Original research article

Tuberculosis prevalence and associated factors among persons infected with human immunodeficiency virus in three West African countries (Benin, Guinea, Senegal)

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ABSTRACT

Background: Tuberculosis (TB) is a leading cause of morbidity and mortality in people living with human immunodeficiency virus (HIV). Data are very scarce on the burden of TB in HIV patients in Sub-saharan African populations. This study aimed to determine the prevalence of pulmonary tuberculosis (PTB) and associated factors among people living with human immunodeficiency virus (HIV) in three West African countries: Benin, Guinea, and Senegal. Methods: A cross-sectional study was conducted among people living with HIV in three outpatient care centres (one in each country). All HIV-positive patients included in this study were routinely screened for PTB using microscopy, GeneXpert and culture. Participants free of TB were reassessed clinically and biologically six months later. Data were analyzed using R-3.4.3 software. Logistic regression was used to identify factors associated with PTB. Results: A total of 2,859 participants were enrolled in the study, of whom 2,820 were screened for TB, 1,000 were ARV-naive (35.46%), and 1,820 were on ARV prior to screening (64.54%). A total of 127 cases of bacteriologically confirmed PTB (BCPTB) were diagnosed: 117 at baseline and 10 at the 6-month visit. The overall prevalence of BCPTB was 7.90% [95% CI: 6.38-9.75] for ARV-naive participants and 2.64% [95% CI: 1.99-3.48] for participants on ARV at the time of screening. Participants from Guinea were more likely to be diagnosed with TB (OR: 2.95 [95% CI: 1.60-5.45], p=0.001). Underweight HIV-positive patients had higher odds of TB diagnosis (OR: 2.09 [95% CI: 1.40-3.12], p<0.001), while overweight/obesity was associated with lower odds of TB (OR: 0.35 [95% CI: 0.15-0.81], p=0.015). Other factors associated with BCPTB in HIV patients were male sex (OR: 1.81 [95% CI: 1.18-2.77], p=0.007), CD4 count <200/ml (OR: 2.24 [95% CI: 1.15-4.37], p=0.018), and irregular disease follow-up (OR: 2.57 [95% CI: 1.29-5.15], p=0.018).

Conclusion: The prevalence of TB among people living with HIV is high in Benin, Guinea and Senegal. These results highlight the need to improve TB screening and diagnosis in PLHIV, especially in ARV-naive patients.

Key words: Tuberculosis, PLHIV, burden, risk factors, West Africa

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Introduction

Tuberculosis (TB) is a major public health issue in sub-Saharan Africa, where the burden of this disease is high [1]. People living with HIV (PLHIV) are particularly vulnerable to TB because of their weakened immune systems. The co-occurrence of HIV and TB is a major challenge for the healthcare systems in Africa because the two diseases are closely linked and can lead to severe health outcomes, if left untreated [2].

TB is the leading cause of death among people living with HIV[3]. This high mortality rate is mainly due to delayed diagnosis or non-diagnosis of TB in this at-risk population [4–7]. In fact, diagnosing TB in PLHIV is difficult because of the frequency of extrapulmonary, disseminated or paucibacillary forms in this population[7]. In addition, several studies have shown that high mortality may also be associated with misdiagnosis of TB. Indeed, autopsy studies of deceased PLHIV have reported that almost half of them had TB [8,9]. Even today, TB remains an underrecognized disease among PLHIV, as the rate of detection in this high-risk population remains low [10].

Thus, there is a compelling need to improve the diagnosis and management of TB in PLHIV. The World Health Organization recommendations for reducing the burden of TB among PLHIV ('3I" strategy) include intensifying TB case detection to ensure highquality anti-TB treatment, preventing TB with Isoniazid by starting antiretroviral treatment rapidly, and combating the transmission of TB infection in health services and community facilities [11]. Intensified case finding (ICF) is a key strategy for reducing the incidence and mortality of TB in PLHIV. It consists of systematically identifying TB at every clinical consultation among PLHIV to treat TB cases at an early stage and prevent transmission in this target population[12]. However, data on the effectiveness of ICF in identifying TB cases among PLHIV in West Africa are limited. Moreover, data on the true prevalence of TB among PLHIV are scarce in the sub-region.

The main objectives of this study were to estimate the prevalence of PTB among PLHIV who had undergone ICF in outpatient HIV clinics as well as the associated factors in three West African countries: Benin, Guinea, and Senegal.

Patients and Methods

Study design and countries involved

This was a multicountry cross-sectional study conducted between October 2015 and March 2017 in Benin, Guinea and Senegal.

Study sites

In each of the countries, the study was conducted at ambulatory HIV care centers located in 3 university hospitals in Cotonou (Centre National Hospitalier Universitaire), Conakry (Centre Hospitalier Universitaire Donka) and Dakar (Centre Hospitalier Universitaire Fann). According to previous data, the prevalence of HIV infection in the population was 1,0 % in Benin, 1,6% in Guinea and 0,4 % in Senegal, respectively during the study period [13].

The incidence of TB in the general population during the study period, was 53, 175, 113 per 100,000 population, respectively, in Benin, Guinea and Senegal [14].

Population

All HIV infected patients who were receiving care in the selected centers and who gave their formal consent were eligible for the study. Those who were already diagnosed with TB and were on treatment prior to the survey were not included. A total number of 1,000 HIV patients per country were planned to be recruited to make 3,000 participants for the three centers. Study procedures included sequential recruitment of participants up to 20 per day to avoid excessive workload for the laboratory teams.

For study procedures, data collection, training of clinical investigators, quality control, we followed the methods described elsewhere by Wachinou and al. [15].

Study procedures

All HIV patients, who were included in the study, were systematically screened for presumptive TB symptoms based on the WHO 4-items questionnaire (cough, fever, night sweats and weight loss) [16]. Each of them were asked to produce two sputum samples (one on the spot and the other one in the early morning) for fluorescence auramine microscopy, Xpert/ MTB/RIF and mycobacterial culture on Lowenstein-Jansen solid media [17]. All bacteriological tests were performed at the TB reference laboratory of each country.

In order to detect any undiagnosed TB case, all HIV patients who were not diagnosed with active TB at the enrolment visit were invited for a new TBrelated investigation six months later. After clinical assessment, they were again requested to produce sputum samples for microscopy and culture. HIV patients with active TB were referred to a basic management unit for treatment. The following data were collected: sociodemographic and anthropometric characteristics, type of HIV, duration of the disease, clinical characteristics such as cough, fever, weight loss, nocturnal sweating, hemoptysis, smoking habits, BCG scar, contact with a TB case, CD4 counts, and TB-status, weight and height. Data were collected by trained clinical investigators who were involved in the study, using a prevalidated questionnaire.

At each site, a local supervisor checked data collection on a weekly basis. Every three months, an external monitor visited to verify the data accuracy by comparing key information like patient eligibility, symptoms, and lab results with original documents. Additionally, a senior lab officer reviewed laboratory results quarterly to ensure all lab procedures were followed correctly.

Diagnostic criteria

BCPTB: A participant was diagnosed with TB based on a positive result of acid-fast bacilli seen on sputum smear microscopy, a positive result of the Xpert MTB/RIF assay or mycobacterial culture, either at the initial assessment or at the sixth-month follow-up visit (for those who were not diagnosed with TB at the first visit).

Nutritional status: This was assessed with Body Mass Index (BMI, kg/m²) that was calculated using the following formula (Weight (in kg) / [Size (in m)]²). Four categories were identified: underweight (BMI <18.5 kg/m²), normal status (BMI= 18.5-24.99 kg/m²), overweight (BMI= 25-29.99 kg/m²) and obesity (BMI ≥30 kg/m²).

Close contact with a TB case: A person who shared the same enclosed living space for one or more nights or for frequent or extended periods during the day with an active TB case [18].

Smoking habits: Participants were categorised into three groups: non-smokers, ex-smokers and current smokers.

BCG vaccination status: This was assessed by examination of the BCG scar mainly on the left forearm. The scar was either present, absent or doubtful.

Data management and analysis

Data were double entered in an access database by two local clerks and clean data were then analyzed using R-3.4.3 software. Categorical variables were expressed as percentages. Comparisons between two categorical variables were made using the chi-square test (or Fisher's exact test if applicable). Potential factors associated with TB were selected from a large literature review. These included: age, sex, close contact with a TB case, BMI, BCG vaccination and smoking habits. A bivariate analysis was performed. This was followed by a multiple logistic regression with all variables showing a p-value less than 0.25 on bivariate analysis. A backward stepwise strategy was performed. The Hosmer-Lemeshow test was used to validate the model.

Results

Baseline characteristics of participants

Overall, 2,859 participants were enrolled in the study out of which 2,820 were screened for TB with 1,000 naïve of ARV (35.46%) and 1,820 on ARV before the screening (64.54%) (Figure 1). Participants

aged 35-49 years were the most represented with 51.57%, 43.66% and 48.87%, respectively for Benin, Guinea and Senegal. They were majoritarily female across the three countries with 69.74% for Benin, 69.30% for Guinea and 60.16% for Senegal. Underweight was found in 15.23% of the participants in Benin, 24.50% in Guinea and 19.26% in Senegal. Most of the participants had HIV1 with an overall proportion of 97.34%. HIV 2 were mostly found in Senegal representing 6.24% of the participants, whereas it only represented 0.10 in Benin and 0.67% in Guinea. The majority of the participants were diagnosed with HIV infection within the last five years across the three countries with 62.38% in Benin, 77.98% in Guinea while in Senegal these participants only represented 32.01%. Close contact with a TB case was reported by 3.73% of participants in Benin, 15.16% in Guinea and 10.76% in Senegal. HIV disease follow-up was irregular in 2.46% of participants in Benin, 10.49% in Guinea and 2.26% in Senegal (Table 1).

Prevalence of BCPTB

Overall, 127 BCPTB cases were diagnosed with 117 cases diagnosed at the initial visit and 10 at 6-month visit (Figure 1). The overall prevalence

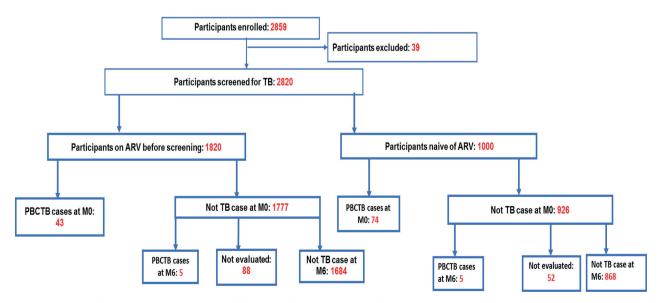


Figure 1. Tuberculosis screening among People living with HIV in three ambulatory HIV care centers in Benin, Guinea and Senegal. BCPTB: Bacteriologically confirmed tuberculosis; TB: tuberculosis; ARV: Antiretroviral therapy; M: month.

	Benin n (%)	Guinea n (%)	Senegal n (%)	All n (%)
Age (years)				
<35	270 (26.52)	411 (39.18)	133 (17.66)	814 (28.87)
35-49	525 (51.57)	458 (43.66)	368 (48.87)	1351 (47.91)
50-64	207 (20.33)	164 (15.63)	210 (27.89)	581 (20.60)
≥65	16 (1.57)	16 (1.53)	42 (5.58)	74 (2.62)
Gender				
Male	308 (30.26)	322 (30.70)	300 (39.84)	930 (32.98)
Female	710 (69.74)	727 (69.30)	453 (60.16)	1890 (67.02)
Body mass index (kg/m²)				
<18.5	155 (15.23)	257 (24.50)	145 (19.26)	557 (19.75)
18.5-24.99	568 (55.80)	622 (59.29)	384 (51.00)	1574 (55.82)
25.0-29.99	192 (18.86)	133 (12.68)	169 (22.44)	494 (17.52)
≥ 30	103 (10.12)	37 (3.53)	55 (7.30)	195 (6.91)
Smoking habits				
Never smoker	983 (96.56)	865 (82.46)	553 (73.44)	2401 (85.14)
Current/Ex-smoker	35 (3.44)	184 (17.54)	200 (26.56)	419 (14.86)
Type of HIV				
HIV 1	1015 (99.71)	1038 (98.95)	692 (91.90)	2745 (97.34)
HIV 2	1 (0.10)	7 (0.67)	47 (6.24)	55 (1.95)
HIV1+HIV2	2 (0.20)	4 (0.38)	14 (1.86)	20 (0.71)
Age of HIV infection (years)				
< 1	408 (40.08)	490 (46.71)	146 (19.39)	1044 (37.02)
1-5	227 (22.30)	328 (31.27)	95 (12.62)	650 (23.05)
6-10	236 (23.18)	188 (17.92)	287 (38.11)	711 (25.21)
> 10	147 (14.44)	43 (4.10)	225 (29.88)	415 (14.72)
Patients on ARV				
Yes	624 (61.30)	608 (57.96)	588 (78.09)	1820 (64.54)
No	394 (38.70)	441 (42.04)	165 (21.91)	1000 (35.46)
Close contact with a TB case				
Yes	28 (3.73)	159 (15.16)	81 (10.76)	278 (9.86)
No	980 (96.27)	890 (84.84)	672 (89.24)	2542 (90.14)
BCG vaccination status				
Present	685 (67.29)	59 (5.62)	573 (76.10)	1317 (46.70)
Doubtful/Absent	333 (32.71)	990 (94.38)	180 (23.90)	1503 (53.30)

Table 1. Demographics and characteristics of People living with HIV in three ambulatory HIV care centres in Benin, Guinea and Senegal (N=2820).

Table 1 (Continues)

	Benin n (%)	Guinea n (%)	Senegal n (%)	All n (%)
HIV Disease monitoring				
Regular	589 (57.86)	502 (47.86)	586 (77.82)	1677 (59.47)
Irregular	25 (2.46)	110 (10.49)	17(2.26)	152 (5.39)
No information	9 (0.88)	_	24 (3.19)	33 (1.17)
Recent diagnosis	395 (38.80)	437 (41.66)	126 (16.73)	958 (33.97)
Fotal	1018	1049	753	2820

Table 2. Prevalence of tuberculosis in on-ARV and ARV-naive people living with HIV screened at three outpatient care centres in Benin, Guinea and Senegal (N=2820).

Type of		Benin		Guinea		Senegal		Total	
	%	IC95%	%	IC95%	%	IC95%	%	IC95%	
ARV naive	3.30	[1.92-5.61]	12.93	[10.09-16.41]	5.45	[2.84-10.21]	7.90	[6.38-9.75]	
On ARV	1.60	[0.86-2.96]	4.93	[3.47-6.98]	1.36	[0.68-2.70]	2.64	[1.99-3.48]	
Total	2.26	[1.50-3.38]	8.29	[6.77-10.13]	2.26	[1.41-3.61]	4.50	[3.80-5.33]	

of BCPTB was 7.90% [95% CI: 6.38-9.75] for ARV naïve participants and 2.64% [95% CI: 1.99-3.48] for participants on ARV at the time of screening. The ratio of the prevalences between ARV naïve and participants on ARV ranged from 2 in Benin to 4 in Senegal. Guinea showed the highest prevalence in both populations: 12.93% (95CI%: 10.09-16.41) for ARV naïve participants and 4.93 (95% CI: 3.47-6.98) for those on ARV at the time of screening (Table 2).

Factors associated with BCPTB in HIV patients

Potential factors associated with TB in HIV patients in the three countries are shown in Table 3. After multivariable analysis, compared to participants from Benin, those living in Guinea had a higher odd of being diagnosed with TB (OR: 2.95 [95% CI: 1.60-5.45], p=0.001). Underweight HIV patients showed a higher odd of being diagnosed with TB (OR: 2.09 [95% CI: 1.40-3.12], p<0.001), while overweight/obesity was associated with a lower odd of TB (OR: 0.35 [95% CI: 0.15-0.81], p=0.015). Other factors associated with BCPTB in HIV patients were: being male: (OR: 1.81 [95% CI: 1.18-2.77], p=0.007), CD4 count <200/ml (OR: 2.24 [95% CI: 1.15-4.37], p=0.018), and irregular follow up of the disease (OR: 2.57 [95%/ 1.29-5.15], p=0.018).

Discussion

This cross-sectional study was conducted in a large population of HIV-infected patients from three sub-Saharan African countries. This study found a high prevalence of BCPTB among PLHIV, with ARV-naive patients showing a much higher prevalence than those on ARV across the three countries. Patients living in Guinea were more likely to have TB than those living in Benin or Senegal. We also found that underweight patients were more likely to develop TB than were overweight or obese patients. Male sex, CD4<200/ml and irregular follow-up were also factors associated with TB in PLHIV.

The high prevalence of tuberculosis in PLHIV is consistent across studies[19,20]. However, the overall prevalence found in our study (4.5%) was lower than that reported in other studies. For example, Ngowi et al. [21], Iliyasu et al. [22] and Assefa et al. [23] reported prevalence rates of 8.5%, 10.5%, and 11%, respectively. Kimerling et al. [24] in Cambodia and Jam

	ТВ					
Variables	Yes	No	cOR (IC95%)	р	aOR (IC95%)	Р
Country						
Benin	23	995	1		1	
Guinea	87	962	3.91 [2.45-6.24]	< 0.001	2.95 [1.60-5.45]	0.001
Senegal	17	736	0.99 [0.53-1.88]		1.24 [0.62-2.47]	0.546
Age (years)						
<35	44	770	1		-	-
35-49	59	1292	0.80 [0.54-1.19]	0.325 -	-	-
50-64	20	561	0.62 [0.36-1.07]		-	-
≥65	4	70	1 [0.35-2.86]	_	-	-
Gender						
Male	65	865	2.22 [1.54-3.12]	.0.001	1.81 [1.18-2.77]	-
Female	62	1828	1	— <0.001 —	1	0.007
Nutritional status						
Normal	62	1512	1		1	
Underweight	59	498	2.89 [1.99-4.19]	<0.001	2.09 [1.40-3.12]	< 0.001
Overweight/obesity	6	683	0.25 [0.10-0.62]		0.35 [0.15-0.81]	0.015
Smoking habits						
Never smoker	96	2305	1	0.000	1	
Current/Ex-smoker	31	388	1.91 [1.26-2.92]	— 0.002 —	1.05 [0.62-1.78]	0.846
Close contact with a TB case						
Yes	20	258	1.76 [1.08-2.89]	0.002	-	-
No	107	2435	1	— 0.023 —	_	_
Type of HIV						
HIV 1	127	2618	-		-	-
HIV 2	0	55	-	0.247	_	_
HIV1+HV2	0	20	-		_	_
Age of HIV infection diagnosis (years)						
< 1	84	960	1		-	-
1-5	22	628	0.40 [0.25-0.65]		0.59 [0.26-1.36]	0.219
6-10	14	697	0.23 [0.13-0.41]	- <0.001 -	0.54 [0.22-1.35]	0.187
> 10	7	408	0.20 [0.09-0.43]		0.66 [0.22-1.96]	0.455
Patients on ARV						
Yes	48	1772	1	0.004	1	-
No	79	921	3.17 [2.19-4.57]	- <0.001 -	0.96 [0.28-3.34]	0.955
BCG vaccination scar						
Present	32	1285	1	0.004	1	_
Doubtful/Absent	95	1408	2.70 [1.80-4.07]	- <0.001 -	0.97 [0.55-1.73]	0.918

Table 3. Factors associated with tuberculosis in people living with HIV in three West African countries (N=2,820).

Table 3 (Continues)

	ТВ					
Variables	Yes	No	cOR (IC95%)	р	aOR (IC95%)	Р
HIV infection follow up						
Regular	33	1644	1		1	-
Irregular	15	137	5.45 [2.89-10.29]	.0.001	2.57 [1.29-5.15]	0.008
No information	1	32	1.56 [0.21-11.73]	- <0.001 -	2.61 [0.26-26.17]	0.414
Recent discovery	78	880	4.41 [2.92-6.69]		1.63 [0.41-6.51]	0.486
CD4 count(/ml)						
>=200	11	844	1		1	
<200	108	1784	4.64 [2.48-8.68]	< 0.001	2.24 [1.15-4.37]	0.018

ARV: antiretroviral; cOR: crude odd ratio; aOR: adjusted odd ratio

et al. in Iran [25] reported overall prevalences of 9% and 24%, respectively. While these discrepancies with the prevalence found in our study could be explained by differences in the prevalence of TB and HIV infection in the studied populations, other background determinants that could not be accounted for may also be involved. This high prevalence of TB in HIV patients suggests the need for prompt TB screening and diagnosis to prevent the spread of TB. It also highlights the fact that PLHIV constitute a reservoir of TB [26] and that intensifying TB detection in this at-risk population will help close the gap in missing TB cases [23].

Our study showed that the TB burden is higher in ARV-naive PLHIV than in ARV patients at the time of screening. This is consistent with results from previous studies [27–30]. This finding confirms, in one hand, the efficacity of antiretroviral (ARV) treatment in reducing the risk of TB in PLHIV. In the other hand, the findings underscore the need for improved TB screening and diagnosis among ARV-naive PL-HIV before the commencement of ARV treatment.

The prevalence of TB among PLHIV varied among countries, with Guinea reporting the highest prevalence, followed by Benin and Senegal. Differences in the burden of TB in these countries as well as differences in healthcare systems and access to care may explain these variations. For example, Guinea was one of the sub-Saharan African countries affected by the Ebola epidemic between 2014 and 2015. This epidemic had a significant impact on already weak health services in African countries. During the epidemic, there was a massive drop in the number of patients in health facilities, especially in HIV treatment centres, with a considerable reduction in the detection of new cases of TB and HIV. It was also noted that HIV prevalence increased significantly during this period [31]. As HIV immunosuppression is one of the main risk factors for TB, it is understandable that the prevalence of this disease among PLHIV in Guinea is higher than that in countries not affected by the Ebola epidemic [32].

This study also identified some factors associated with TB in PLHIV. Underweight patients were more likely to be diagnosed with TB (OR: 2.09 [95% CI: 1.40-3.12], p<0.001), while overweight/obese patients had lower odds (OR: 0.35 [95% CI: 0.15-0.81], p=0.015). Malnutrition weakens the immune system, rendering PLHIV more vulnerable [33]. Similar associations were reported by Enju et al. in Tanzania [34] and Moore et al. in Uganda [35]. This association underscores the need for nutritional support for PLHIV.

Although our study included a majority of women and that HIV prevalence is higher in the female population than in the male population [36], we found that male PLHIV had a higher risk of developing TB than female PLHIV (OR: 1.81 [95% CI: 1.18-2.77], p=0.007). This finding corroborates that of Enju et al. in Tanzania [34], Kribet et al. in Ethiopia[[37], and Gupte et al. in India [38]. Gupte et al. explained this finding by the fact that men were more immunosuppressed than women at the start of ARV treatment [38]. This is also in line with the epidemiological curiosity of a higher notification of TB in men than in women generally [39].

Not surprisingly, a low CD4 count (<200/ml (OR: 2.24 [95% CI: 1.15-4.37], p=0.018)) was associated with the occurrence of TB in HIV-positive patients in our study, as described in the literature [22,30,37,38,40,41].

Irregular follow-up of HIV infection was associated with TB diagnosis. Irregular patients are more likely to be off antiretroviral therapy, which is the most effective preventive treatment for TB. The risk of TB was associated with a follow-up period of less than 6 months in the study by Abgrall et al. [40]. Several studies have reported that stages 3 and 4 of HIV infection, long duration of HIV infection, and interruption of antiretroviral therapy are associated with the occurrence of TB in PLHIV [22,30,42]. In addition, the proportion of deaths among PLHIV on anti-TB treatment and not receiving antiretrovirals in Africa is 16%-35% [43]. Therefore, these studies suggest that monitoring and surveillance of PLHIV should be very frequent, and that antiretroviral therapy should be started as early as possible. This was demonstrated by a study in Uganda, which found that ARV use led to a 61% reduction in TB incidence and a 52% reduction in TB-related mortality after the first six years of followup on ARV therapy [35].

Our study has several strengths. First, it was an extensive study with a large sample size in three sub-Saharan African countries with different but comparable epidemiological profil regarding HIV and TB. In addition, the diagnostic methods used are in line with the WHO recommendations for the diagnosis of TB in PLHIV [16]. It also provides useful data (comparison of TB prevalence between ARV-treated and ARV-naive PLHIV populations) for deciding patient management strategies.

Despite these strengths, our study has several limitations that need to be acknowledged. First, we acknowledge that our study's focus on three large university centers may not fully represent the epidemiological landscape of TB in HIV patients across the entire countries of Benin, Guinea, and Senegal. These centers, while providing high-quality care and serving large HIV populations, typically have better resources (human, material, organisational) than peripheral health facilities. This selection bias might have influenced our findings, particularly in terms of TB detection rates. However, the consistency of our findings with previous literature regarding risk factors for TB, especially the protective effect of antiretroviral therapy among PLHIV [44] suggests that our main conclusions remain robust despite this limitation. Future studies should consider including both urban and rural healthcare facilities of varying sizes to provide a more comprehensive picture of TB epidemiology in HIV patients in these regions. Second, to avoid excessive workload for the laboratory teams, a maximum of 20 participants were recruited per day. This may have prevented us from measuring the true prevalence of TB in HIV patients. Thus, this true prevalence may have been higher if all eligible participants were included, reinforcing the idea of a high burden of TB in HIV patients, especially in those naïve to ARV.

Third, another limitation of this study is the noninclusion of urine lipoarabinomannan (LAM) testing in our TB screening strategy. Although WHO strongly recommends LAM testing for TB screening among PLHIV, particularly those with low CD4 counts, this diagnostic tool was not yet implemented in the routine TB care services of the participating countries during the study period. Future studies should incorporate LAM testing to enhance TB case detection among PLHIV in these settings. Fourth, while our unadjusted analysis suggested an association between ever smoking history and TB prevalence, this relationship did not persist after adjusting for potential confounders. This finding contrasts with several previous studies that have demonstrated a significant association between smoking and TB risk [45,46]. This discrepancy might be explained by the relatively small number of smokers in our study population, limiting our statistical power to detect such an association. Additionally, other risk factors such as HIV status and socioeconomic conditions might have had a stronger influence on TB prevalence in our study setting. Fifth, we also acknowledge the limitation of combining current and former smokers in our analysis. This decision was

primarily driven by the small number of participants in each category, which would have further reduced our statistical power if analyzed separately. Indeed, analyzing these groups separately could have provided valuable insights into the potential differential effects of current versus past smoking on TB risk. Future studies with larger sample sizes should consider examining these groups independently.

Conclusion

This study provides important insights into the prevalence and associated factors of TB in PLHIV three West African countries (Benin, Guinea, Senegal). The findings indicate a high prevalence of TB in PLHIV, reinforcing the necessity of enhancing TB screening and diagnosis for PLHIV, especially in patients naïve of ARV. Additionally, it emphasizes the significance of providing nutritional support to underweight PLHIV and maintaining consistent follow-up. The findings of this study have important implications for the management and control of TB in PLHIV, and further research is needed to develop effective strategies for the prevention and control of TB in this vulnerable population.

References

- Zumla A, Petersen E, Nyirenda T, Chakaya J. Tackling the tuberculosis epidemic in sub-Saharan Africa – unique opportunities arising from the second European Developing Countries Clinical Trials Partnership programme 2015–2024. Int J Infect Dis 2015;32:46–9.
- World Health Organization. Global tuberculosis report 2013. Geneva: World Health Organization; 2013.
- Loveday M, Zweigenthal V. TB and HIV integration: obstacles and possible solutions to implementation in South Africa. Trop Med Int Health 2011;16:431–8.
- Tesfaye B, Alebel A, Gebrie A, Zegeye A, Tesema C, Kassie B. The twin epidemics: prevalence of TB/HIV co-infection and its associated factors in Ethiopia; a systematic review and meta-analysis. PLoS One 2018;13: e0203986.
- 5. Abdool Karim SS, Naidoo K, Grobler A, Padayatchi N, Baxter C, Gray A, et al. Timing of initiation of antiretroviral

drugs during tuberculosis therapy. N Engl J Med 2010; 362:697–706.

- Getahun H, Gunneberg C, Granich R, Nunn P. HIV infection-associated tuberculosis: the epidemiology and the response. Clin Infect Dis 2010;50:S201–7.
- Schutz C, Meintjes G, Almajid F, Wilkinson RJ, Pozniak A. Clinical management of tuberculosis and HIV-1 co-infection. Eur Respir J 2010;36(6):1460-81.
- Omar T, Variava E, Moroe E, Billioux A, Chaisson R, Lebina L, et al. Undiagnosed TB in adults dying at home from natural causes in a high TB burden setting: a postmortem study. Int J Tuberc Lung Dis 2015;19:1320–5.
- Gupta RK, Lucas SB, Fielding KL, Lawn SD. Prevalence of tuberculosis in post-mortem studies of HIV-infected adults and children in resource-limited settings: a systematic review and meta-analysis. AIDS 2015;29:1987–2002.
- Yang Q, Han J, Shen J, Peng X, Zhou L, Yin X. Diagnosis and treatment of tuberculosis in adults with HIV. Medicine (Baltimore) 2022;101:e30176.
- 11. World Health Organization. Guidelines for intensified tuberculosis case-finding and isoniazid preventive therapy for people living with HIV in resource-constrained settings. Geneva: World Health Organization; 2011. Available from: https://apps.who.int/iris/handle/10665/44472
- Kranzer K, Houben RM, Glynn JR, Bekker LG, Wood R, Lawn SD. Yield of HIV-associated tuberculosis during intensified case finding in resource-limited settings: a systematic review and meta-analysis. Lancet Infect Dis 2010;10:93–102.
- World Bank Open Data. Prevalence of HIV, total (% of population ages 15–49). Available from: https://data.world bank.org
- World Health Organization. Tuberculosis country profiles. 2019. Available from: https://worldhealthorg.shinyapps .io/tb_profiles/
- 15. Wachinou AP, Ade S, Mbaye MN, Bah B, Baldé N, Gninkoun J, et al. Tuberculosis prevalence and associated factors among persons with diabetes mellitus after intensified case finding in three West African countries. Multidiscip Respir Med 2021;16:712.
- World Health Organization. Systematic screening for active tuberculosis: an operational guide. Geneva: World Health Organization; 2015. Available from: https://apps .who.int/iris/handle/10665/181164
- World Health Organization. TB diagnostics and laboratory services, information note. Available from: https:// www.who.int/tb/dots/lab.pdf
- World Health Organization. Recommendations for investigating contacts of persons with infectious tuberculosis in low- and middle-income countries. Available from: https://apps.who.int/iris/handle/10665/77741
- Brennan A, Maskew M, Larson BA, Tsikhutsu I, Bii M, Vezi L, et al. Prevalence of TB symptoms, diagnosis and treatment among people living with HIV not on ART presenting at outpatient clinics in South Africa and

Kenya: baseline results from a clinical trial. BMJ Open 2020;10:e035794.

- Bajema KL, Bassett IV, Coleman SM, Ross D, Freedberg KA, Wald A, et al. Subclinical tuberculosis among adults with HIV: clinical features and outcomes in a South African cohort. BMC Infect Dis 2019;19:23.
- Ngowi BJ, Mfinanga SG, Bruun JN, Morkve O. Pulmonary tuberculosis among people living with HIV/AIDS attending care and treatment in rural northern Tanzania. BMC Public Health 2008;8:341.
- 22. Iliyasu Z, Babashani M. Prevalence and predictors of tuberculosis coinfection among HIV-seropositive patients attending the Aminu Kano Teaching Hospital, northern Nigeria. J Epidemiol 2009;19:81–7.
- Assefa D, Melaku Z, Gadissa T, Negash A, Hinderaker S, Harries A. Intensified tuberculosis case finding among people living with the human immunodeficiency virus in a hospital clinic in Ethiopia. Int J Tuberc Lung Dis 2011; 15:411–3.
- Kimerling ME, Schuchter J, Chanthol E, Kunthy T, Stuer F, Glaziou P, et al. Prevalence of pulmonary tuberculosis among HIV-infected persons in a home care program in Phnom Penh, Cambodia. Int J Tuberc Lung Dis 2002;6:988–94.
- Jam S, Sabzvari D, SeyedAlinaghi S, Fattahi F, Jabbari H. Frequency of Mycobacterium tuberculosis infection among Iranian patients with HIV/AIDS by PPD test. Acta Med Iran 2010;48:67–71.
- Sulis G, Roggi A, Matteelli A, Raviglione MC. Tuberculosis: epidemiology and control. Mediterr J Hematol Infect Dis 2014;6:e2014070.
- Kufa T, Chihota V, Mngomezulu V, Charalambous S, Verver S, Churchyard G, et al. The incidence of tuberculosis among HIV-positive individuals with high CD4 counts: implications for policy. BMC Infect Dis 2016;16:266.
- Kufa T, Mabuto T, Muchiri E, Charalambous S, Rosillon D, Churchyard G, et al. Incidence of HIV-associated tuberculosis among individuals taking combination antiretroviral therapy: a systematic review and meta-analysis. PLoS One 2014;9:e111209.
- 29. Nicholas S, Sabapathy K, Ferreyra C, Varaine F, Pujades-Rodríguez M, AIDS Working Group of Médecins Sans Frontières. Incidence of tuberculosis in HIV-infected patients before and after starting combined antiretroviral therapy in 8 sub-Saharan African HIV programs. J Acquir Immune Defic Syndr 2011;57:311–8.
- Sadirova D, Grigoryan R, Parpieva N, Barotova V, Trubnikov A, Kalandarova L, et al. Incidence rate and risk factors for tuberculosis among people living with HIV: a 2015–2017 cohort from Tashkent, Uzbekistan. Int J Environ Res Public Health 2021;18:5746.
- Camara BS, Delamou A, Diro E, Béavogui AH, El Ayadi AM, Sidibé S, et al. Effect of the 2014/2015 Ebola outbreak on reproductive health services in a rural

district of Guinea: an ecological study. Trans R Soc Trop Med Hyg 2017;111:22–9.

- Leuenberger D, Hebelamou J, Strahm S, De Rekeneire N, Balestre E, Wandeler G, et al. Impact of the Ebola epidemic on general and HIV care in Macenta, Forest Guinea, 2014. AIDS 2015;29:1883–7.
- Madhu M, Udaya Kumar V, Dhingra S, Kumar N, Singh S, Ravichandiran V, et al. Nutritional aspects of people living with HIV amidst COVID-19 pandemic: an insight. Curr Pharmacol Rep 2022;8:350–64.
- 34. Enju L, Makubi A, Drain P, Spiegelman D, Sando D, Nan L, et al. Tuberculosis incidence rate and risk factors among HIV-infected adults with access to antiretroviral therapy in Tanzania. AIDS 2015;29:1391–9.
- Moore D, Liechty C, Ekwaru P, Were W, Mwima G, Solberg P, et al. Prevalence, incidence and mortality associated with tuberculosis in HIV-infected patients initiating antiretroviral therapy in rural Uganda. AIDS 2007;21: 713–9.
- UNAIDS. Global AIDS report 2016. Geneva: UNAIDS; 2016.
- 37. Kibret KT, Yalew AW, Belaineh BG, Asres MM. Determinant factors associated with occurrence of tuberculosis among adult people living with HIV after antiretroviral treatment initiation in Addis Ababa, Ethiopia: a case control study. PLoS One 2013;8:e64488.
- Gupte AN, Kadam D, Sangle S, Rewari BB, Salvi S, Chavan A, et al. Incidence of tuberculosis in HIV-infected adults on first- and second-line antiretroviral therapy in India. BMC Infect Dis 2019;19:1–9.
- Wachinou AP, Ade S, Agodokpessi G, Awanou B, Affolabi D, Bekou W, et al. Diagnosis and treatment outcomes of tuberculosis in relation to gender and HIV status in South Benin. J Tuberc Res 2017;5:189–200.
- 40. Abgrall S, Del Giudice P, Melica G, Costagliola D. HIV-associated tuberculosis and immigration in a high-income country: incidence trends and risk factors in recent years. AIDS 2010;24:763–71.
- Karo B, Haas W, Kollan C, Gunsenheimer-Bartmeyer B, Hamouda O, Fiebig L, et al. Tuberculosis among people living with HIV/AIDS in the German ClinSurv HIV Cohort: long-term incidence and risk factors. BMC Infect Dis 2014;14:148.
- Cui Z, Lin M, Nie S, Lan R. Risk factors associated with tuberculosis among people living with HIV/AIDS: a pairmatched case-control study in Guangxi, China. PLoS One 2017;12:e0173976.
- 43. Mukadi YD, Maher D, Harries A. Tuberculosis case fatality rates in high HIV prevalence populations in sub-Saharan Africa. AIDS 2001;15:143–52.
- 44. Soares KA, Ehrlich J, Camará M, Chaloub S, Emeka E, Gando HG, et al. Implementation of WHO guidelines on urine lateral flow LAM testing in high TB/HIV burden African countries. Eur Respir J 2023;62:2103053.

- Shinde M, Dixit S, Patel M, Sharma A, Satam J, Patil Y, et al. Relationship between smoking and pulmonary tuberculosis based on positive sputum smears. GMS Hyg Infect Control 2024;19:Doc58.
- 46. Sujana SP, Hamda FH, Siddiq MA, Latif YI, Asyary A. The association between secondhand smoke exposure and risk of developing active tuberculosis in individuals with latent tuberculosis infection: a systematic literature review. Ann Ig 2025 doi: 10.7416/ai.2025.2685. Epub ahead of print.

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