

# Clinical Forms of Tuberculosis and Associated Factors among People Living with HIV Hospitalised at the Infectious Diseases Department of the Libreville University Hospital Centre in 2024

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Received: 02 Dec 2025; Accepted: 03 Jan 2026; Published: 18 Jan 2026

**Citation:** Essomeyo Ngue Mebale Magalie, Manomba B Charleine, Ntsame Owono Marion, et al. Clinical Forms of Tuberculosis and Associated Factors among People Living with HIV Hospitalised at the Infectious Diseases Department of the Libreville University Hospital Centre in 2024. *Microbiol Infect Dis*. 2026; 10(1): 1-6.

## ABSTRACT

**Background:** Tuberculosis (TB) remains a leading cause of morbidity and mortality among people living with HIV (PLHIV), with a wide spectrum of pulmonary and extrapulmonary manifestations. Data on TB localisations and associated factors among hospitalised PLHIV in Gabon remain limited.

**Methods:** We conducted a retrospective study in 2024 at the Infectious and Tropical Diseases Department of the Libreville University Hospital Centre. Adult PLHIV hospitalised for bacteriologically confirmed or clinically diagnosed TB were included. Sociodemographic, clinical, and biological data were extracted from medical records.

**Results:** Among 1,014 hospitalised patients, 76 (7.4%) PLHIV with TB were included. Women accounted for 77.6% of cases, and the mean age was 42±12.2 years. Pulmonary TB predominated (63.2%), while extrapulmonary involvement, isolated or multifocal, was observed in 36.8% of patients. The most frequent extrapulmonary sites were digestive (13.2%), lymph node (9.2%), and pleural (9.2%). Severe immunosuppression (CD4 <200 cells/mm<sup>3</sup>) was present in 71.4% of patients, with a mean CD4 count of 180.2±178.6 cells/mm<sup>3</sup>. Opportunistic infections were documented in 19.7% of cases, mainly oral candidiasis and cerebral toxoplasmosis (14.4%). Tobacco use was significantly associated with multifocal TB ( $p=0.01$ ). Overall in-hospital mortality was 15.8%, and the mean length of stay was 8.6 ± 4.2 days.

**Conclusion:** TB among hospitalised PLHIV in Libreville is characterised by advanced immunosuppression, a high burden of extrapulmonary disease, and substantial mortality. Strengthening early HIV and TB diagnosis and addressing behavioural risk factors remain critical.

## Keywords

HIV-tuberculosis coinfection, Extrapulmonary tuberculosis, Opportunistic infections, CD4 count, Gabon.

## Introduction

Tuberculosis (TB) is an infectious and contagious disease transmitted through the airborne route and most commonly affecting the respiratory system. Dissemination to other organs

results in extrapulmonary tuberculosis. Tuberculosis remains the leading cause of death from infectious diseases worldwide, with an estimated 1.23 million deaths in 2024 according to the World Health Organization (WHO) report [1].

Human immunodeficiency virus (HIV) infection continues to represent a major global public health challenge. It is characterised by cellular immunosuppression, which constitutes a major risk

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factor for the development of tuberculosis, placing people living with HIV (PLHIV) at particularly high risk of developing this disease. According to the most recent estimates reported by the Joint United Nations Programme on HIV/AIDS (UNAIDS) in 2024, approximately 40.8 million people were living with HIV worldwide, including 25.9 million in sub-Saharan Africa. During the same year, about 630,000 AIDS-related deaths were recorded, representing a reduction of nearly 70% compared with the peak observed in 2004, while 1.3 million new HIV infections were reported [2].

The HIV pandemic has led to a substantial increase in tuberculosis incidence and TB-associated mortality [3]. HIV-tuberculosis coinfection constitutes a deadly synergy, with each disease accelerating the progression of the other. Despite the widespread availability of antiretroviral therapy (ART), tuberculosis remains the leading cause of hospitalisation and death among people infected with HIV [3]. In 2024, approximately 150,000 PLHIV died from HIV-tuberculosis coinfection worldwide [1].

To reduce this excess mortality, the World Health Organization has recommended since 2003 the initiation of antiretroviral therapy within two weeks to two months after the start of anti-tuberculosis treatment in coinfecting patients with CD4 T-lymphocyte counts below 200 cells/mm<sup>3</sup> [4].

In Gabon, the National Tuberculosis Control Programme (Programme National de Lutte contre la Tuberculose, PNLT) is responsible for the detection of new cases, contact tracing, and diagnosis of infected individuals, and reports these data to the Ministry of Health for national surveillance purposes. However, detailed information on the different clinical forms and anatomical localisations of tuberculosis is not systematically documented. Although several national studies have previously addressed HIV-tuberculosis coinfection, no study has specifically focused on extrapulmonary tuberculosis localisations among PLHIV in Gabon.

In this context, the objective of the present study was to describe the clinical forms and anatomical localisations of tuberculosis among HIV-infected hospitalised patients and to identify factors associated with these forms at the Infectious and Tropical Diseases Department (SMIT) of the Libreville University Hospital Centre (CHUL).

## Methods

### Study design and settings

This was a retrospective observational study conducted at the Infectious and Tropical Diseases Department (SMIT) of the Libreville University Hospital Centre (CHUL), Gabon. The study was based on routinely collected medical records over a 12-month period, from January to December 2024.

The SMIT is the national referral centre for the management of HIV infection and other infectious diseases in Gabon. Each year, approximately 5,000 PLHIV are followed on an outpatient basis

for HIV care at this centre.

### Study population

The study population consisted of adult patients infected with HIV-1 who were hospitalised at the SMIT during the study period for tuberculosis.

Inclusion criteria were age  $\geq 18$  years, confirmed HIV-1 infection, hospitalisation for bacteriologically confirmed or clinically diagnosed tuberculosis, receipt of anti-tuberculosis treatment, and being either antiretroviral therapy-naïve or already receiving antiretroviral therapy.

Patients with incomplete medical records or without documented consent for the use of anonymised data for research purposes were excluded.

### Diagnostic procedures and study material

The study material consisted of individual medical records of eligible hospitalised patients. Suspicion of tuberculosis constituted the main indication for admission.

Tuberculosis diagnosis was based on bacteriological confirmation and/or clinical criteria. A rapid molecular diagnostic test, GeneXpert MTB/RIF, was systematically performed in patients from the day following admission. This assay detects *Mycobacterium tuberculosis* DNA and rifampicin resistance within approximately two hours and is recommended for rapid confirmation of tuberculosis.

The GeneXpert MTB/RIF assay can be performed on various biological samples; in this study, it was conducted on gastric aspirate fluid. Medical records included patients already receiving antiretroviral therapy as well as patients newly diagnosed with HIV infection who were ART-naïve at the time of admission.

Only records of patients who had provided written informed consent for the anonymous use of their data for research purposes were included in the analysis.

### Variables

The following variables were extracted from medical records: Sociodemographic variables: age, sex, marital status, medical history, habits and lifestyle; Clinical variables: anatomical localisation of tuberculosis, presence of opportunistic infections, use of cotrimoxazole prophylaxis, and antiretroviral therapy status; Biological variables: CD4 T-lymphocyte count and presence of renal impairment.

### Data collection procedures

Data were collected using a standardised data collection form specifically designed for this study. All variables were extracted retrospectively from hospital medical records by trained investigators.

## Statistical analysis

Data were entered into Microsoft Excel 2016 and subsequently analysed using Stat View version 5.0 software (SAS Institute Inc., Cary, NC, USA). Quantitative variables were described using means and standard deviations or medians with interquartile ranges (IQR), depending on their distribution. Qualitative variables were summarised as absolute counts and percentages. Comparisons of proportions were performed using the chi-square ( $\chi^2$ ) test or Fisher's exact test when expected cell counts were less than five. All statistical tests were two-sided. Statistical significance was set at  $p < 0.05$ .

## Ethical considerations

Patients were included voluntarily after providing informed consent for the use of their data for research purposes. The study was conducted in accordance with the ethical principles of the Declaration of Helsinki (2013 revision).

Authorisation for data use was obtained from the Director of Medical Affairs of the Libreville University Hospital Centre (CHUL); the Head of the Department of Medicine and Medical Specialties. All data were anonymised prior to analysis. A unique identification number was assigned to each participant to ensure confidentiality, oral consent was obtained for data use and confidentiality was kept throughout the study.

## Results

### Baseline characteristics of the study population

During the study period, 76 patients with tuberculosis, representing 7.4% of the 1,014 patients hospitalised in the department, were included in the analysis. Women accounted for the majority of cases (77.6%), and the mean age was  $42 \pm 12.2$  years, ranging from 21 to 68 years. Nearly three quarters of patients were living alone (72.3%). Most patients did not have diabetes, while half reported alcohol and/or tobacco use.

Tuberculosis was the circumstance of HIV diagnosis in 63.2% of cases. Pulmonary tuberculosis was the predominant clinical form, observed in 98.7% of patients. Opportunistic infections were documented in 19.7% of cases. Among patients with available immunological data, 68.2% had severe immunosuppression defined by a CD4 count below 200 cells/mm<sup>3</sup>. At admission, 46.1% of patients were receiving antiretroviral therapy and 47.4% were on cotrimoxazole prophylaxis. Overall mortality during hospitalisation was 15.8% (Table 1).

### Clinical forms and anatomical distribution of tuberculosis

Pulmonary tuberculosis alone accounted for 63.2% of cases, while extrapulmonary involvement, either isolated or as part of multifocal disease, was observed in 36.8% of patients. Multifocal tuberculosis represented 35.5% of all cases. The most frequent extrapulmonary sites were digestive, lymph node, and pleural localisations, together accounting for 31.6% of patients.

Oral candidiasis and cerebral toxoplasmosis were the most

commonly associated opportunistic infections, together affecting 14.4% of the study population (Table 2).

**Table 1:** General characteristics of the population.

| Variables                        | N  | %    |
|----------------------------------|----|------|
| Female                           | 59 | 77.6 |
| Male                             | 17 | 22.4 |
| Age <30 years                    | 11 | 14.5 |
| Age 30-60 years                  | 55 | 72.4 |
| Age >60 years                    | 10 | 13.1 |
| Single                           | 54 | 72.0 |
| Cohabiting                       | 13 | 17.4 |
| Married                          | 7  | 9.3  |
| Widow                            | 1  | 1.3  |
| Diabetes (Yes)                   | 3  | 3.9  |
| Diabetes (No)                    | 73 | 96.1 |
| Tobacco use (Yes)                | 6  | 7.9  |
| Alcohol use (Yes)                | 32 | 42.1 |
| TB as circumstance of diagnosis  | 48 | 63.2 |
| Pulmonary TB                     | 75 | 98.7 |
| Associated OIs (Yes)             | 15 | 19.7 |
| CD4 <200 cells/mm <sup>3</sup> * | 15 | 68.2 |
| On ART                           | 35 | 46.1 |
| Cotrimoxazole use                | 36 | 47.4 |
| Discharged alive                 | 64 | 84.2 |
| Death                            | 12 | 15.8 |

\*CD4 available for a subset of patients.

**TB\***: tuberculosis

**Table 2:** Tuberculosis forms, anatomical sites, and associated opportunistic infections.

| Variables                  | N  | %    |
|----------------------------|----|------|
| Pulmonary TB               | 48 | 63.2 |
| Isolated extrapulmonary TB | 1  | 1.3  |
| Multifocal TB              | 27 | 35.5 |
| Digestive TB               | 10 | 13.2 |
| Lymph node and others      | 7  | 9.2  |
| Neuromeningeal TB          | 2  | 2.6  |
| Bone TB                    | 2  | 2.6  |
| Pleural TB                 | 7  | 9.2  |
| Oral candidiasis           | 5  | 6.7  |
| Oral candidiasis + prurigo | 1  | 1.3  |
| Hepatitis                  | 1  | 1.3  |
| Pneumocystosis             | 1  | 1.3  |
| Toxoplasmosis              | 6  | 7.8  |
| Herpes zoster              | 1  | 1.3  |
| None                       | 61 | 80.3 |

### Comparison between pulmonary and multifocal tuberculosis

Patients with pulmonary and multifocal tuberculosis were predominantly aged 30-60 years in both groups, with a female predominance (sex ratio M/F = 0.29). Hypertension was the only comorbidity observed in both groups, while diabetes was documented exclusively among patients with pulmonary tuberculosis.

Alcohol and tobacco use were more frequent in patients with multifocal tuberculosis, with a statistically significant association observed for tobacco use ( $p = 0.01$ ). Tuberculosis represented the circumstance of HIV diagnosis in more than half of patients in both groups. Associated opportunistic infections were significantly more frequent in the pulmonary tuberculosis group ( $p = 0.008$ ).

The mean CD4 count was  $180.2 \pm 178.6$  cells/mm<sup>3</sup>, and severe immunosuppression was present in nearly three quarters of patients in both groups. Most patients were discharged alive. However, mortality was higher among patients with pulmonary tuberculosis compared with those with multifocal disease. The mean length of hospital stay was  $8.6 \pm 4.2$  days (Table 3).

**Table 3:** Pulmonary versus multifocal tuberculosis and associated factors among PLHIV.

| Variables                       | Pulmonary TB |      | Multifocal TB |      | p value |
|---------------------------------|--------------|------|---------------|------|---------|
|                                 | N            | %    | N             | %    |         |
| <30 years                       | 7            | 14.6 | 4             | 14.8 | 0.91    |
| 30-60 years                     | 34           | 70.8 | 20            | 74.1 |         |
| >60 years                       | 7            | 14.6 | 3             | 11.1 |         |
| Female                          | 37           | 77.1 | 21            | 77.8 | 0.94    |
| Male                            | 11           | 22.9 | 6             | 22.2 |         |
| Hypertension                    | 2            | 4.2  | 2             | 7.4  | 0.94    |
| Diabetes                        | 3            | 6.3  | 0             | 0    | 0.18    |
| Alcohol use                     | 18           | 37.5 | 13            | 48.1 | 0.36    |
| Tobacco use                     | 1            | 2.1  | 5             | 31.8 | 0.01    |
| CTX use                         | 24           | 50.0 | 11            | 40.7 | 0.44    |
| On ART                          | 24           | 50.0 | 10            | 37.1 | 0.27    |
| TB as circumstance of diagnosis | 30           | 62.5 | 17            | 62.9 | 0.96    |
| Associated OIs                  | 14           | 29.2 | 1             | 3.7  | 0.008   |
| CD4 <200 cells/mm <sup>3</sup>  | 10           | 71.4 | 5             | 71.4 |         |
| Hospital stay $\geq 10$ days    | 19           | 60.4 | 7             | 25.9 | 0.22    |
| Death                           | 10           | 20.8 | 2             | 7.4  | 0.12    |

## Discussion

This study, conducted in 2024 at the Infectious and Tropical Diseases Department (SMIT) of the Libreville University Hospital Centre (CHUL), aimed to describe the anatomical localisations of tuberculosis among people living with HIV-1 and to identify associated factors in a hospital setting.

A marked female predominance was observed, with a sex ratio of 0.28. This finding is consistent with that reported by Mutombo and colleagues in the Democratic Republic of Congo, where women represented 78.9% of the study population [5], but contrasts with the results of Diarra and colleagues in Bamako, who reported a male predominance of 60.42% [6]. These discrepancies suggest that sex distribution among HIV-tuberculosis coinfecting patients is strongly influenced by sociocultural factors and health-seeking behaviours. Women are more likely to access healthcare services regularly and adhere to treatment, increasing their representation in hospital-based cohorts. Conversely, men may present later in the course of disease, often at more advanced and clinically severe

stages.

The most represented age group was 30-60 years (72.4%), in line with findings reported by Mutombo, who also identified adults aged 40-60 years as the most affected group [5]. This confirms that young and middle-aged adults remain the population most impacted by HIV-tuberculosis coinfection. In our study, most patients were living alone (73.3%), a finding that contrasts with that of Diarra and colleagues, who reported that 68.75% of patients were married [6]. Half of our patients reported alcohol and/or tobacco use (50%), while fewer than 5% had diabetes. These results differ from those reported in the DRC, where diabetes prevalence reached 8.1% and alcohol and tobacco use were observed in 42.2% and 24.1% of cases, respectively [5]. The relatively young age of our population may partly explain the lower prevalence of diabetes observed.

Pulmonary tuberculosis was the predominant clinical form in our study (98.7%). Similar findings were reported by Ngombe and colleagues and Diarra and colleagues, with pulmonary involvement accounting for 63.4% and 43.75% of cases, respectively [7,6]. This predominance is expected, as the lung is the primary target organ of tuberculosis, which is transmitted via airborne droplets from respiratory secretions. Consequently, pulmonary forms represent the main source of transmission within communities.

The overall mortality rate in our study was 15.2%, comparable to that reported by Kettani and colleagues in Casablanca (21.7%) and Mutombo and colleagues in the DRC (13.5%) among HIV-tuberculosis coinfecting patients [5,8]. The combination of HIV and tuberculosis, both associated with profound immunosuppression, substantially increases the risk of death, particularly in the absence of early diagnosis and timely treatment. In Gabon, a previous study reported an even higher case fatality rate of 26% among coinfecting patients [9], highlighting persistent challenges in disease management.

Extrapulmonary tuberculosis accounted for more than one third of cases in our study (36.8%). The most frequent anatomical localisations were digestive (13.2%), lymph node (9.2%), and pleural (9.2%), together representing approximately one third of cases. These findings are consistent with those reported by Diarra and colleagues, who observed extrapulmonary forms in 33.3% of cases [6]. Other studies conducted in Libreville, Lomé, and Sétat-Casablanca also identified lymph node involvement as the most frequent extrapulmonary localisation, with proportions ranging from 4.4% to 18.3%, followed by pleural forms [10-12]. Ntsame and colleagues additionally reported neuromeningeal and lymph node involvement in 13.8% of cases in Libreville [9]. These similarities suggest a stable pattern of extrapulmonary tuberculosis in HIV-infected populations across different African settings.

The high prevalence of alcohol consumption and tobacco use observed in our cohort may contribute to increased susceptibility to tuberculosis and more severe disease progression. These behaviours are known to impair macrophage function, alter

cellular immunity, and increase both the risk of Mycobacterium tuberculosis infection and progression to severe forms, particularly in immunocompromised individuals.

Oral candidiasis and cerebral toxoplasmosis (n = 11; 14.4%) were the most frequently associated opportunistic infections in our study. Similar findings were reported by Ntsame and colleagues, who identified opportunistic infections, including cerebral toxoplasmosis and progressive multifocal leukoencephalopathy, in 7.4% of cases [9]. Profound immunosuppression (CD4 <200 cells/mm<sup>3</sup>) likely explains the high frequency of these infections, particularly among patients with uncontrolled HIV infection or poor adherence to antiretroviral therapy. Riziki and colleagues also reported tuberculosis and cerebral toxoplasmosis as major causes of hospitalisation among PLHIV [13]. Together, these findings reflect persistent diagnostic and therapeutic delays and the continued burden of opportunistic infections in African contexts.

A comparison between pulmonary and multifocal tuberculosis revealed both shared and distinct clinical characteristics. In both groups, patients were predominantly young adults with a female predominance, consistent with the feminisation of HIV infection reported in several African studies and by the WHO. Only 6.3% of patients had diabetes, a proportion similar to that reported by Mutombo and colleagues (8.1%) [5]. Patients with multifocal tuberculosis reported higher alcohol consumption (n = 13/27) and tobacco use (n = 5/27) compared with those with pulmonary tuberculosis, with a statistically significant association observed for tobacco use. This finding is consistent with that reported by Noubom and colleagues in Cameroon, who highlighted smoking as a risk factor for tuberculosis [15].

The mean CD4 count in our population was 180.2 ± 178.6 cells/mm<sup>3</sup>, and severe immunosuppression (CD4 <200 cells/mm<sup>3</sup>) was present in 71.4% of patients. This proportion is higher than that reported by Dagnra and colleagues in Lomé (55.8%) [16], suggesting delayed access to care and suboptimal adherence to antiretroviral therapy in our cohort. The mean duration of hospitalisation was 8.6 ± 4.2 days, similar to that reported by Ntsame and colleagues (7.0 [6.0-8.0] days) [9]. In-hospital mortality in the multifocal tuberculosis group reached 15.2%, exceeding that reported by Laouali and colleagues in Niger (10.42%) [17], possibly reflecting delays in diagnosis and treatment initiation.

Several limitations should be acknowledged. The retrospective design exposes the study to potential selection bias, and the limited number of exploitable records reduces the representativeness of the sample. Furthermore, the single-centre nature of the study limits the generalisability of the findings. Nevertheless, the study provides important insights into the clinical spectrum and outcomes of HIV-tuberculosis coinfection in Gabon.

## Conclusion

HIV-tuberculosis coinfection remains frequent among people living with HIV, predominantly affecting young adults with advanced

immunosuppression. The predominance of pulmonary forms and the substantial proportion of extrapulmonary localisations, particularly digestive, lymph node, and pleural, reflect delayed diagnosis and rapid disease progression, favoured by low CD4 counts and behavioural risk factors such as tobacco and alcohol use. The frequent occurrence of opportunistic infections, notably oral candidiasis and cerebral toxoplasmosis, further underscores the immunological vulnerability of this population and contributes to persistently high mortality.

These findings highlight the need to strengthen integrated strategies for early HIV and tuberculosis screening, improve access to and continuity of antiretroviral therapy, and ensure systematic management of modifiable risk factors, particularly alcohol and tobacco use.

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