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Research Article

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Tuberculosis in Senegal: Treatment Pathway and Diagnostic Delay

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ABSTRACT

In Senegal, tuberculosis is endemic, and tuberculosis patients are supposed to be properly cared for in all healthcare facilities, but a significant proportion of them reach the top of the healthcare pyramid to receive adequate care, and there is little information available on the therapeutic pathway of tuberculosis patients prior to their admission at the reference facilities.

Objective: To describe the therapeutic pathway of patients hospitalized in the national reference department with a diagnosis of tuberculosis and to identify the missed opportunities (for diagnosis and treatment).

Methods: Retrospective study on the records of hospitalized tuberculosis patients from 2020 to 2022. The identification of factors associated with multifocal TB was carried out using a logistic regression model. The cumulative incidence of death was assessed using Kaplan-Meier curves, and the identification of prognostic factors was done using a Cox regression models.

Results: We included 363 patients with a median (IQR) age of 39 (30-50) years, including 61.6% of men and 51.6% of people living with HIV. Before their admission at the national reference department, 88.6% had been seen at another healthcare facility. Missed opportunities for tuberculosis diagnosis were identified in 62.4% of them; otherwise, missed opportunities for tuberculosis treatment occurred in 28.7% of cases and missed opportunities for HIV infection screening in 43.4% of cases. Tuberculosis was unifocal in 30.4% of cases, bifocal in 35.8%, and multifocal in 33.8%. Multifocal tuberculosis was associated with the existence of a missed opportunity for tuberculosis treatment (OR = 3.2. The fatality rate was 7/100 person-months: 7.3/100 person-months among people living with HIV compared to 6.8/100 person-months among others. After adjustment, age > 55 years (HR = 1.6; p – 0.038) and diabetes as a comorbidity (HR = 2; p – 0.024) were prognostic factors for tuberculosis; the risk of death was associated with a CD4+ T-cell count < 50/mm^3 in people living with HIV, being 10 times higher in those with a CD4+ T-cell count < 50/mm^3.

Conclusion: Tuberculosis was common, particularly among people living with HIV, whose therapeutic pathway with missed opportunities for diagnosis and treatment could contribute to their advanced immunosuppression upon arrival at the national reference department and, consequently, help explain the high lethality of tuberculosis.

Keywords: Therapeutic Pathway, Missed Opportunities, Tuberculosis, Senegal

Background

Tuberculosis (TB) is a public health problem in low- and middle-income countries (LMICs), where it is steadily increasing, mainly due to population growth and the emergence of the human immunodeficiency virus (HIV) [1]. The annual number of TB cases is estimated at 10 million, with 1.5 million deaths[1], mainly in LMICs. It is a target disease of the Global Fund with public health guidelines at the country level where the fight against TB is coordinated by a national program. This is the case in Senegal, where TB is endemic, with 14,688 cases diagnosed in 2022, 80% of which were contagious [2]. The HIV epidemic

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there is concentrated, and the healthcare system pyramidal, with university hospital centers (UHCs) at the top which bring together different specialties and thus the most complex patients, some of whom are referred by other healthcare facilities where adequate care could not be provided, particularly due to diagnostic and therapeutic problems. The Infectious and Tropical Diseases Department (ITDD) at the Fann National University Hospital Center (FNUHC) as the national reference center for infectious diseases provides an opportunity to document patients' treatment pathways and identify missed opportunities for diagnosis and treatment. We therefore conducted this study with the objectives of describing the treatment pathway of patients hospitalized at the ITDD between 2020 and 2022 with a diagnosis of TB and identifying the missed opportunities (for diagnosis and treatment) during their therapeutic pathway.

Methods

We conducted a retrospective cohort study on the records of patients hospitalized at the ITDD between January 1, 2020, and December 31, 2022, with a diagnosis of TB. The data were collected from patients' medical records and entered a Kobo toolbox database designed for the purposes of the study. Statistical analyses were performed using version 16.1 of the Stata software. The primary variable of interest was TB disease confirmed by smear microscopy, nucleic acid amplification tests, or histology on various pathological specimens.

A missed opportunity for TB diagnosis was the failure to screen for TB in a patient with a cough lasting ≥ 2 weeks, night sweats, fever, weight loss > 3 kg, or recent contact with a TB case (or chronic cougher). A missed opportunity for TB treatment was the absence of TB treatment in cases where tuberculosis was diagnosed. A missed opportunity for HIV screening was the absence of HIV serology in cases of tuberculosis. Each quantitative variable was represented by its mean with standard deviation or its median with interquartile range (IQR). For each qualitative variable, the percentages and 95% confidence intervals (95% CI) of the different categories were presented. Descriptive statistics were used to compare patients' characteristics according to HIV serostatus, using χ^2 tests.

The factors associated with multifocal TB were identified using a logistic regression model constructed according to a manual top-down procedure with the following independent variables: age (<35/35–45/46–55/>55), sex (male/female), history of tuberculosis (yes/No), history of hospitalization (yes/No) presence of comorbidity such as diabetes, high blood pressure, sickle cell disease, HIV infection, asthma (Yes/No), missed opportunity for TB diagnosis Yes/No), and missed opportunity for TB treatment (Yes/No). The cumulative incidence of death was assessed using Kaplan-Meier curves. The comparison of survival curves between PLHIV and others was performed using the log-rank test. Prognostic factors were identified using a Cox model constructed according to a manual downward procedure with the following explanatory variables:: age (<≤55/>55), sex (male/female), history of tuberculosis or hospitalization (yes/No), presence of diabetes as comorbidity, presence of other progressive opportunistic infection (Yes/No), LT CD4+ cell count (<50/≥50), missed opportunity for TB diagnosis Yes/No), and missed opportunity for TB treatment (Yes/No).

Results

The study population consisted of 363 patients, of whom 92 (25.3%) were hospitalized in 2020, 139 (38.3%) in 2021, and 132 (36.4%) in 2022. Their characteristics are presented in Table I. The median age (IQR) age was 39 (30-50) years. Seventy-two (19.9%; 95% CI = 15.9% - 24.9%) reported being vaccinated with BCG, 7.7% (95% CI = 5.2%-10.9%) against COVID-19, and 1.1% (95% CI = 0.3%-2.8%) against pneumococcus. Among people living with HIV (PLHIV), 93.1% (95% CI = 88.5%–96.3%) were infected with HIV-1, 5.9% (95% CI = 2.9%–10.2%) with HIV-2, and 1% (95% CI = 0.1%–3.8%) with both HIV-1 and HIV-2. One, 41, and 146 PLHIV were classified at WHO stage 2, WHO stage 3, and WHO stage 4, respectively. Other opportunistic infections (OIs) were found in 52.1% (95% CI = 44.7%– 59.4%) of them. Fifty-eight (31.2%; 95% CI = 24.6-38.4) PLHIV were on cotrimoxazole and 54.3% (95% CI = 46.8% - 61.5%) were antiretroviral therapy (ART)-nave. The latest CD4 count ranged from 1/mm³ to 282/mm³, with a mean of 96 ± 75/mm³. The last plasma viral load was known for 4 patients at 12 copies/mL, 370 copies/mL, 35,498,428 copies/mL, and 2,941,932 copies/mL Before admission to ITDD, 88.6% (95% CI = 84.9%-91.7%) had been seen at another healthcare facility, which could have been a health center, hospital, or private facility. Among them, 95.3% (95% CI = 92.4%–97.3%) had presented with cough, fever, weight loss, or night sweats, and TB was diagnosed in 34.5% (95% CI = 29.2%–40.2%) of them; Missed opportunities for TB diagnosis were identified in 65.5% (95% CI = 59.8% - 70.8%). Among the 105 patients diagnosed with TB prior to admission to the .ITDD, 71.3% (95% CI = 61.8%–79.8%) were placed on anti-tuberculosis treatment; missed opportunities for TB treatment occurred in 28.7% (95% CI = 20.2%–38.2%); HIV serology was performed in 56.2% (95% CI = 46.2% - 65.9%) and missed opportunities for HIV screening were identified in 43.8% (95% CI = 34.1% - 53.8%). The median duration (IIQ) of anti-tuberculosis treatment was 30 (13-65) days; duration < 6 months for 87% (95% CI = 77.1%-93.6%). The comparison of the sociodemographic characteristics of PLHIV with those of patients who were not living with HIV is presented in Table II. The mean age was 40.6 ± 12.4 years compared to 41.2 16.7 years among others; p = 0.359. The proportion of patients under 35 and those of patients over 55 were lower among PLHIV. The proportion of divorced and widowed individuals was higher among PLHIV, while the proportion of single individuals was lower. The level of education was lower among PLHIV. The average monthly income of PLHIV was lower.

Table 1: Characteristics of patients hospitalized with a diagnosis of tuberculosis from 2020 to 2022 in the infectious and tropical diseases department

Variables N = 363	%	95% CI[a]
Age (years)		
< 35	37.5	32.6-42.6
35-45	27.8	23.4-32.7
45-55	16.5	13-20.7
>55	18.2	14.5-22.5
Sex		
Female	38.4	33.5-43.5
Male	61.6	56.5-66.5
Residence area		
Urban	47.9	42.5-53.2
Suburban	43.0	37.8-48.4
Rural	09.1	06.3-12.6
Education level		
Unspecified	49.9	44.6-55.1
Not at school	08.8	06.1-12.2
Up to high school diploma	08.3	05.6—11.6
Post-secondary/college	18.2	14.3-22.5
At least undergraduate degree	14.9	11.4-19.0
Average monthly income (US$)		
< 200	37.3	30.7-44.1
200 – 1000	58.0	51.1-64.7
> 1000	04.7	02.3-09.8
History of tuberculosis	14.1	10.6-18.1
Previous hospitalization	44.9	40.0 -50.2
Comorbidity		
HIV infection	51.6	46.5-57
High blood pressure	07.2	04.7-10.1
Diabetes	06.3	03.8-09.7
Sickle cell disease	01.9	00.8 – 03.9
Lifestyle habits		
Smoking	18.5	14.6-23
Alcohol consumption	08.2	05.5-11.5
Cocaine use	00.3	00.0- 01.6
Phytotherapy	02.0	00.8-04.0

[a] 95% confidence interval

Table 2: Comparison of sociodemographic characteristics of patients hospitalized with a diagnosis of tuberculosis from 2020 to 2022 in the infectious and tropical diseases department according to HIV serostatus

Characteristics	HIV serostatus				p-value
	HIV– N = 175		HIV+ N = 188		
	%	95% CI[a]	%	95% CI	
Age (years)					< 0.001
≤ 35	44	36.5 - .51.7	31.4	24.8 – 38.5	
35-45	19.4	13.8 – 26.1	35.6	28.8 - 42.9	
45-55	13.7	09.0 – 19.7	19.2	13.8 - 25.5	
>55	22.9	16.9 – 29.8	13.8	09.2 - 19.6	
Sex					< 0.001
Male	72.6	65.3 - 79.0	51.3	.43.9 - 58.7	
Female	27.4	21.0 - .34.7	48.7	41.3 - 56.0	
Marital status					< 0.001
Single	38.9	31.5 – 46.7	23	17.2 - 29.7	
Divorced	04.8	2.1 – 9.2	13.9	09.3 - 19.7	
Married	51.5	43.6 – 59.3	47.1	39.7 - 54.5	
Widower	04.8	2.1 – 09.2	16	11.1 - 22.1	
Education level					< 0.001
Unspecified	40.6	33.2 – 48.2	58.5	51.1 - 65.6	
Not at school	00.0		01.6	00.3 – 04.6	
Up to high school diploma	08.6	04.9 – 13.7	07.5	04.1 – 12.2	
Post-secondary/college	03.4	01.3 – 07.3	12.8	08.3 – 18.4	
At least undergraduate degree	24.6	18.4 – 31.6	12.2	07.9 – 17.8	
Average monthly income (US$)					0.003
< 200	28.3	20.0 – 37.9	46.2	36.5 – 56.2	
200 – 1000	63.2	53.3 – 72.4	52.8	42.9 – 62.6	
> 1000	08.5	04.0 – 15.5	01.0	.00.2 – 05.1	
Lifestyle habits					
Smoking	21.1	05.8 – 15.1	16	11.0 – 22.2	0.214
Alcohol consumption	10.3	06.2 – 15.8	06.1	03.1 -10.6	0.147
Cocaine use	00.0		00.9	00.2 – 05.4	0.325
Phytotherapy	02.3	00.6 – 05.7	01.7	00.3 – 04.8	0.670

[a] 95% confidence interval

A history of tuberculosis was found in 16% (95% CI = 11%–22%) of PLHIV compared with 12% (95% CI = 7.6%–17.7%); p = 0.278; and a history of hospitalization in 4.2% (95% CI = 1.8%–8.2%) of PLHIV compared to 8.1% (95% CI = 4.5%–13.1%); p = 0.219. The most common comorbidities were high blood pressure, diabetes, and sickle cell disease. Diabetes was less common among PLHIV: 3.7% versus 9.1%; p = 0.034. The prevalence of high blood pressure and sickle cell diseuse did not differ according to HIV status. The most common locations of TB were pulmonary (94.6%; 95% CI = 91%–97.1%), neurological (42%; 95% CI = 35.7%–48.4%), lymph node (39.9%; 95% CI = 33.7%–46.4%), pleural (21.8%; 95% CI = 16.8%–27.5%), peritoneal (18.5%; 95% CI = 13.8%–24%), splenic (10.7%; 95% CI = 7.1%– 15.3%), digestive (10.3%; 95% CI = 6.8%–14.8%), bone (8.2%; 95% CI = 5.1%–12.4%), and hepatic (6.6%; 95% CI = 3.8%–10.5%). TB was unifocal in 30.4% (95% CI = 25.6%–35.5%) of cases, bifocal in 35.8% (95% CI = 28.9% - 39.0%) and multifocal in 33.8% (95% CI = 11% – 22%); multifocal TB was associated with a missed opportunity for TB treatment (OR = 3.2; 95% CI = 1.2 – 8.3). The frequencies of the different locations according to HIV serostatus are presented in Table III. Miliary tuberculosis was found in 0.8% (95% CI = 0.2%-4.2%) of PLHIV compared with 2.6% (95% CI = 0.5%-7.5%) in others; p = 0.256. The frequency of extrapulmonary tuberculosis and multifocal TB did not differ according to HIV serostatus. The anti-tuberculosis treatment regimens are presented in Table IV.

Table 3: Locations of tuberculosis of patients hospitalized with a diagnosis of tuberculosis from 2020 to 2022 in the infectious and tropical diseases department according to HIV serostatus

Locations	HIV serostatus				p-value
	HIV-		HIV+		
	%	95% CI[a]	%	95% CI	
Pulmonary	95.6	90.1 -98.6	93.8	88.1 -97.3	0.530
Neurological	44.7	35.4 - 54.4	39.5	31.0 - 48.5	0.412
Ganglion	27.2	19.3 - 36.3	51.2	42.2 - 60.0	< 0.001
Pleural	23.7	16.2 - 32.6	20.2	13.6 - 28.1	0.506
Peritoneal	20.2	13.2 - 28.7	17.1	11.0 - 24.7	0.532
Splenic	03.5		17.1		0.001
Digestive	08.8	04.3 - 15.5	11.6	06.6 - 18.4	0.465
Bone	12.3	06.9 - 19.7	04.7	01.7 - 09.8	0.031
Hepatic	06.1	02.5 - 12.4	07.0	3.2.12.8	0.793
Pericardial	04.4	01.4 - 09.9	04.6	01.7 - 09.8	0.921
Urinary	01.7	00.2 - 06.2	01.6	00.2 - 05.5	0.901

[a] 95% confidence interval

Table 4: Anti-tuberculosis treatment regimens of patients hospitalized with a diagnosis of tuberculosis from 2020 to 2022 in the infectious and tropical diseases department

Treatment regimens	%	95% CI[a]
2RHZE+4RH	60.3	54.9 - 65.4
2RHZE+10RH	32.9	27.9 - 38.0
2RHZE	2.00	0.8 - 04.1
4RH	00.9	00.2 - 02.5
2RHZE + 10RH	00.6	00.0 –0 2.4
10RH	00.3	00.0 – 01.6
2RH+4RHZE	00.3	00.0 – 01.6
2RHE+4RH	00.3	00.0 – 01.6
2RHZE + 10 RH	00.3	00.0 – 01.6
2RHZE +10RH	00.3	00.0 – 01.6
2RHZE +4RH	00.3	00.0 – 01.6
2RHZE+10RH	00.3	00.0 – 01.6
2RHZE+12RH	00.3	00.0 – 01.6
2RHZE+4RE	00.3	00.0 – 01.6
2RHZE+6RH	00.3	00.0 – 01.6
2RHZE/4EH	00.3	00.0 – 01.6

[a]95% confidence interval

The tuberculosis treatment regimens did not differ according to HIV serostatus. The average duration of treatment was 8.2 ± 2.9 months. Treatment was directly observed in 77.6% of cases; less frequently in PLHIV: 72.8% versus 82.7%; p = 0.026. ART was modified during hospitalization for one patient. The delay in introducing ART after the start of anti- tuberculosis treatment was 2 weeks for 107 patients, 4 weeks for 39 patients, 6 weeks for one patient, while 26 died before ART was introduced. A double dose of Dolutegravir was prescribed to 137 patients, while 3 received a single dose. The average length of hospital stay was 14.6±10.2 days: 16 ± 10.7 days for PLHIV compared to 13 ± 5.2 days for non-HIV individuals, p=0.002. The probability of death was 33.6% (95% CI = 28.8%–38.7%) and the case fatality rate was 7/100 person-months: 7.3/100 person- months among PLHIV versus 6.8/100 person-months among others; Log-Rank test, p = 0.752. The survival curves are shown in Figure 1. After adjustment, the risk of death was associated with diabetes and advanced age (Table V). More specifically, among PLHIV, the risk of death was associated with a CD4+ LT < 50/mm^3 (Table VI); the risk of death was 10 times higher among PLHIV with a CD4+ LT < 50/mm^3.

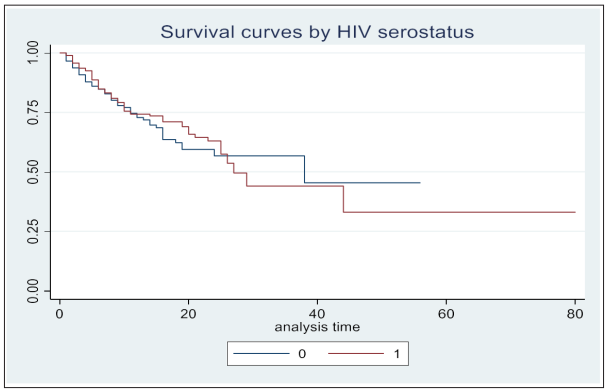

Figure 1: Survival Curves for Tuberculosis Patients Hospitalized at ITDD in 2020-2022 by HIV Serostatus

Table 5: Crude and adjusted hazard ratios of characteristics of patients hospitalized with a diagnosis of tuberculosis at the infectious and tropical diseases department on death from Cox regression models

Characteristics	Univariate analysis (N= 361)		Multivariate analysis (N = 361)	
	HR[a] (95% CI[b])	p-value	HR* (95% CI)	p-value
Age (tears)				
≤ 55	1		1	
>55	1.7(1.1 - 2.5)	0.011	1.6(1.1-2.4)	0.024
Sex				
Female	1		1	0.094
Male	1.2(0.9-1.8)	0.433	1.2(0.9-1.8)	0.237
History of TB				
NO	1		1	
Yes	1.2(078-1.9)	0.240	1.1 (07 – 1.9)	0.598
History of hospitalization				
NO	1			
Yes	1.1(0.7-1.5)	0.687		
Diabetes				
No	1		1	
Yes	2.0(1.2-3.5)	0.013	1.8 (1.03 –3.2)	0.038
HIV infection				
No	1			
Yes	0.9(0.7-1.3)	0.755		
BCG vaccination				
No	1			
Yes	0.9(0.5-1.6)	0.759		
COVID-19 vaccination				
No	1			
Yes	1.0(0.5-2.1)	0.925		
Pneumococcal vaccine				
No	1			
Yes	1.0(0.8-1.5)	0.736		
Missed opportunity for TB screening				
No	1			
Yes	1.2(0.8-1.9)	0.286		
Missed opportunity for TB treatment				
No	1			
Yes	1.0(0.4-2.1)	0.967		

Characteristics	Univariate analysis (N= 361)		Multivariate analysis (N = 361)	
	HR[a] (95% CI[b])	p-value	HR[*] (95% CI)	p-value
Missed opportunity for HIV screening				
No	1			
Yes	1.0(0.5-1.9)	0946		

[a]hazard ratio [b]95% confidence interval [*]Adjusted,

Table 6: Crude and adjusted hazard ratios of characteristics of hospitalized people living with HIV diagnosed with tuberculosis at the infectious and tropical diseases department on death from Cox regression models

Characteristics	Univariate analysis N = 188		Multivariate analysis N = 188	
	HR[a] (95% CI[b])	p-value	HR* (95% CI)	p-value
Age (years)				
≤ 55	1		1	
>55	1.4(0.7-2.6)	0.273	0.8(0.1-5.8)	0.853
Sex				
Female	1		1	
Male	1.2(0.8-1.9)	0.462	8.1(0.7-93.9)	0.094
History of TB				
No	1			
Yes	1.4(0.8-2.7)	0.243		
History of hospitalization				
No	1			
Yes	0.9(0.5-1.9)	0.646		
Other progressive opportunistic infection				
No	1			
Yes	1.04(0.6-1.7)	0.884		
Antiretroviral therapy naive				
No	1			
Yes	1.2(0.8-2.1)	0.328		
Antiretroviral therapy introduction delay				
2 weeks	1			
4 weeks	1.1(0.5-2.3)	0.802		
6 weeks	5(0.7-37.5)	0.119		
LT CD4+ < 50				
No	1		1	
Yes	4(0.8-21.7)	0.101	9.7(1.3-7.3)	0.027
Diabetes				
No	1			
Yes	1.8(0.7-5.1)	0.235		
Missed opportunity for TB screening				
No	1			
Yes	1.3(0.8-2.2)	0.271		
Missed opportunity for TB tratment				
No	1			
Yes	0.8(0.5-1.3)	0.405		
Missed opportunity for HIV screening				
No	1			
Yes	0.8(0.3-2.3)	0.708		

[a]hazard ratio [b]95% confidence interval [*]Adjusted

Discussion

Between 2020 and 2022, 363 tuberculosis patients with a median age of 39 years and 61.6% men were hospitalized at the ITDD. Among them were 188 PLHIV, more than half of whom were at WHO stage IV and ART-naïve with a mean CD4+ LT of 96/mm^3. Before admission to the ITDD, 88.6% had been seen at another health facility, with missed opportunities for TB diagnosis in 27.3%, missed opportunities for TB treatment in 31.2%, and missed opportunities for HIV screening in 42.9%. HIV infection was not a prognostic factor for TB, but a low CD4 count was in PLHIV. Our study was exhaustive in the national reference department during 2020-2022. The study population, most of whom could not be properly treated at other levels of the healthcare pyramid, reflects the difficulties of managing TB in LMICs. The diagnosis of TB was made according to the highest standards in LMICs; the diagnosis of HIV infection was made according to WHO recommendations.

The characteristics of our study population in terms of age, sex, and area of residence are consistent with those reported for sub-Saharan African countries[3–6]. Like our study, others have reported that the first recourse for care was not specialized services in Senegal, where 27.2% of patients resorted to traditional healers[7]. In one health district in 2022, delays in consultation were reported in 60% of TB cases and delays in prescribing smear tests in 50.8% of cases [8]. At the national level, one in three TB cases had not been detected or reported by the health system in 2024 [8,9]. According to Keugoung et al., many opportunities (screening, education, system strengthening) are not being seized in sub-Saharan Africa [10] ; a significant delay between the onset of symptoms and seeking care has been reported in South Africa[11]. Like our study, Cherif M et al reported a case of multifocal TB following a missed opportunity to treat TB [12]. This is biologically plausible because an infection, if left unchecked, spreads.

The characteristics of our study population should be like those of patients with TB requiring specialized care in LMICs. The results of our study should be generalizable in these countries, subject to a different diagnostic approach. The main limitation of our study was the completeness of the data, which did not allow us to adjust the associations studied for plasma HIV RNA.

Conclusion

TB was common in Senegal, with a hospital prevalence of 20.3% in the national reference department for infectious diseases. It was particularly common among PLHIV whose therapeutic pathway, with missed opportunities for diagnosis and treatment, could contribute to their advanced immunodeficiency and high mortality rates. The patients' pathway prior to admission to the ITDD may contribute to delays in receiving appropriate care. It would therefore be appropriate to improve the diagnostic and therapeutic capabilities of frontline health workers regarding TB, but also with regard to HIV infection.

Conflicts of interest

No author declares potential competing interests.

Acknowledgements

Data availability

Data are available on reasonable request. Aggregate data can be obtained through a formal request procedure. Researchers interested in obtaining access to the data are advised to contact the corresponding author (DA). Data will be shared in accordance with applicable data protection regulations and ethical considerations.

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