Clinical Medicine Insights: Circulatory, Respiratory and Pulmonary Medicine

ORIGINAL RESEARCH

Pulmonary Hypertension in Patients with Treated Pulmonary Tuberculosis: Analysis of 14 Consecutive Cases

Ala Eldin H. Ahmed[1,2], Ahmed S. Ibrahim[3] and Somia M. Elshafie[2]

[1]Department of Medicine, University of Khartoum, Khartoum, Sudan. [2]Department of Respiratory Medicine, Elshaab Teaching Hospital, Khartoum Sudan. [3]Department of Cardiology, Elshaab Teaching Hospital, Khartoum Sudan.
Corresponding author email: drahahmed@hotmail.com

Abstract

Background: Pulmonary tuberculosis (PTB) is an increasing global health problem that continues to cause significant morbidity and mortality. The impact of PTB has been measured in terms morbidity and mortality and little attention has been paid to continuing respiratory disability in those who were cured. Pulmonary hypertension (PHT) is a serious respiratory disability that results from structural lung damage and chronic hypoxia. This study was conducted to investigate the presence of PHT in a cohort of treated PTB patients who presented with shortness of breath.

Methods: This is a cross-sectional study that included 14 consecutive patients who were cured of PTB and presented with shortness of breath. Demographic and clinical data were recorded for all patients. PHT was diagnosed using Doppler echocardiography.

Results: Fourteen patients who were treated for PTB and were found to have PHT were studied. All patients were sputum smear negative at the time of the study. The mean age (SD) was 43.1 (13.6) and half of the patients were males. The mean number of years since PTB was diagnosed (SD) was 9.4 (10.9). All patients had abnormal chest x-rays. The commonest radiological abnormality was fibrocavitation which occurred in 50% of patients. Estimated pulmonary artery systolic pressure (PASP) of 51 to 80 mm/Hg was found in 9 patients (64.3%) whereas PASP of 40 to 50 mm/Hg was found in 4 patients (28.6%) and one patient had PASP more than 80 mm/Hg.

Conclusions: Different grades of PHT occurred in this cohort of treated PTB patients on average about 9 years after cure. The findings of this study support implementation of strategies for early detection and prevention of PTB. For those who were cured from PTB, longer periods of disability should be implemented in assessment of disease burden.

Keywords: tuberculosis, pulmonary hypertension, echocardiography

Clinical Medicine Insights: Circulatory, Respiratory and Pulmonary Medicine 2011:5 1–5

doi: 10.4137/CCRPM.S6437

This article is available from http://www.la-press.com.

Introduction

PTB continues to be a major global health problem causing significant morbidity and mortality in spite of modern and effective chemotherapy.[1] Many factors contribute to the increase in PTB worldwide including homelessness, poverty, immigration, lack of public health infrastructure, limited access to medical care, in addition to the HIV epidemic, and these factors are likely to continue in the foreseeable future.[2] The impact of PTB has traditionally been measured in terms of morbidity and mortality. Treatment success in PTB has been defined in terms of microbiological cure rates and little attention has been paid to the impact of PTB as a cause of disability in those who survived the disease.[1] Given the high incidence of PTB and the high success rate of modern therapy there is an unknown but substantial number of patients who survived PTB worldwide.[1]

Studies that assessed the impact of treated PTB as a cause of disability have focused on impairment of lung function.[3–5] These studies have shown significant residual lung function impairment in more than 50% of treated PTB patients and both obstructive and restrictive ventilatory defects have been described.[3–5] It is known that persisting physiological impairment leads to gas exchange abnormalities and development of pulmonary hypertension which is a cause of severe disability and reduced longevity.[6–8] However, few studies described pulmonary hypertension in treated PTB patients and most of the available information is from the pre-chemotherapy era.[9] We therefore conducted this study to investigate the presence of pulmonary hypertension in a cohort of patients who survived PTB as a result of treatment and presented with shortness of breath. This is a pilot study of a project that aims to follow up survivors of PTB with a view to assess prevalence and progression of physiological impairment, radiological abnormalities and PHT in these patients.

Materials and Methods

This is a descriptive cross-sectional study that included 14 consecutive patients with treated PTB who presented with shortness of breath. Patients were recruited from the respiratory department of a tertiary referral hospital: Elshaab Hospital, Khartoum, Sudan. Ethical approval for the study was obtained from the ethical committee of the hospital and all patients gave informed consent to take part in the study. Patients with a history of treated pulmonary tuberculosis diagnosed on basis of positive sputum smear test who presented with shortness of breath were investigated for the presence of PHT and if found to have PHT were included in the study. All patients received antituberculous therapy at the time of diagnosis as in the protocol of Sudan National Tuberculosis Program. The daily regimen is composed of intramuscular streptomycin for two months, oral pyrazinamide for two months, oral rifampicin for six months and oral isoniazid for six months. All patients had chest radiographs and these were reviewed. Data on age, sex, history of tuberculosis including time and method of diagnosis and treatment received and its duration were collected using a structured questionnaire. All patients underwent a full clinical examination and physical signs were recorded using a specially designed clinical sheet. Patients with cardiac valvular lesions and those who were HIV positive were excluded from the study. Patients underwent Doppler echocardiography using a *GE Vivid 3Pro and Esaote MyLab™50 XVision* echocardiography machine. Tricuspid regurgitation was identified in the best possible view for proper continuous wave alignment. Right atrium/right ventricle pressure gradient (RA/RVPG) was calculated using simplified Bernoulli equation.[10] PASP was identified using the equation PASP = RA/RV PG + right atrial pressure mm/Hg estimated using IVC collapsibility index.[10] PHT was considered as PASP $\geq$ 40 mm/Hg.[10]

Results

A total of 30 patients who were treated for PTB and presented with shortness of breath were screened for the presence of PHT. Fourteen of these patients were found to have PHT and were included in the study. Table 1 shows the demographic and clinical characteristics of the 14 patients studied. There were equal numbers of men and women with a mean age of 43.7 years. All patients were initially diagnosed on basis of a positive sputum smear test, but none was sputum smear positive at the time of inclusion in the study. The mean number of years since PTB was diagnosed was 9.4 years. Eight patients completed treatment and the rest defaulted. Seventy nine percent

Table 1. Demographic and clinical characteristics of the 14 patients with treated pulmonary tuberculosis and pulmonary hypertension.

Characteristic	Number (percentage)
Age in years mean (SD)	43.1 (13.6)
Gender	
Males	7 (50%)
Females	7 (50%)
Sputum smear test	
Positive when first diagnosed	14 (100%)
Positive at time of inclusion in study	0 (0%)
Years since TB was first diagnosed mean (SD)	9.4 (10.9)
Completed Tuberculosis therapy	
Yes	8 (57%)
Defaulted	6 (43%)
Smoking	
Current smokers	1 (7%)
Previous smokers	2 (14%)
Non smokers	11 (79%)

of the patients were non smokers. Table 2 shows the radiological abnormalities at the time the study was conducted. All patients had abnormal chest radiographs. Fifty percent of the patients had residual fibrocavitatory changes and one patient had a fibrothorax. Table 3 shows the echocardiographically estimated pulmonary artery systolic pressure of the 14 patients. Most of the patients had moderately severe PHT (PASP 51–80 mm/Hg) whereas only one patient had severe PHT (PASP more than 80 mm/Hg).

Discussion

This study documents the presence of PHT in a cohort of symptomatic patients who were treated from PTB in a country with high tuberculosis burden.[2] Our study was designed to exclude other possible causes of PHT in this cohort of patients in that we excluded

Table 2. Radiological abnormalities among the 14 patients with treated pulmonary tuberculosis and pulmonary hypertension.

Chest-X-ray abnormality	Number (percentage)
Fibrocavitatory	7 (50%)
Fibrosis	5 (36%)
Bullae and fibrosis	1 (7%)
Fibrothorax	1 (7%)

Table 3. Estimated pulmonary artery systolic pressure among the 14 patients with treated pulmonary tuberculosis and pulmonary hypertension.

Estimated pulmonary artery systolic pressure	Number (percentage)
40–50 mm/Hg	4 (28.6%)
51–80 mm/Hg	9 (64.3%)
More than 80 mm/Hg	1 (7.1%)

all patients with cardiac valvular lesions and those who were HIV positive.[11] The percentage of smokers among the study population was low at 21% making chronic obstructive pulmonary disease as a possible cause of PHT very unlikely.[6–8] Furthermore, all patients we studied were sputum smear positive at the time when they were first diagnosed and had residual radiological abnormalities that are known to result from PTB thus excluding other forms of interstitial lung disease as a possible cause of PHT.

Previous studies that assessed the presence of PHT in PTB patients were mostly from the pre-chemotherapy era and PHT and cor pulmonale were diagnosed by electrocardiography or at postmortem.[9,12–14] Our study is different in that all our patients received modern anti-tuberculous chemotherapy and were microbiologically cured. We utilized Doppler echocardiography to diagnose pulmonary hypertension in our patients. While Doppler echocardiography estimates PASP, it is by far the best method for non invasive diagnosis of PHT and we considered it to be acceptable for this report.[15,16] Values of pulmonary artery systolic pressure obtained with measurement of the maximum velocity of tricuspid valve regurgitation using continuous wave Doppler echocardiography correlate strongly with those found on right heart catheterization.[17]

The mechanism of development of PHT in treated PTB patients is thought to result from residual pulmonary structural damage and pulmonary function abnormalities leading to gas exchange abnormalities and chronic hypoxia.[9,18] It has also been suggested that repeated secondary respiratory tract infections, caused by residual chest x-ray abnormalities, play an important role in the pathogenesis of PHT in treated PTB patients.[9,18] All our patients had abnormal chest radiographs that were caused by PTB, but we did not measure lung function in our study population. However,

all of our patients presented with shortness of breath and it has been shown that symptoms of pulmonary function impairment generally do not occur in patients with chronic lung disease until the forced expiratory volume in the first second has fallen to 50% of that predicted;[19] therefore, it is likely that the patients we studied had significant lung function impairment.

The occurrence of PHT in the course of chronic pulmonary disease is associated with accelerated morbidity and increased mortality.[6–8] A remarkable finding in this study is the young age of the patients diagnosed with PHT—mean age 43 years. These patients are much younger when compared with patients who have PHT in association with chronic obstructive pulmonary disease whose mean age was 66 years.[20] Clearly, these patients developed a serious respiratory disability at a relatively young age as a result of a disease which they contracted on average more than 9 years previously and from which they were cured.

This study was not designed to measure the prevalence of PHT in treated PTB patients; rather, it is a case series that documents the presence of a serious respiratory morbidity in a cohort of symptomatic patients after successful treatment of PTB. Studies of the prevalence of residual lung function abnormalities in treated PTB patients have shown persistent pulmonary function impairment in up to 65% of these patients.[3–5,21] Similarly, residual radiological abnormalities have been documented in 86% of treated PTB patients.[21] However, the prevalence of PHT in patients with residual lung function and radiological abnormalities has not been documented in these studies.[3–5,21] Nevertheless, persistent lung function impairment and residual radiological abnormalities are thought to cause PHT in patients with PTB.[9,18] Also, the effect of physiological impairment leading to chronic hypoxia and structural lung damage as causes of PHT are well documented in chronic lung disease.[6–8] Given the global scale of PTB and the increasing number of patients who have survived the disease because of effective therapy, we can postulate that the problem of PHT in treated PTB patients is likely to be substantial.[1,2] However, a specially designed study to document prevalence of PHT in treated PTB is needed.

PHT of variable degrees occurs in patients with treated PTB. PHT as a measure of pulmonary impairment contributes important burdens of PTB in microbiologically cured patients that may cause excess mortality. Current assessment of PTB burden assumes that tuberculosis causes disability before and then immediately after diagnosis and treatment.[22] Given the results of this study, such an approach clearly underestimates this burden and should take into account longer period of disability in cured patients. The findings of this study support early case detection and treatment of latent PTB and employment of other preventative strategies.

Disclosure

This manuscript has been read and approved by all authors. This paper is unique and is not under consideration by any other publication and has not been published elsewhere. The authors and peer reviewers of this paper report no conflicts of interest. The authors confirm that they have permission to reproduce any copyrighted material.

References

1. World Health Organization. Global tuberculosis control: epidemiology, strategy, financing. WHO report 2009. WHO/HTM/TB/2009.411. Geneva, Switzerland: WHO. 2009:314.
2. Corbett EL, Watt CJ, Walker N, et al. The growing burden of tuberculosis: global trends and interactions with the HIV epidemic. *Arch Intern Med*. 2003;163:1009–21.
3. Pasipanodya JG, Miller TL, Vecino M, et al. Pulmonary impairment after tuberculosis. *Chest*. 2007;131:1817–24.
4. Maguire GP, Anstey NM, Ardian M, et al. Pulmonary tuberculosis, impaired lung function, disability and quality of life in a high-burden setting. *Int J Tuberc Lung Dis*. 2009;13(12):1500–6.
5. Menezes AMB, Hallal PC, Perz-Padilla R, et al; for the Latin American Project for the Investigation of Obstructive Lung Disease (PLATINO) Team: Tuberculosis and airflow obstruction: evidence from the PLATINO study in Latin America. *Eur Respir J*. 2007;30:1180–5.
6. Naeije R. Pulmonary hypertension and right heart failure in chronic obstructive pulmonary disease. *Ann Thorac Soc*. 2005;2:20–2.
7. Naeije R, Barberà JA. Pulmonary hypertension associated with COPD. *Critical Care*. 2001;5(6):286–9.
8. Chaouat A, Naeije R, Weitzenbium E. Pulmonary hypertension in COPD. *Eur Respir J*. 2008;32:1371–85.
9. Kapoor SC. Pathogenesis of cor pulmonale in pulmonary tuberculosis. *Ind J Tuberc*. 1986;33:167–70.
10. The task force for the diagnosis and treatment of pulmonary hypertension of the European Society of Cardiology and the European Respiratory Society. Guidelines for the diagnosis and treatment of pulmonary hypertension. *Eur Heart J*. 2009;30:2493–537.
11. Farber HW, Loscalzo J. Pulmonary arterial hypertension. *N Eng J Med*. 2004;351:1655–65.
12. Nemet G, Rosenblatt MB. Cardiac failure secondary to chronic pulmonary tuberculosis. *Am Rev Tuberc*. 1937;xxxv:713.
13. Levinsky L. Tuberculosis and Cardiopulmonary Failure. *Dis Chest*. 1961;40:564–71.
14. Heries F, Widimsky J. Tuberculosis of the Lungs in the Pathogenesis of Cor Pulmonale. *Acta Univ Carol Med*. 1956;2:267.
15. McGoon M, Gutterman D, Steen V, et al. Screening, early detection, and diagnosis of pulmonary arterial hypertension: ACCP evidence-based clinical practice guidelines. *Chest*. 2004;126 Suppl 1:14S–34S.

16. Naeije R, Torbicki A. More on the noninvasive diagnosis of pulmonary hypertension: Doppler echocardiography revisited. *Eur Respir J*. 1995; 8:1445–9.
17. Berger M, Haimowitz A, van Tosh A, Berdoff RL, Goldberg E. Quantitative assessment of pulmonary hypertension in patients with tricuspid regurgitation using continuous wave Doppler ultrasound. *J Am Coll Cardiol*. 1985; 6:359–65.
18. Kapoor SC. Cor pulmonale in pulmonary tuberculosis: a preliminary report of 66 patients. *Ind J Tuberc*. 1959;6(2):51–64.
19. Sutherland ER, Cherniack RM. Current concepts: management of chronic obstructive pulmonary disease. *N Engl J Med*. 2004;350:2689–97.
20. Scharf SM, Iqbal M, Keller C, Criner G, Lee S, Fessler HE. Hemodynamic characterization of patients with severe emphysema. *Am J Respir Crit Care Med*. 2002;166:314–22.
21. Banu Rekha VV, Ramachandran R, Kuppa Rao KV, et al. Assessment of long term status of pulmonary TB patients successfully treated with short course chemotherapy. *Ind J Tuberc*. 2009;56:132–40.
22. Lopez AD, Mathers CD, Ezzati M, Jamison DT, Murray CJ. Global and regional burden of disease and risk factors, 2001: systematic analysis of population health data. *Lancet*. 2006;367:1747–57.