INT J TUBERC LUNG DIS 23(2):195–202

http://dx.doi.org/10.5588/ijtld.18.0234

Prevalence of lung function impairment in cured pulmonary tuberculosis patients in Cotonou, Benin

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SUMMARY

SETTING: National teaching hospital for the management of respiratory diseases, Cotonou, Benin.

OBJECTIVE: 1) To estimate the prevalence of lung function impairment (LFI) and associated factors in patients cured of pulmonary tuberculosis (PTB); and 2) to determine the link between human immunodeficiency virus (HIV) infection and LFI occurrence.

DESIGN: We performed a cross-sectional study in cured patients with smear-positive TB (PTB+) treated between 2012 and 2015. We recruited two control groups of 70 HIV-infected (HIV+/TB–) and 70 HIV-negative participants without TB (HIV–/TB–). We performed spirometry in all participants to identify LFI (obstructive, restrictive or mixed) and the 6-min walk test (6-MWT) in PTB+ participants. We assessed the factors associated with LFI using logistic regression.

RESULTS: Of 4711 subjects with PTB, 241 were contacted and 189 were included. The median age was 37 years; 128 (68.0%) were male. Overall, 85 cured PTB+ patients had LFI (45.0%). Extent of initial radiological lesions, time between symptom onset and treatment, and female sex were independently associated with LFI. Fifty-five (29.1%) cured PTB+ patients had an abnormal 6-MWT; those with LFI had a higher risk of poor exercise tolerance (OR 2.23; interquartile range 1.16–4.30). We did not find any association between HIV infection and LFI.

CONCLUSION: LFI is very common in cured PTB+ patients from Benin and significantly impacts exercise tolerance.

KEY WORDS: spirometry; TB; HIV; Benin

ACCORDING TO THE World Health Organization (WHO), there were 10.4 million new tuberculosis (TB) cases in 2016, 12% of whom were co-infected with the human immunodeficiency virus (HIV).[1] The overall success rate of first-line treatment was 83%. However, both treated and cured patients are prone to suffer from life-long lung conditions which may alter their quality of life (QoL).[2]

Despite anti-tuberculosis treatment, remodelling of the pulmonary parenchyma can lead to various respiratory functional disorders which are responsible for increased morbidity.[3–5] Studies of respiratory function in previously treated pulmonary TB (PTB) patients have shown restrictive, obstructive or mixed patterns.[3,6,7] In 2016, scholars called for better linkages between TB control programmes and respiratory medicine services as well as better understanding of the burden of respiratory disability at the end of anti-tuberculosis treatment to improve QoL.[8]

HIV infection itself can lead to respiratory disorders.[9–12] A recent meta-analysis showed a high prevalence of chronic obstructive pulmonary disease (COPD) in the global population with HIV.[13] It is probable that the high prevalence of TB and HIV in Africa leads to increased prevalence of lung function impairment (LFI), particularly post-TB; however, this situation is poorly documented.

No data are available on the burden of post-TB LFI in Benin. Assessing the LFI attributable to PTB could be useful for planning strategies to reduce its long-term impact. We aimed to assess the prevalence of LFI and to identify the associated factors in previously treated and cured smear-positive patients (PTB+) in Cotonou, Benin. In particular, we sought to assess the impact of HIV infection on LFI in cured PTB patients.

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Article submitted 26 March 2018. Final version accepted 23 August 2018.

METHODS

Study population and design

We conducted a cross-sectional study from April to July 2016 at the Centre national hospitalo-universitaire de Pneumophtisiologie (CNHU-PP) in Cotonou. We included individuals aged ⩾18 years with known HIV status treated between 2012 and 2015 for PTB+ and considered cured for at least 6 months. We excluded pregnant women, individuals who had been retreated for TB, those treated for multidrug-resistant TB, those with TB relapse, neuromuscular degenerative disease, any ongoing or recent cardiovascular disease, resting tachycardia, active thrombophlebitis and/or recent pulmonary embolism, and those with thoracic abnormalities. Participants in the study were selected by simple random draw.

To validate spirometry results in the study population, we recruited two control groups among HIV-infected out-patients on antiretroviral therapy from an HIV treatment centre in Cotonou, without TB history or suspicion (HIV+/TB–), and healthy volunteers (HIV–/TB–) in the general population. Control groups were matched by sex, age and size with PTB+ patients.

Ethical approval

The study protocol was approved by the National Ethics and Research Committee, Cotonou.

Study procedures

After providing informed consent, all participants underwent physical examination, and data on anthropometric parameters were collected. Clinical, biological and radiological data relating to the initial TB disease were collected in their medical charts using standardised questionnaires. Information about TB symptoms, smear results and the time between symptom onset and anti-tuberculosis treatment was collected. Information on tobacco smoking and exposure to biomass fuels was collected based on participants' statements.

In accordance with American Thoracic Society/European Respiratory Society (ERS) standards, a Spirodoc® spirometer (Medical International Research, Rome, Italy) was used for pulmonary function testing (Appendix*). The forced vital capacity (FVC), forced expiratory volume in one second (FEV_1), FEV_1/FVC ratio (Tiffeneau Index) and the mid-expiratory flow rate 25–75% of the FVC (MEF25–75%) were used to diagnose LFI.

To avoid mis-estimation of LFI prevalence, and due to the absence of spirometry equations in Beninese adults, Perfura's equations (Appendix Table A.1) derived from African Black Bantu in Cameroon were used as a reference to calculate theoretical values,[14] instead of the equations recommended for African Americans by the ERS and pre-parametrised in the Spirodoc device. All tests were performed by a chest physician trained in spirometry. The upper limit of normal (ULN) and lower limit of normal (LLN) of each spirometry parameter were determined using 90% confidence intervals (CIs) (Appendix Table A.1). Exercise tolerance in PTB+ patients was assessed using the 6-min walk test (6-MWT)[15] (Appendix). The level of dyspnoea was measured using the modified Medical Research Council (mMRC) Dyspnoea Scale, blood pressure, peripheral oxygen saturation (SpO_2) and heart rate (HR) before and immediately after the 6-MWT. Theoretical distances for the 6-MWT were computed based on Enright's equations.[16]

Definitions

LFI was defined as the presence of spirometry abnormalities characterised by restrictive, obstructive or mixed LFI patterns. Normal spirometry was defined as FEV_1, FVC and FEV_1/FVC ratio >LLN. An obstructive pattern was defined as a FEV_1/FVC ratio <LLN with normal FVC (LLN⩽FVC⩽ULN). A restrictive pattern was defined as FVC<LLN and a normal FEV_1/FVC ratio. A mixed pattern was defined as FVC<LLN and FEV_1/FVC<LLN. Poor tolerance of exercise was defined as a 6-MWT distance <LLN. Dyspnoea ⩾2/5 after the 6-MWT or ⩾1/5 at rest on the mMRC Dyspnoea Scale was considered clinically abnormal. For analysis of radiological features, we proposed a scoring of lung radiological lesion extensions based on dividing each lung field in three parts (Appendix Table A.2).

Study size

With an expected LFI prevalence of 50%, and $\alpha = 5\%$, we estimated that 171 subjects with cured PTB+ would be needed to estimate the prevalence of LFI with a precision of 7.5%. We recruited a convenience sample of 70 subjects in each control group.

Statistical analysis

We compared characteristics between groups using Pearson's χ^2 test, Fisher's exact test, Student's *t*-test or the Mann-Whitney test, as appropriate. Factors associated with LFI were identified using logistic regression with a backward stepwise procedure; age, sex and tobacco smoking were included in the regression logistic model. We also modelled variations in spirometry parameters between PTB+, HIV+TB– and the HIV–TB– groups using multiple linear regression. $P < 0.05$ was considered statistically significant. We performed analyses using R Studio v 0.99.893 (R Development Core Team, Vienna, Austria).

* The appendix is available in the online version of this article, at http://www.ingentaconnect.com/content/iuatld/ijtld/2019/00000023/00000002/art000 .....

Table 1 Comparative characteristics of PTB patients, with control groups (PLHIV and healthy subjects)

Variables	Former PTB (n =189) n (%)	PLHIV controls (n =70) n (%)	Healthy controls (n =70) n (%)	P value
Age, years, median [IQR]	37 [30–47]	41.5 [35.5–49.5]	39 [33.5–52]	0.04
Male	128 (67.7)	48 (68.6)	48 (68.6)	0.98
Weight, kg, median [IQR]	61 [53.5–70.5]	64.50 [58.5–72.0]	68.50 [62.0–80.0]	<0.05
Height, m, median [IQR]	1.68 [1.6–1.7]	1.68 [1.6–1.7]	1.67 [1.6–1.7]	0.74
BMI, kg/m^2, median [IQR]	21.23 [19.4–23.6]	22.249 [20 – 25]	24.40 [21.9–28.7]	0.005
Comorbidities				
Asthma	9 (4.8)	5 (7.1)	4 (5.7)	0.78
COPD	0	0	0	—
Diabetes mellitus	21 (11.1)	2 (2.9)	2 (2.9)	0.021
Arterial hypertension	19 (10.05)	5 (7.14)	9 (12.85)	0.43
Respiratory symptoms				
Dyspnoea	25 (13.2)	0	0	<0.001
Sputum	21 (11.1)	3 (4.28)	0	0.005
Cough	27 (14 .3)	5 (7.14)	0	0.002
Chronic bronchitis	9 (4.8)	0	0	0.03
Chest pain	6 (3.2)	1 (1.42)	0	0.26
Respiratory signs				
Crackles rales	4 (2.1)	0	0	0.22
Sibilant rales	0	1 (1.42)	0	0.16
HIV co-infection	20 (10.6)	—	—	
Education level				0.008
None	34 (18.0)	10 (14.3)	3 (4.3)	
Primary school	66 (34.9)	25 (35.7)	19 (27.1)	
Secondary school	65 (34.4)	29 (41.4)	30 (42.9)	
University degree	24 (12.7)	6 (8.6)	18 (25.7)	
Place of residence: Cotonou	175 (92.6)	67 (95.7)	61 (87.1)	0.15
Tobacco smoking	38 (20.1)	9 (13.0)	5 (7.1)	0.029
Exposure to biomass[†]	46 (24.3)	5 (7.1)	6 (8.6)	<0.05
Occupational exposure to pulmonary irritants*	40 (21.1)	17 (24.3)	10 (14.3)	0.31
Lung function impairment	85 (45.0)	19 (27.1)	16 (23.0)	<0.001
Obstructive pattern	62 (32.8)	12 (17.14)	15 (21.4)	0.02
Restrictive pattern	18 (9.5)	7 (10.0)	1 (1.4)	0.07
Mixed pattern	5 (2.6)	0	0	0.22
Time since TB treatment completion, months, median [IQR]	28 [18–38]	—	—	

* Includes taxi/motorcycle drivers, auto mechanics, masons, painters, carpenters, petrol station assistants, welders, bakers, sellers of adulterated gasoline.
[†] Exposure due to firewood use.
PTB = pulmonary TB; PLHIV = people living with HIV; IQR = interquartile range; BMI = body mass index; COPD = chronic obstructive pulmonary disease; HIV = human immunodeficiency virus; TB = tuberculosis.

RESULTS

Of 4711 patients treated for TB in the Centre national hospitalier de Pneumo-Phtisiologie, 426 with cured PTB+ were randomly selected, 241 were contacted by telephone, and 189 were included in this study (Figure 1). Participants were predominantly male (68%); the median age was 37 years (interquartile range 30–47) (Table 1), and 10.6% ($n = 20$) were HIV-infected.

Spirometry characteristics and prevalence of lung function impairment

Spirometry characteristics of participants are given in Table 2. We found LFI in 85 participants, with an overall LFI prevalence of 45.0% (95%CI 37.8–52.4): 62 (32.8%) participants had obstructive LFI, 19 (10.1%) had restrictive and 4 (2.1%) had a mixed pattern. Eleven (5.8%) participants with a Tiffeneau Index <LLN and bronchoreversibility were considered to be asthmatic.

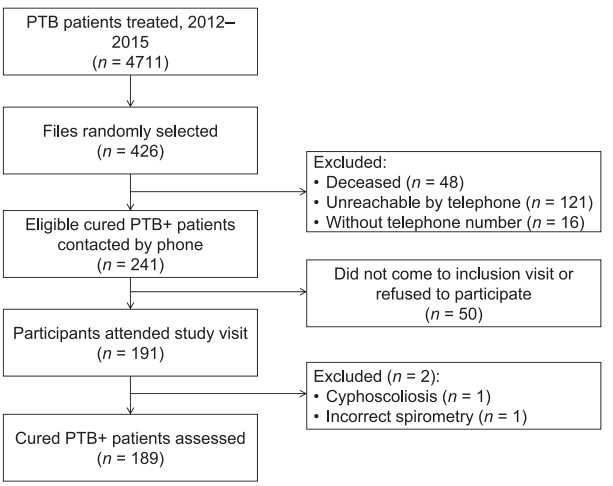

Figure 1 Participant selection. PTB+ = smear-positive pulmonary tuberculosis.

Table 2 Spirometry characteristics and prevalence of LFI in PTB patients

Spirometry parameters	*n* (%)
FVC, l, median [IQR]	3.1 [2.5–3.7]
Abnormal FVC (FVC < LLN)	22 (11.6)
FEV_1, l/s, median [IQR]	2.4 [1.9–2.9]
Abnormal FEV_1 (FEV_1 < LLN)	37 (19.6)
MEF25–75%, median [IQR]	2.36 [1.7–3.2]
Abnormal MEF25–75% (MEF < LLN)	56 (29.6)
Tiffeneau Index (FEV_1/FVC), median [IQR]	0.81 [0.73–0.87]
Abnormal result: (FEV_1/FVC) < LLN	66 (34.9)
Abnormal result: (FEV_1/FVC) < LLN + bronchoreversibilty	11 (5.8)
Presence of LFI	
Yes	85 (45.0)
No	104 (55.0)
Obstructive pattern	62 (33.0)
Minor	43 (23.0)
Moderate	19 (10.0)
Severe	0
Restrictive pattern	19 (10.0)
Minor	6 (3.2)
Moderate	11 (6.0)
Severe	2 (1.0)
Mixed pattern	4 (2.1)
Minor	0
Moderate	0
Severe	4 (2.1)

LFI = lung function impairment; PTB = pulmonary tuberculosis; FVC = forced vital capacity; IQR = interquartile range; LLN = lower limit of normal; FEV_1 = forced expiratory volume in one second; MEF = mid-expiratory flow.

Factors associated with lung function impairment in cured pulmonary tuberculosis-positive patients

Factors independently associated with LFI were female sex, being underweight, time from symptom onset to treatment >32 days and increasing TB radiological lung lesion extension (Table 3). Being overweight and obese were associated with a reduced risk of LFI. Age, smoking status, exposure to biomass and occupational exposure to pulmonary pollutants were not associated with the risk of LFI.

Lung function impairment and spirometry parameters in control groups

Individuals in the control groups had lower exposure to tobacco and/or biomass. Overall, 9 (27.1%) HIV+/TB– controls and 15 (22.9%) HIV–/TB– controls had LFI diagnosed ($P < 0.001$) (Table 1). PTB+ participants were approximately three times more likely to have LFI than healthy controls (odds ratio [OR] 2.76, 95%CI 1.47–5.16; $P = 0.001$). HIV+/TB– controls were not more likely to have LFI than HIV–/TB– controls (OR 1.25, 95%CI 0.58–2.70; $P = 0.55$). Among PTB+ patients, 33% had a non-reversible obstructive pattern, compared with 17.1% among HIV+/TB– controls and 21.2% among HIV–/TB– controls ($P = 0.02$) (Table 1). FEV_1, FVC, and MEF25–75% values and the Tiffeneau Index differed significantly between cured PTB+ patients and HIV+/TB– and HIV–/TB– healthy controls (respectively, $P < 0.005$, $P = 0.019$, $P < 0.001$, and $P < 0.02$; Figure 2). After adjusting for age, sex, exposure to tobacco and biomass, the four spirometry parameters were significantly dependent on the study group ($P < 0.05$). Compared with HIV–/TB– controls, FVC in PTB+ participants was lower on average by –0.34 l (95%CI –0.56 to –0.12), FEV_1 was lower by –0.37 l (95%CI –0.73 to –0.2), MEF25–75% was lower by –0.46 l (95%CI –0.73 to –0.2) and the Tiffeneau Index was lower by –3% (95%CI –0.06 to 0.0) (Table 4). There was no difference in spirometry parameters between HIV-infected and non-HIV-infected PTB+ participants. There were no statistically significant differences between the spirometry parameters in HIV–/TB– and HIV+/TB– controls.

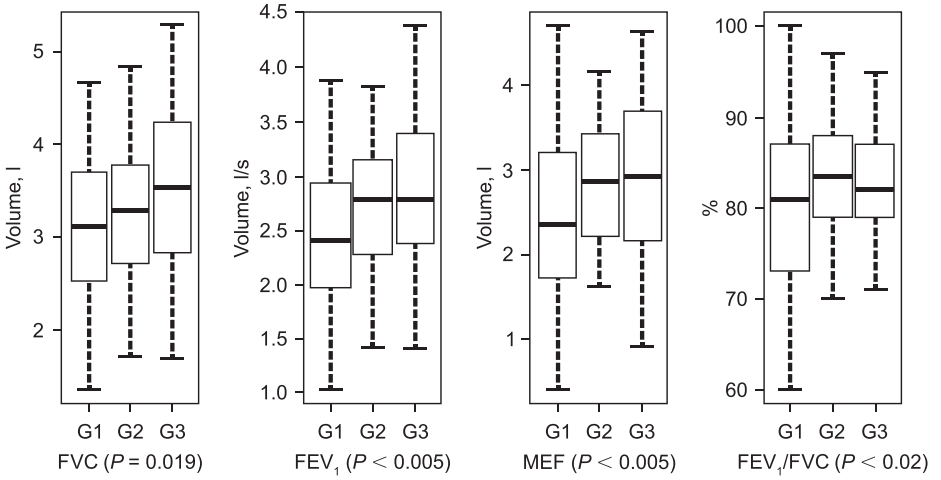

Figure 2 Comparative analysis of spirometry parameters in PTB patients and in control groups. G1 = former PTB patients; G2 = HIV-infected, no PTB (controls); G3 = non-HIV-infected, no PTB (controls); FVC = forced vital capacity; FEV_1 = forced expiratory volume in one second; MEF = mid-expiratory; PTB = pulmonary tuberculosis; HIV = human immunodeficiency virus.

Table 3 Factors associated with lung function impairment in cured PTB patients ($n = 189$)

		Univariate analysis		Multivariate analysis	
Variables	*n*	OR (95%CI)	*P* value	aOR (95%CI)	*P* value
Age, years			0.80		0.87
⩽40	116	1		1	
>40	73	0.93 (0.49–1.74)		0.94 (0.44–1.99)	
Sex			0.02		0.004
Male	128	1		1	
Female	61	2.10 (1.13–3.90)		2.98 (1.4–6.34)	
BMI			0.04		0.01
Normal weight (18 <BMI <25 kg/m^2)	132	1		1	
Underweight (BMI ⩽18 kg/m^2) (lean corpulence)	23	2.32 (0.91–5.88)		2.50 (0.90–6.66)	
Overweight and obese (BMI >25 kg/m^2)	34	0.60 (0.47–0.71)		0.40 (0.26–0.52)	
Occupational exposure to pulmonary irritants*			0.71		
No	149	1			
Yes	40	1.13 (0.56–2.30)			
Place of residence			0.46		
Cotonou	14	1			
Outside Cotonou	175	1.5158 (0.49–4.70)			
Tobacco smoking			0.13		0.25
No	151	1		1	
Yes	38	0.57 (0.27–1.19)		0.61 (0.26–1.45)	
Exposure to biomass†			0.07		0.58
No	143	1		1	
Yes	46	1.85 (0.94–3.62)		1.23 (0.58–2.61)	
HIV status			0.63		
Negative	169	1			
Positive	20	0.79 (0.30–2.04)			
Smear status			0.55		
1–9 AFB/100 fields	27	1			
10–99 AFB/10 fields	42	0.70 (0.26–1.86)			
1–10 AFB/fields	80	1.13 (0.47–2.71)			
>10 AFB/fields	40	1.25 (0.46–3.33)			
Time between symptom onset and anti-tuberculosis treatment, days			0.02		0.04
⩽32	95	1		1	
>32	94	1.95 (1.05–3.64)		2.0 (1.01–3.59)	
Time since TB treatment completion, years			0.61		
⩽2.33	95	1			
>2.33	94	1.16 (0.63–2.14)			
Radiological features present on initial CXR‡					
Alveolar syndrome	117	1.04 (0.52–2.06)	0.9		
Interstitial syndrome	70	1.22 (0.68–2.18)	0.9		
Cavitation	114	1.49 (0.82–2.71)	0.18		
Miliary TB	5	1.23 (0.24–6.26)	0.8		
Pleural damage	5	0.81 (0.13–4.96)	0.8		
Extent of pulmonary damage on initial CXR†			0.003		0.005
Unilateral, 1/3 field	28	1		1	
Bilateral, 1/3 field or 2/3 unilateral	38	0.56 (0.18–1.72)	0.31	0.54 (0.16–1.79)	
2/3 field + 1/3 controlateral field	23	2.30 (0.74–7.19)	0.15	1.96 (0.57–6.76)	
Unilateral complete field	14	3.80 (0.98–14.66)	0.05	2.95 (0.69–12.94)	
Bilateral 2/3 field	32	1.64 (0.57–4.72)	0.35	1.51 (0.47–4.74)	
1 complete field + 1/3 contralateral field	8	2.11 (0.43–10.42)	0.35	1.42 (0.25–7.91)	
1 complete field + 2/3 contralateral field	23	4.82 (1.47–15.87)	0.009	3.33 (0.90–12.35)	
Bilateral, 2 lower lung fields	4	6.33 (0.57–6.9)	0.13	2.79 (0.82–9.54)	

* Includes taxi and motorcycle drivers, mechanics, masons, carpenters, painters, petrol station agents, welders, bakers, sellers of adulterated gasoline, etc.
† Exposure to biomass due to firewood use.
‡ Number of participants with initial CXR, n =170.
PTB = pulmonary TB; OR = odds ratio; CI = confidence interval; aOR = adjusted OR; BMI = body mass index; HIV = human immunodeficiency virus; AFB = acid-fast bacilli; CXR = chest X-ray; TB = tuberculosis.

Exercise tolerance and persistent symptoms

Participants with LFI reported cough more frequently than those without LFI (19, 22.4% vs. 8, 7.7%; OR 3.5, 95%CI 1.3–9.2; $P = 0.004$). There was no difference in other symptoms between participants with LFI and those without LFI. The mean 6-MWT distance walked was 558.7 ± 88.3 m; 53 (29.9%) participants had a 6-MWT distance <LLN for their age. Thirty-one (39.2%) participants with LFI had an abnormal 6-MWT compared with 22 (22.5%) participants without LFI ($P = 0.01$), with a higher risk of poor tolerance (OR

Table 4 Spirometry parameters of PTB+, HIV+/TB– and HIV–/TB– groups on multiple linear regression ($n = 329$)

Variables	FVC ($P < 0.0005$)*		FEV_1 ($P < 0.0005$)*		MEF25–75% ($P < 0.0005$)*		FEV_1/FVC ($P < 0.0001$)*	
	Adjusted coefficient (95%CI)	*P* value†	Adjusted coefficient (95%CI)	*P* value†	Adjusted coefficient (95%CI)	*P* value†	Adjusted coefficient (95%CI)	*P* value†
Age								
Increasing of 5 years	−0.081 (−0.12 to −0.05)	<0.001	−0.09 (−0.12 to −0.06)	<0.001	−0.13 (−0.18 to −0.09)	<0.001	−0.01 (−0.012 to −0.0001)	0.003
Sex								
Female vs. male	−0.97 (−1.15 to −0.78)	<0.001	−0.76 (−0.9 to −0.62)	<0.001	−0.69 (−0.9 to −0.46)	<0.001	0.02 (−0.01 to 0.04)	0.09
Tobacco smoking								
Yes vs. no	0.1 (−0.14 to 0.34)	00.429	0.04 (−0.14 to 0.23)	00.63	−0.06 (−0.34 to 0.23)	00.68	−0.02 (−0.05 to 0.01)	0.209
Exposure to biomass								
Yes vs. no	−0.31 (−0.54 to −0.08)	00.009	−0.24 (−0.42 to −0.06)	00.008	−0.24 (−0.53 to 0.03)	00.087	−0.01 (−0.04 to 0.02)	0.571
Study group (participants vs. healthy control)		00.021		<0.001		00.001		0.013
Former PTB vs. healthy	−0.36 (−0.58 to −0.13)	00.002	−0.37 (−0.54 to −0.2)	<0.001	−0.48 (−0.73 to −0.2)	<0.001	−0.03 (−0.06 to 0.0)	0.057
HIV-TB co–infected vs. healthy	−0.23 (−0.63 to 0.16)	00.239	−0.3 (−0.59 to 0)	00.052	−0.37 (−0.84 to 0.1)	00.127	−0.04 (−0.09 to 0.01)	0.098
HIV+ control vs. healthy control	−0.23 (−0.48 to 0.03)	00.085	−0.15 (−0.35 to 0.05)	00.137	−0.06 (−0.37 to 0.25)	00.714	0.01 (−0.02 to 0.05)	0.417

* Global contribution of different variables in the model (Fisher's global test).
† Specific contribution of each variable in the model.
PTB+ = smear-positive pulmonary TB; HIV+TB– = HIV-infected, no TB; HIV–TB– = non-HIV-infected, no TB; FVC = forced vital capacity; CI = confidence interval; FEV1 = forced expiratory volume in one second; MEF = mid-expiratory flow; TB = tuberculosis; HIV = human immunodeficiency virus.

2.23, 95%CI 1.16–4.3) of physical exercise. They also had an increased risk of desaturation (30.4% with SpO_2 <92%) during effort (OR 3.45, 95%CI 1.47–8.21).

DISCUSSION

LFI affected almost half of cured PTB+ Beninese patients. Sex, body mass index, time to anti-tuberculosis treatment and extension of initial radiological lesions were the main factors associated with LFI. Spirometry parameters were significantly lower in former PTB+ patients than in controls. Individuals with LFI had a higher risk for desaturation during effort, with poorer exercise tolerance and persistent respiratory symptoms.

TB is an important risk factor for LFI. Previously treated PTB+ patients had an approximately three times higher risk of LFI than HIV–/TB– controls. A high prevalence of LFI has been found in PTB+ patients from Cameroon and Togo, with rates reaching 45.4% and 67%, respectively.[17,18] The prevalence in Togo was higher despite geographical proximity and morphological similarities between the Beninese and Togolese. This difference may be because the study from Togo used African-American spirometry norms, which have been shown to overestimate the frequency of LFI among Black populations living in Africa.[14,19]

The obstructive pattern was predominant. Tobacco smoking and exposure to biomass may have played a part in pulmonary obstructive defects but were not significantly associated with LFI. Treated and cured PTB itself is a recognised (but uncommon) risk factor for COPD, and can lead to increased COPD prevalence in high TB endemic areas.[20,21] PTB leads to hyperplasia and hypertrophy of mucous glands, increased mucosal secretion in bronchial smooth muscle tissue and reduction of bronchial calibre, which leads to bronchial obstruction.[22] Respiratory infectious diseases occurring in childhood, notably before the introduction of expanded immunisation programmes in Benin, may also have played a role in healthy controls, as shown in about one-third of obstructive cases in adulthood.[23,24]

The frequency of restrictive and mixed pattern varies between studies and contexts. Only 10% of study participants had pulmonary restriction and 2% had mixed impairment. Studies in Tanzania[25] reported restrictive patterns in 13% of study participants and 19% had mixed defects; restrictive patterns were more frequent (36%) while mixed patterns were less frequent (5%) in Cameroon.[17] Post-TB restrictive patterns would be due to severe destruction of lung parenchyma because of caseous necrosis and cavity formation during TB. Mixed ventilatory syndromes could be the result of fibrosing and destructive

tuberculous lesions with loss of pulmonary parenchyma.

Our study showed that cured TB can lead to LFI with persistent respiratory symptoms such as cough, sputum and dyspnoea.[26] As reported previously, exercise tolerance was worse in PTB+ patients with LFI.[18,27] These patients had an increased risk of oxygen desaturation during exercise with a significant reduction in distance travelled at the 6-MWT. LFI is therefore an important factor for poor cardiorespiratory tolerance during physical activities and could have a significant impact on QoL, as shown in Togo.[18]

A delay of >1 month between symptom onset and treatment initiation was independently associated with a higher risk of LFI, confirming the results of several studies on the role of diagnostic and treatment delays as risk factors for LFI in PTB+ patients.[17,18,28] As delayed care prolongs the infectious process and aggravates parenchymal damages, this results in long-term LFI despite bacteriological cure. The extent of initial radiological lesions rather than the type of lesions was significantly associated with LFI. Our radiographic score was significantly and inversely associated with spirometry parameters. As reported previously, extensive initial radiological lesions lead to more LFI after healing.[29]

We did not find any association between HIV infection and LFI. Our analysis showed that having PTB was an important factor in altering all spirometry parameters; however, being HIV+ did not increase the risk of LFI. There were no differences in pulmonary function in HIV co-infected TB patients and non-HIV-infected TB patients One possible explanation may be that HIV-infected patients develop atypical PTB with less extensive parenchymal lesions. As cell-mediated immunity is responsible for the formation of tuberculous lesions, lung lesions are uncommon in HIV-TB co-infected patients due to cellular immunodeficiency.[30] We found no association between smoking or exposure to biomass with LFI. Tobacco smoking was generally low in our study setting but exposure to biomass is quite common in semi-urban or rural settings. The study sample size may have lacked statistical power to show a link between these factors and LFI.

Our results suggest that interventions to reduce the long-term impact of PTB on lung function should be implemented. A study from Uganda demonstrated the feasibility of pulmonary rehabilitation in people with post-TB lung disease, and reported that this significantly improved QoL, exercise capacity and respiratory outcomes.[31] Implementation of exercise training or respiratory rehabilitation programmes after anti-tuberculosis treatment could therefore reduce the occurrence of LFI and persistent respiratory symptoms.

Our study had three main limitations. First, there are no validated spirometry equations for people from Benin. We used equations derived from a Bantu-Cameroonian population, which may not be perfectly adapted to the Beninese population because the morphotypes of West African Beninese and central African Bantu-Cameroonian may differ. It should be noted that the high LFI prevalence found in HIV–/TB– controls raises the problem of adapting Cameroonian equations to the Beninese population. Second, our study was monocentric and only those who could be contacted by telephone could participate in our study. Our study population may thus not necessarily be representative of former PTB+ patients in Cotonou. Finally, the lack of knowledge on pre-TB lung functions of study participants could constitute a bias for the attribution of LFI to TB. By validating our observations with comparison with HIV–/TB– and HIV+/TB– control groups using the same methods, we were nevertheless able to show unambiguously the high prevalence of LFI in treated and cured former PTB+.

CONCLUSION

PTB, even when treated and cured, exposes individuals to severe LFI which can limit cardiorespiratory capacity. The time between symptom onset and treatment, extent of radiological lesions in the lungs and female sex were strongly related to LFI in our context. Whether national TB programmes should focus on active screening and treatment of LFI as part of a holistic approach for TB management requires further research.

Acknowledgements

The study was co-financed by Soutien Pneumologique International, Paris, and the Association pour le Développement et la Pneumologie et l'Allergologie francophone, Nice, France. However, the contents were solely the responsibility of the authors and do not necessarily represent the official views of these associations.

The authors thank participants of the study and the CNHPP staff in Cotonou, Benin, and the staff of the respiratory physiology laboratory at the University of Bordeaux, Bordeaux, France, for logistic support. The study was conducted as part of the Francoise Barré-Sinoussi Scholarship for AF.

Conflicts of interest: none declared.

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APPENDIX

PROCEDURE FOR SPIROMETRY AND THE 6-MIN WALK TEST (6MWT)

Realization and criteria for validation of spirometry tests

We used acceptability and reproducibility criteria as recommended by the American Thoracic Society/ European Respiratory Society. Spirometry was performed in all participants in a seated position with the nose closed. Patients benefited from spirometry pre- and post-bronchodilatation tests; separated by 10 min of waiting for bronchodilation. A minimum of three and a maximum of six spirometry tests were performed to determine the correct flow-volume curve. Each test was separated by a rest period of 1 min.

6-min walk test

The duration of the test is 6 min and involves walking on flat terrain as fast as possible back and forth. We explained the test to participants as follows: "You will now do a 6-min walking test. The object of this test is to walk as fast as you can for 6 min. We will inform you of the time elapsed and the time left. You can slow down if necessary and even stop, but it is best to keep walking, even slowly. You are encouraged to do your best in order to walk as far as possible within 6 min. You should stop if you have chest pains, dizziness, palpitations or abnormal shortness of breath. When the 6 min have elapsed, we will tell you to stop so that we can record the distance you have covered."

This test allowed us to measure the walking perimeter of the participants, as well as the cardio-respiratory adaptive capacities of the individual to assess exercise tolerance, shortness of breath rating and oxygenation at the end of the test. Blood pressure, oxygen saturation and shortness of breath were measured at the end of the test to evaluate the cardiorespiratory adaptation of participants.

Table A.1 Spirometry reference equations for African Black Bantu people in Cameroon[15]

Parameters	Equations	Coefficient of determination R^2	RSD
Male			
FEV_1, l	–1.93–0.027 age+3.609 high	0.485	0.56 361
FVC, l	–2.549–0.029 age+4.266 high	0.477	0.63537
PEF, l/s	–0.814–0.038 age+5.429 high	0.124	2.00442
MEF25–75%	1.321–0.035 age–0.034 high	0.233	1.12148
FEV_1/FVC	0.959–0.00043 age–0.00043 high	0.009	0.07118
Female			
FEV_1, l	–1.398–0.023 age+2.848 high	0.397	0.4645
FVC, l	–1.791–0.023 age+3.276 high	0.390	0.5159
PEF, l/s	–4.453–0.038 age+6.695 high	0.229	1.301
MEF25–75%	−1.221–0.025 age+3.271 high	0.175	0.9235
FEV_1/FVC	0.993–0.00022 age–0.045 high	0.006	0.05564

RSD = residual standard deviation; FEV_1 = forced expiratory volume in one second; FVC = forced vital capacity; PEF = peak expiratory flow; MEF = mid-expiratory flow.

Table A.2 Radiological lesion extension

Extension of radiological lesion	Score
Unilateral, 1/3 field	1
Bilateral 1/3 field or 2/3 unilateral	2
2/3 field + 1/3 controlateral field	3
Unilateral complete field	4
Bilateral 2/3 field	5
1 complete, field + 1/3 contralateral field	6
1 complete, field + 2/3 contralateral field	7
Bilateral, 2 lower lung fields	8

RÉSUMÉ

CADRE : Centre national hospitalier et universitaire de Pneumophtisiologie de Cotonou, Bénin.

OBJECTIF : Estimer la prévalence des troubles fonctionnels respiratoires (LFI) et les facteurs associés chez des patients guéris de tuberculose pulmonaire (TBP). Le lien entre le statut virus de l'immunodéficience humaine (VIH) et les LFI a été secondairement recherché.

MÉTHODE : Nous avons donc réalisé une étude transversale chez des patients guéris de TBP à frottis positif (TBP+) traités entre 2012 et 2015. Nous avons recruté deux groupes témoins de 70 participants VIH-positifs (VIH+/TB–) et de 70 séronégatifs sans tuberculose (VIH–/TB–). Nous avons effectué une spirométrie chez tous les participants pour identifier les LFI (obstructifs, restrictifs ou mixtes) et un test de marche de 6 min (6MWT) chez les anciens tuberculeux. Nous avons identifié les facteurs associés aux LFI par régression logistique.

RÉSULTATS : Sur 4711 sujets TBP, 241 ont été contactés et 189 ont été inclus. L'âge médian était de 37 ans, 128 (68,0%) étaient des hommes. Au total, 85 patients TBP+ guéris avaient un LFI (45,0% ; IC95% 37,8–52,4). L'étendue des lésions radiologiques initiales, le délai entre les symptômes et le traitement, et le sexe féminin étaient indépendamment associés aux LFI. Cinquante-cinq (29,1%) patients TBP+ guéris présentaient une anomalie au 6MWT ; ceux avec un LFI avaient un risque plus élevé de mauvaise tolérance à l'exercice (OR 2,23 ; intervalle interquartile 1,16–4,30). Nous n'avons trouvé aucune association entre l'infection par le VIH et les LFI.

CONCLUSION : Les LFI sont assez fréquents chez les patients TBP+ traités et guéris au Bénin ; et altèrent significativement leur tolérance à l'effort.

RESUMEN

MARCO DE REFERENCIA: El hospital nacional de formación en neumología de Cotonú, en Benin.

OBJETIVO: Estimar la prevalencia de deterioro de la función respiratoria y los factores asociados, en los pacientes curados de tuberculosis pulmonar (TBP). En un segundo tiempo se analizó el vínculo entre la infección por el virus de la inmunodeficiencia humana (VIH) y el deterioro de la función respiratoria.

MÉTODO: Se llevó a cabo un estudio transversal en pacientes curados de TBP con baciloscopia positiva (TBP+) tratados del 2012 al 2015. Se conformaron dos grupos testigos de 70 personas infectadas por el VIH sin TB y 70 personas sin infección por el VIH ni TB. En todos los participantes se practicó una espirometría con el fin de detectar la disfunción respiratoria (perfiles obstructivos, restrictivos o mixtos) y los participantes tratados por TBP+ realizaron la prueba de la marcha de 6 minutos (6MWT). Se analizaron los factores asociados con el deterioro de la función respiratoria mediante un modelo de regresión logística.

RESULTADOS: De los 4711 participantes tratados por TBP, se contactaron 241 y se incluyeron 189 en el estudio. La mediana de la edad fue 37 años, 128 eran de sexo masculino (68,0%). En general, 85 pacientes curados de TBP+ presentaban deterioro de la función respiratoria (45,0%). La magnitud inicial de las lesiones radiográficas, el lapso entre el inicio de los síntomas y el tratamiento y el sexo femenino se asociaron de manera independiente con el deterioro de la función respiratoria. En 55 pacientes curados de TBP+ (29,1%) el resultado de la prueba de la 6MWT fue anormal; los pacientes con disfunción respiratoria exhibieron un mayor riesgo de baja tolerancia al ejercicio (cociente de posibilidades 2,23; amplitud intercuartil 1,16–4,30). No se observó ninguna asociación entre la infección por el VIH y la disfunción respiratoria.

CONCLUSIÓN: El deterioro de la función respiratoria es muy frecuente en los pacientes curados de una TBP+ en Benin y tiene una repercusión notable en su tolerancia al ejercicio.