respiratory symptoms         11/21 (54.3)         67/124 (54)         0.888           Gattriant Symptoms         21/124 (15.9)         0.7124 (54)         0.888           Gattriant Symptoms         21/124 (16.9)         0.810         0.810           Additional sites of MTBC isolatio         1         0.53         0.63           Pulmonary         14/21 (66.6)         89/124 (71.7)         0.63           Addominal <sup>6</sup> 8/21 (38.1)         21/124 (15.9)         0.63           Genitourinary         7/21 (33.3)         26/124 (20.9)         0.21           Skin, joint, bone, and soft tissue         0/21 (0)         3/124 (2.4)         0.099 <sup>d</sup> Jymph node         1/21 (4.7)         3/124 (2.4)         0.39           Bore marrow positive TB culture         3/19 (15.7)         16/112 (2.1)         0.63           Miliary         8/19 (42.1)         3/19 (12.32.1)         0.33           Cavitary         0/19 (0)         8/112 (2.1)         0.33           Cavitary	Symptoms onset, days, median (IQR)	76 (37–118)	64 (29–131)	0.631
Weight loss         14/21 (14.5)         71/123 (57.7)         0.441           Night sweats         8/21 (38.1)         6/123 (56.1)         0.126           Respiratory symptoms         12/12 (54.3)         6/123 (56.1)         0.888           Gastrointestinal symptoms         12/12 (19.0)         21/124 (16.9)         0.81           Additional sites of MTBC isolation         9/124 (71.7)         0.63           Abdominal*         8/21 (38.1)         21/124 (16.9)         0.025           Central nervous system         2/21 (9.5)         18/124 (14.5)         0.54           Genitorinary         7/21 (33.3)         26/124 (20.9)         0.21           Jskin, joint, bone, and soft tissue         0/21 (0)         3124 (2.4)         0.0994           Lymph node         1/21 (4.7)         3/124 (2.4)         0.034           Bone marrow positive TB culture         3/19 (15.7)         16/112 (14.2)         0.66           Milary         3/19 (42.1)         3/124 (2.1)         0.33           Cavitary         0/19 (0)         8/112 (21.1)         0.33           Gavitary         3/19 (42.1)         5/112 (49.1)         0.33           Cavitary         0/19 (0)         8/112 (21.1)         0.33           Laborator         16	Fever	17/21 (80.9)	106/124 (85.4)	0.592
Night sweats8/21 (38.1)69/123 (56.1)0.126Respiratory symptoms11/21 (54.3)69/124 (54)0.888Gastroirtestinal symptoms4/21 (19.0)21/124 (16.9)0.818Gastroirtestinal symptoms4/21 (19.0)21/124 (16.9)0.63Additional sites of MTBC isolation89/124 (71.7)0.63Pulmonary14/21 (66.6)89/124 (15.9)0.025Central nervous system2/21 (9.5)18/124 (14.5)0.54Genitourinary7/21 (33.3)26/124 (20.9)0.21Skin, joint, bone, and soft tissue0/21 (0.7)3/124 (2.4)0.54Bone marrow positive TB culture3/6 (50)3/25 (12)0.034Chest radiography pattern1/19 (15.7)16/112 (12.1)0.99Chest radiography pattern9/19 (0.7)16/112 (12.1)0.39Cavitary0/19 (0)8/112 (7.1)-Other8/19 (42.1)50/12 (41.3)0.001Laboratory test results at diagnosis16/20 (80)50/121 (41.3)0.001Hemoglobin_c10 g/dl.16/20 (80)50/121 (41.3)0.001Hemoglobin_10 g/dl.16/20 (80)50/121 (41.3)0.001Hemoglobin_210 g/dl.17.14-2.4)2.6 (1.9-3.1)0.001 <sup>b</sup> Albumin_2 g/dl.17.14-2.4)2.6 (1.9-3.1)0.001 <sup>b</sup> Mycobacterium hovis6/21 (2.8.5)7/124 (4.5)0.001 <sup>b</sup> Mycobacterium hovis6/21 (2.8.5)9/124 (4.5)0.001 <sup>b</sup> In-hospital TB related mortality4/21 (19)6/124 (4.8)0.01	Weight loss	14/21 (14.5)	71/123 (57.7)	0.441
Respiratory symptoms         11/21 (54.3)         67/124 (54)         0.888           Gastrointestinal symptoms         Juse of immunosuppressive drugs         4/21 (19.0)         21/124 (16.9)         0.81           Additional sites of MTBC isolation	Night sweats	8/21 (38.1)	69/123 (56.1)	0.126
Gastroittestinal symptoms $4/21 (19.0)$ $21/124 (16.9)$ $0.81$ Additional sites of MTBC isolation $  -$	Respiratory symptoms	11/21 (54.3)	67/124 (54)	0.888
Use of immunosuppressive drugs         4/21 (19.0)         21/124 (16.9)         0.81           Additional sites of MTBC isolation           0.63           Pulmonary         14/21 (66.6)         89/124 (71.7)         0.63           Abdominal <sup>6</sup> 2/21 (9.5)         18/124 (14.5)         0.54           Central nervous system         2/21 (9.5)         18/124 (14.5)         0.54           Genitourinary         7/21 (33.3)         26/124 (20.9)         0.21           Skin, joint, bone, and soft tissue         0/21 (0         3/124 (2.4)         0.54           Bone marrow positive TB culture         3/6 (50)         3/25 (12)         0.034           Chest radiography pattern          8/124 (14.3)         0.61           Miliary         8/19 (42.1)         36/112 (32.1)         0.39           Cavitary         0/19 (0)         8/112 (7.1)         -           Other         8/19 (42.1)         5/5112 (49.1)         0.33           Leborotry test results at diagnosis         -         -         -           Hemoglobin sci0 g/dL (UQR)         9 (7.5-9.7)         10.5 (9-12)         0.003 <sup>b</sup> Hemoglobin sci0 g/dL (UQR)         16/20 (80)         50/121 (41.3)         0.001 <sup>b</sup> <t< td=""><td>Gastrointestinal symptoms</td><td></td><td></td><td></td></t<>	Gastrointestinal symptoms			
Additional sites of MTBC isolation         Pulmonary         14/21 (66.6)         89/124 (71.7)         0.63           Abdominal <sup>6</sup> 8/21 (38.1)         21/124 (16.9)         0.025           Central nervous system         2/21 (9.5)         18/124 (14.5)         0.54           Genitourinary         7/21 (33.3)         26/124 (20.9)         0.21           Skin, joint, bone, and soft tissue         0/21 (0,         3/124 (2.4)         0.54           Bone marrow positive TB culture         3/6 (50)         3/25 (12)         0.034           Chett radiography pattern         3/19 (15.7)         16/112 (32.1)         0.36           Miliary         8/19 (42.1)         3/112 (32.1)         0.33           Cavitary         0/19 (0)         8/112 (7.1)         -           Other         8/19 (42.1)         55/112 (49.1)         0.33           Laboratory test results at diagnosis         -         -         -           Hemoglobin, median g/dL (IQR)         9/7.5–9.7)         10.5 (9–12)         0.003 <sup>b</sup> Hemoglobin s/10 g/dL         16/20 (80)         50/121 (41.3)         0.001           Leukocytes, median cells/µL (IQR)         173 (88–302)         290 (185–372)         0.007 <sup>b</sup> Albumin, nedian g/dL (IQR)         173 (88–302) </td <td>Use of immunosuppressive drugs</td> <td>4/21 (19.0)</td> <td>21/124 (16.9)</td> <td>0.81</td>	Use of immunosuppressive drugs	4/21 (19.0)	21/124 (16.9)	0.81
Pulmonary         14/21 (66.6)         89/124 (71.7)         0.63           Abdominal <sup>6</sup> 8/21 (38.1)         21/124 (16.9)         0.025           Central nervous system         2/21 (9.5)         18/124 (14.5)         0.54           Genitourinary         7/21 (33.3)         26/124 (20.9)         0.21           Skin, joint, bone, and soft tissue         0/21 (0)         3/124 (2.4)         >0.99 <sup>d</sup> Lymph node         1/21 (4.7)         3/124 (2.4)         0.54           Bone marrow positive TB culture         0/65 (50)         3/124 (2.4)         0.54           Bone marrow positive TB culture         0/61 (0)         3/124 (2.4)         0.54           Bone marrow positive TB culture         0/21 (0)         3/124 (2.4)         0.54           Miliary         65 (50)         3/124 (2.4)         0.54           Miliary         8/19 (15.7)         16/112 (14.2)         0.63           Cavitary         0/19 (0)         8/112 (7.1)         -           Other         8/19 (42.1)         36/112 (32.1)         0.33           Laboratory test results at diagnosis         -         -         -           Hemoglobin, median g/dL (QR)         9 (7.5-9.7)         10.5 (9-12)         0.003           Hemoglobin	Additional sites of MTBC isolation			
Abdominale8/21 (38.1)21/124 (16.9)0.025Central nervous system2/21 (9.5)18/124 (14.5)0.54Genitourinary7/21 (33.3)26/124 (20.9)0.21Skin, joint, bone, and soft tissue0/21 (0)3/124 (2.4)0.54Jymph node1/21 (4.7)3/124 (2.4)0.54Bone marrow positive TB culture3/6 (50)3/25 (12)0.034Chest radiography pattern15/12 (14.7)3/25 (12)0.34Normal3/19 (15.7)16/112 (14.2)0.86Miliary8/19 (42.1)3/112 (32.1)0.39Cavitary0/19 (0)8/112 (7.1)-Other8/19 (42.1)5/112 (49.1)0.33Laboratory test results at diagnosis1Hemoglobin, median g/dL (1QR)9 (7.5–9.7)10.5 (9–12)0.003 <sup>b</sup> Hemoglobin ≤10 g/dL16/20 (80)50/121 (41.3)0.001Leukocytes, median cells/µL (1QR)9 (7.5–9.7)10.5 (9–12)0.003 <sup>b</sup> Platelets, median cells/µL (1QR)17.14-2.4)2.6 (1.9–3.1)0.001 <sup>b</sup> Abumin ≤2 g/dL11/3 (88-302)290 (185–372)0.077 <sup>b</sup> Albumin ≤2 g/dL11/18 (61.1)27/106 (25.4)0.001 <sup>b</sup> Mycobacterium bovis6/21 (28.5)59/124 (47.5)0.1Mycobacterium tuberculosis15/21 (71.4)65/124 (52.4)In -hospital TB related mortality4/21 (19)6/124 (4.8)0.017	Pulmonary	14/21 (66.6)	89/124 (71.7)	0.63
Central nervous system2/21 (9.5)18/124 (14.5)0.54Genitourinary7/21 (33.3)26/124 (20.9)0.21Skin, joint, bone, and soft tissue0/21 (0)3/124 (2.4)>0.99 <sup>d</sup> Jymph node1/21 (4.7)3/124 (2.4)0.54Bone marrow positive TB culture3/6 (50)3/25 (12)0.034Chest radiography pattern3/19 (15.7)16/112 (14.2)0.86Miliary8/19 (42.1)36/112 (32.1)0.39Cavitary0/19 (0)8/112 (7.1)-Other0/19 (0)8/112 (7.1)-Other0/19 (0)5/112 (49.1)0.003 <sup>b</sup> Hemoglobin, median g/dL (IQR)9 (7.5–9.7)10.5 (9–12)0.003 <sup>b</sup> Hemoglobin ≤10 g/dL16/20 (80)50/121 (41.3)0.001Leukocytes, median cells/µL (IQR)6 (4-8.9)7 (4.4–10.7)0.45 <sup>b</sup> Platelets, median cells/µL (IQR)173 (88-302)290 (185–372)0.07 <sup>b</sup> Albumin _s2 g/dL11/18 (61.1)27/106 (25.4)0.001 <sup>b</sup> Mycobacterium bovis6/21 (28.5)59/124 (47.5)0.001 <sup>b</sup> Mycobacterium tuberculosis15/21 (71.4)65/124 (52.4)1.12In-hospital TB related mortality4/21 (19)6/24 (4.8)0.017	Abdominal <sup>c</sup>	8/21 (38.1)	21/124 (16.9)	0.025
Genitourinary         7/21 (33.3)         26/124 (20.9)         0.21           Skin, joint, bone, and soft tissue         0/21 (0)         3/124 (2.4)         >0.99 <sup>d</sup> Lymph node         1/21 (4.7)         3/124 (2.4)         0.54           Bone marrow positive TB culture         3/6 (50)         3/124 (2.4)         0.54           Bone marrow positive TB culture         3/6 (50)         3/12 (2.4)         0.34           Chest radiography pattern         -         0.34         0.34           Miliary         8/19 (15.7)         16/112 (14.2)         0.86           Miliary         8/19 (42.1)         36/112 (32.1)         0.39           Cavitary         0/19 (0)         8/112 (7.1)         -           Other         8/19 (42.1)         55/112 (49.1)         0.33           Laboratory test results at diagnosis         -         -         -           Hemoglobin, median g/dL (IQR)         9/7.5-9.7)         10.5 (9-12)         0.003 <sup>b</sup> Hemoglobin ≤10 g/dL         16/20 (80)         50/121 (41.3)         0.001           Leukocytes, median cells/µL (IQR)         173 (88-302)         290 (185-372)         0.007 <sup>b</sup> Albumin ≤2 g/dL         171 (1.4-2.4)         26 (1.9-3.1)         -0.001 <sup>b</sup>	Central nervous system	2/21 (9.5)	18/124 (14.5)	0.54
Skin, joint, bone, and soft tissue0/21 (0)3/124 (2.4)>0.99dLymph node1/21 (4.7)3/124 (2.4)0.54Bone marrow positive TB culture3/6 (50)3/25 (12)0.034Chest radiography patternVormal3/19 (15.7)16/112 (14.2)0.86Miliary8/19 (42.1)36/112 (32.1)0.39Cavitary0/19 (0)8/112 (7.1)-Other8/19 (42.1)55/112 (49.1)0.33Laboratory test results at diagnosisHemoglobin, median g/dL (IQR)9 (7.5–9.7)10.5 (9–12)0.003bHemoglobin ≤10 g/dL16/20 (80)50/121 (41.3)0.001Leukocytes, median cells/µL (IQR)6 (4–8.9)7 (4.4–10.7)0.45bPlatelets, median cells/µL (IQR)1.71 (88–302)290 (185–372)0.007bAlbumin $\leq 2$ g/dL11/18 (61.1)27/106 (25.4)0.001bMycobacterium bovis6/21 (28.5)59/124 (47.5)0.1Mycobacterium bovis6/21 (28.5)59/124 (47.5)0.1Mycobacterium tuberculosis15/21 (71.4)65/124 (52.4)In-hospital TB related mortality4/21 (19)6/124 (52.4)	Genitourinary	7/21 (33.3)	26/124 (20.9)	0.21
Iymph node         1/21 (4.7)         3/124 (2.4)         0.54           Bone marrow positive TB culture         3/6 (50)         3/25 (12)         0.034           Chest radiography pattern	Skin, joint, bone, and soft tissue	0/21 (0)	3/124 (2.4)	>0.99 <sup>d</sup>
Bone marrow positive TB culture         3/6 (50)         3/25 (12)         0.034           Chest radiograph pattern	Lymph node	1/21 (4.7)	3/124 (2.4)	0.54
Chest radiography pattern           Normal         3/19 (15.7)         16/112 (14.2)         0.86           Miliary         8/19 (42.1)         36/112 (32.1)         0.39           Cavitary         0/19 (0)         8/112 (7.1)         -           Other         8/19 (42.1)         55/112 (49.1)         0.33           Laboratory test results at diagnosis         -         -         -           Hemoglobin, median g/dL (IQR)         9 (7.5–9.7)         10.5 (9–12)         0.003 <sup>b</sup> Hemoglobin s_10 g/dL         16/20 (80)         50/121 (41.3)         0.001           Leukocytes, median cells/µL (IQR)         6 (4–8.9)         7 (4.4–10.7)         0.45 <sup>b</sup> Platelets, median cells/µL (IQR)         173 (88–302)         290 (185–372)         0.007 <sup>b</sup> Albumin, median g/dL (IQR)         17 (1.4–2.4)         2.6 (1.9–3.1)         <0.001 <sup>b</sup> Albumin _2 g/dL         11/18 (61.1)         27/106 (25.4)         0.002           Mycobacteriul species	Bone marrow positive TB culture	3/6 (50)	3/25 (12)	0.034
Normal         3/19 (15.7)         16/112 (14.2)         0.86           Miliary         8/19 (42.1)         36/112 (32.1)         0.39           Cavitary         0/19 (0)         8/112 (7.1)         -           Other         8/19 (42.1)         55/112 (49.1)         0.33           Laboratory test results at diagnosis         -         -         -           Hemoglobin, median g/dL (IQR)         9 (7.5–9.7)         10.5 (9–12)         0.003 <sup>b</sup> Hemoglobin ≤10 g/dL         16/20 (80)         50/121 (41.3)         0.001           Leukocytes, median cells/µL (IQR)         6 (4–8.9)         7 (4.4–10.7)         0.45 <sup>b</sup> Platelets, median cells/µL (IQR)         173 (88–302)         290 (185–372)         0.007 <sup>b</sup> Albumin, median g/dL (IQR)         1.7 (1.4–2.4)         2.6 (1.9–3.1)         <0.001 <sup>b</sup> Albumin ≤2 g/dL         11/18 (61.1)         27/106 (25.4)         0.002           Mycobacterial species	Chest radiography pattern			
Miliary $8/19$ (42.1) $36/112$ (32.1) $0.39$ Cavitary $0/19$ (0) $8/112$ (7.1) $-$ Other $8/19$ (42.1) $55/112$ (49.1) $0.33$ Laboratory test results at diagnosis $ -$ Hemoglobin, median g/dL (IQR) $9$ (7.5–9.7) $10.5$ (9–12) $0.003^{b}$ Hemoglobin $\leq 10$ g/dL $16/20$ (80) $50/121$ (41.3) $0.001$ Leukocytes, median cells/µL (IQR) $6$ (4–8.9) $7$ (4.4–10.7) $0.45^{b}$ Platelets, median cells/µL (IQR) $173$ (88–302) $290$ (185–372) $0.077^{b}$ Albumin, median g/dL (IQR) $1.7$ (1.4–2.4) $2.6$ (1.9–3.1) $<0.001^{b}$ Albumin $\leq 2$ g/dL $11/18$ (61.1) $27/106$ (25.4) $0.002$ Mycobacterial species $59/124$ (47.5) $0.1$ Mycobacterium bovis $6/21$ (28.5) $59/124$ (47.5) $0.1$ Mycobacterium tuberculosis $15/21$ (71.4) $6/124$ (52.4) $0.007$	Normal	3/19 (15.7)	16/112 (14.2)	0.86
Cavitary Other0/19 (0)8/112 (7.1)-Other8/19 (42.1)55/112 (49.1)0.33Laboratory test results at diagnosis55/112 (49.1)0.33Hemoglobin, median g/dL (IQR)9 (7.5–9.7)10.5 (9–12)0.003bHemoglobin $\leq 10$ g/dL16/20 (80)50/121 (41.3)0.001Leukocytes, median cells/µL (IQR)6 (4–8.9)7 (4.4–10.7)0.45bPlatelets, median cells/µL (IQR)173 (88–302)290 (185–372)0.077bAlbumin, median g/dL (IQR)1.7 (1.4–2.4)2.6 (1.9–3.1)<0.001b	Miliary	8/19 (42.1)	36/112 (32.1)	0.39
Other8/19 (42.1)55/112 (49.1)0.33Laboratory test results at diagnosis $Iagnosis$ $Iagnosis$ $Iagnosis$ $Iagnosis$ Hemoglobin, median g/dL (IQR)9 (7.5–9.7)10.5 (9–12) $0.003^b$ Hemoglobin $\leq 10$ g/dL16/20 (80) $50/121$ (41.3) $0.001$ Leukocytes, median cells/µL (IQR)6 (4–8.9)7 (4.4–10.7) $0.45^b$ Platelets, median cells/µL (IQR)173 (88–302)290 (185–372) $0.077^b$ Albumin, median g/dL (IQR)1.7 (1.4–2.4)2.6 (1.9–3.1) $<0.001^b$ Albumin $\leq 2$ g/dL11/18 (61.1)27/106 (25.4) $0.002$ Mycobacterial species $Syl24$ (47.5) $0.1$ Mycobacterium bovis6/21 (28.5) $59/124$ (47.5) $0.1$ Mycobacterium tuberculosis15/21 (71.4) $65/124$ (52.4) $0.017$	Cavitary	0/19 (0)	8/112 (7.1)	-
Laboratory test results at diagnosis       9 (7.5–9.7)       10.5 (9–12)       0.003 <sup>b</sup> Hemoglobin, median g/dL (IQR)       9 (7.5–9.7)       10.5 (9–12)       0.003 <sup>b</sup> Hemoglobin $\leq 10$ g/dL       16/20 (80)       50/121 (41.3)       0.001         Leukocytes, median cells/µL (IQR)       6 (4–8.9)       7 (4.4–10.7)       0.45 <sup>b</sup> Platelets, median cells/µL (IQR)       173 (88–302)       290 (185–372)       0.077 <sup>b</sup> Albumin, median g/dL (IQR)       1.7 (1.4–2.4)       2.6 (1.9–3.1)       <0.001 <sup>b</sup> Albumin $\leq 2$ g/dL       11/18 (61.1)       27/106 (25.4)       0.002         Mycobacterial species       59/124 (47.5)       0.1         Mycobacterium bovis       6/21 (28.5)       59/124 (47.5)       0.1         Mycobacterium tuberculosis       15/21 (71.4)       65/124 (52.4)       0.017	Other	8/19 (42.1)	55/112 (49.1)	0.33
Hemoglobin, median g/dL (IQR)9 (7.5–9.7)10.5 (9–12)0.003bHemoglobin $\leq 10$ g/dL16/20 (80)50/121 (41.3)0.001Leukocytes, median cells/µL (IQR)6 (4–8.9)7 (4.4–10.7)0.45bPlatelets, median cells/µL (IQR)173 (88–302)290 (185–372)0.077bAlbumin, median g/dL (IQR)1.7 (1.4–2.4)2.6 (1.9–3.1)<0.001b	Laboratory test results at diagnosis			
$ \begin{array}{llllllllllllllllllllllllllllllllllll$	Hemoglobin, median g/dL (IQR)	9 (7.5–9.7)	10.5 (9–12)	0.003 <sup>b</sup>
Leukocytes, median cells/µL (IQR)6 (4-8.9)7 (4.4-10.7)0.45bPlatelets, median cells/µL (IQR)173 (88-302)290 (185-372)0.077bAlbumin, median g/dL (IQR)1.7 (1.4-2.4)2.6 (1.9-3.1)<0.001b	Hemoglobin ≤10 g/dL	16/20 (80)	50/121 (41.3)	0.001
Platelets, median cells/µL (IQR)173 (88-302)290 (185-372) $0.077^{b}$ Albumin, median g/dL (IQR)1.7 (1.4-2.4)2.6 (1.9-3.1)<0.001^{b}Albumin $\leq 2$ g/dL11/18 (61.1)27/106 (25.4)0.002Mycobacterial species59/124 (47.5)0.1Mycobacterium bovis6/21 (28.5)59/124 (47.5)0.1Mycobacterium tuberculosis15/21 (71.4)65/124 (52.4)0.017In-hospital TB related mortality4/21 (19)6/124 (4.8)0.017	Leukocytes, median cells/µL (IQR)	6 (4–8.9)	7 (4.4–10.7)	0.45 <sup>b</sup>
Albumin, median g/dL (IQR)       1.7 (1.4–2.4)       2.6 (1.9–3.1)       <0.001 <sup>b</sup> Albumin ≤2 g/dL       11/18 (61.1)       27/106 (25.4)       0.002         Mycobacterial species       59/124 (47.5)       0.1         Mycobacterium bovis       6/21 (28.5)       59/124 (47.5)       0.1         Mycobacterium tuberculosis       15/21 (71.4)       65/124 (52.4)       0.017	Platelets, median cells/µL (IQR)	173 (88–302)	290 (185–372)	0.077 <sup>b</sup>
Albumin ≤2 g/dL       11/18 (61.1)       27/106 (25.4)       0.002         Mycobacterial species	Albumin, median g/dL (IQR)	1.7 (1.4–2.4)	2.6 (1.9–3.1)	<0.001 <sup>b</sup>
Mycobacterial species         59/124 (47.5)         0.1           Mycobacterium tuberculosis         15/21 (71.4)         65/124 (52.4)         0.017           In-hospital TB related mortality         4/21 (19)         6/124 (4.8)         0.017	Albumin $\leq 2 \text{ g/dL}$	11/18 (61.1)	27/106 (25.4)	0.002
Mycobacterium bovis         6/21 (28.5)         59/124 (47.5)         0.1           Mycobacterium tuberculosis         15/21 (71.4)         65/124 (52.4)         0.1           In-hospital TB related mortality         4/21 (19)         6/124 (4.8)         0.017	Mycobacterial species			
Mycobacterium tuberculosis         15/21 (71.4)         65/124 (52.4)           In-hospital TB related mortality         4/21 (19)         6/124 (4.8)         0.017	Mycobacterium bovis	6/21 (28.5)	59/124 (47.5)	0.1
In-hospital TB related mortality         4/21 (19)         6/124 (4.8)         0.017	Mycobacterium tuberculosis	15/21 (71.4)	65/124 (52.4)	
	In-hospital TB related mortality	4/21 (19)	6/124 (4.8)	0.017

Note. Data are n/N (%) of cases, unless otherwise indicated. n values across categories might be less than the counts in the column headings due to missing data. IQR, interquartile range; BMI, body mass index; BCG, bacille calmette-guérin; HIV, human immunodeficiency virus; TB, tuberculosis.

<sup>a</sup> *p* values were determined by the  $\chi^2$  test.

 $^{\rm b}\,\,p$  values were determined by the Mann–Whitney U test.

 $^{\rm c}\,$  Ascites, gastrointestinal biopsies, intraabdominal lymph nodes, or fecal samples.

<sup>d</sup> *p* values were determined by Fisher's exact test.

diagnosis, one suffered from chronic ulcerative colitis and was under immunosuppressive treatment, and one was diagnosed with acute myeloid leukemia. Regarding four bacteremic patients who died, three were HIV-negative, and the fourth had unknown HIV status (not tested).

#### Discussion

In this study, the rates of MTBC-bacteremia among HIVinfected and non-infected patients were not significantly different. Anemia, hypoalbuminemia, and low BMI were associated with MTBC-bacteremia. In addition, patients presenting with mycobacteremia had higher in-hospital TB-related mortality. These findings are relevant and may help deciding which patients may present mycobacteremia, prioritize resources, and define short-term prognosis.

Blood cultures are not part of routine diagnostic approach for TB in most settings, especially in resource-limited regions. Moreover, mycobacteremia and its associated characteristics have been widely described in the HIV-infected population for which blood cultures are more frequently requested. Of note, in this study encompassing 15 years of culture-proven TB cases, a significant proportion of the patients had a blood culture performed, and the positivity rate was similar among HIV-infected and uninfected patients. Therefore, we believe that bacteremia among the latter is underdiagnosed.

Low hemoglobin levels were shown to be associated with mycobacteremia in similar studies, although an explanation has not been provided. In our study, this association remained significant even after adjusting for HIV status in multivariate analysis. A relationship between inflammatory anemia and worse TB outcome in HIV-infected patients, together with increased levels of hepcidin, a peptide that regulates iron levels and that increases as part of the acute phase inflammatory response was recently reported.<sup>11</sup> Moreover, although the number of bone marrow cultures was limited in this study, 50% of the patients with bacteremia had also a positive bone marrow culture. In fact, anemia has been proposed as a predictor of positive bone marrow cultures for TB among HIV-infected patients.<sup>12</sup> Therefore, bone marrow infiltration by mycobacteria may also account for this finding, although not systematically investigated.

We found low levels of albumin associated with mycobacteremia. Albumin levels are a marker of malnutrition, but acute hypoalbuminemia is also common in severely ill patients as result of decreased synthesis, and capillary leakage.<sup>13</sup> Hypoalbuminemia has also been reported as a short-term mortality predictor in TB in both HIV-infected and uninfected patients, mostly attributed to low BMI.<sup>14</sup>

Previous reports have not provided information regarding the causative species of bacteremia. Although *M. bovis* is more frequently related to extrapulmonary disease, the rates of bacteremia were not different in our study. This emphasizes the concept that disseminated TB and extrapulmonary TB are not interchangeable terms (although easily confused), since dissemination may depend on the host rather than the causative mycobacteria species.

Finally, we found higher in-hospital mortality among patients with bacteremia.<sup>15</sup> This may be related to high bacillary burden, reflected on the short turnaround time for culture results compared to other reports.<sup>16</sup> However, as a limitation of this study, we acknowledge the small number of MTBC-bacteremia analyzed and this precluded a multivariate analysis.

In conclusion, larger studies with a systematic approach for TB diagnosis incorporating blood cultures are necessary to characterize the phenomenon completely, especially in the HIV-negative population. Nevertheless, this study supports the use of blood cultures as a potential tool for diagnosis and short-term prognosis of TB.

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#### **Conflicts of interest**

The authors declare no conflicts of interest.

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