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Original article

Effect of pulmonary hypertension on outcome of pulmonary tuberculosis

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ABSTRACT

Background: This study performed at the National Research Institute of Tuberculosis and Lung Disease, Tehran, Iran, aimed to evaluate the effect of concomitant pulmonary hypertension on the outcome of pulmonary tuberculosis.
Methods: New cases of pulmonary tuberculosis were recruited for the study. Pulmonary hypertension was defined as systolic pulmonary arterial pressure ≥35 mm Hg estimated by transthoracic Doppler echocardiography. We assessed the relationship between pulmonary hypertension and mortality during the six-month treatment of tuberculosis.
Results: Of 777 new cases of pulmonary tuberculosis, 74 (9.5%) had systolic pulmonary arterial pressure ≥35 mm Hg. Ten of them (13.5%) died during treatment compared to 5% of cases with pulmonary arterial pressure less than 35 mm Hg ($p = 0.007$). Logistic regression analysis showed that pulmonary hypertension and drug abuse remained independently associated with mortality (OR = 3.1; 95% CI: 1.44–6.75 and OR = 4.4; 95% CI: 2.35–8.17, respectively).
Conclusion: A significant association was found between mortality and presence of pulmonary hypertension and drug abuse among new cases of pulmonary tuberculosis.

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Introduction

Pulmonary tuberculosis (TB) continues to be a major health problem worldwide. In spite of effective chemotherapy, excess morbidity and mortality are attributed to TB. Because treatment success in pulmonary TB has been defined as mycobacteriological response, little attention has been paid to the related chronic disabilities in those who survived the disease.[1] Despite successful treatment, a significant permanent damage of lung function has been reported in more than 50% of pulmonary TB patients. They may be obstructive or restrictive[2] and lead to gas exchange abnormalities and development of pulmonary hypertension.[3]

Pulmonary hypertension (PH) is a serious disorder with poor prognosis. It is defined as a mean pulmonary arterial pressure (PAP) of more than 25 mm Hg at rest.[4] Recently, new therapeutic options have been developed for treating PH that improve quality of life and prognosis of the disease.[5] Symptoms of PH consisting of dyspnea, palpitations, fatigue, and syncope are vague that postpone detection of it.[4] As a result, an appropriate plan for screening PH is necessary among high risk groups of patients.

Few studies described PH in treated TB patients but most of them were conducted during pre-chemotherapy era.[6] Studies about PH during active pulmonary TB are very scarce.[7] Moreover, according to different definitions of the disease and various screening methods and population groups, the results are widely different.

This study was aimed to evaluate the effects of PH in the outcome of active pulmonary TB. Due to the growing range of therapeutic options, early diagnosis of pulmonary hypertension may change patient survival.

Materials and methods

This retrospective cohort study was conducted on inpatient new cases of pulmonary tuberculosis that were diagnosed in the National Research Institute of Tuberculosis and Lung Diseases (NRITLD), Tehran, Iran between 2005 and 2009. A diagnosis of TB was made by positive smear and culture results for *Mycobacterium tuberculosis* or histopathological findings. New cases of TB were defined as those who had received either no anti-TB drugs or less than one month of treatment in the past. TB treatment has been initiated at the time of diagnosis, as recommended by the World Health Organization (WHO) guidelines,[8] consisting of isoniazid, rifampin, ethambutol and pyrazinamide for two months as initial phase and isoniazid and rifampin for the next four months as maintenance phase. All the patients were referred to peripheral health centers for continuing medication under the directly observed treatment (DOT) strategy in accordance with our National Tuberculosis Program (NTP). The outcome of treatment was defined according to WHO guidelines. Death due to any reason during the course of tuberculosis treatment was considered.[8]

For calculation of pulmonary artery pressure firstly tricuspid valve regurgitant jet was identified by color Doppler echocardiography (Vivid 7 dimension; Mann healthcare, GE). Then the trans-tricuspid pressure gradient was calculated using modified Bernoulli equation and right atrium pressure was added to obtained peak pulmonary artery pressure. For this study we considered pulmonary hypertension as peak systolic pulmonary arterial pressure equal or more than 35 mm Hg estimated by resting transthoracic echocardiography.

Recorded data of all new cases of pulmonary tuberculosis from our hospital registry were preset for recent study. Demographic, characteristics and other variables were entered in SPSS (version 11.5) software.

The relationship between pulmonary hypertension and the outcome of TB treatment was assessed controlling for confounding factors (age, sex, smoking, drug abuse, symptoms and adverse effects of anti TB drugs) by regression analysis. The χ^2 test was used for categorical variables, and whenever necessary, the Fisher exact test was utilized. Continuous variables with normal distribution were analyzed by *t*-Student test, and Mann–Whitney *U* test in case of abnormal distribution. A p-value < 0.05 was considered statistically significant.

The scientific and ethics committee of the NRITLD approved the study protocol.

Results

A total of 777 new cases of pulmonary tuberculosis were diagnosed in the study period. Systolic pulmonary arterial pressure more than 35 mm Hg was detected in 74 (9.5%) by Doppler echocardiography. Right heart catheterization was not performed.

Characteristics of patients and clinical factors for both groups are showed in Table 1.

Males comprised 357 (45.9%). Mean (±SD) age of patients was 54.51 ± 21.73; 84% were of Iranian nationality. HIV test was performed in 309 patients with 36 (4.7% of all cases) positive cases. All TB patients with PAP $\geq$ 35 mm were HIV negative.

There was no significant difference between patients with PAP above and below 35 mm Hg concerning gender, smoking status, opium addiction, and history of hemoptysis.

Cases with pulmonary hypertension were older and present dyspnea and chest pain more often.

Adverse effects of anti-TB medications occurred in 26 (35%) patients with PAP $\geq$ 35 mm Hg and in 38% patients of the control ($p = 0.68$). The major adverse effect was drug-induced hepatitis, which was not different between two groups ($p = 0.18$).

The outcome of TB treatment was known for 700 patients. Ten patients with PAP $\geq$ 35 mm Hg (13.5%) died during treatment in comparison to 5% of cases without PH ($p = 0.007$) (Fig. 1).

To determine the independent association of risk factors (gender, age > 65, nationality, smoking status, and PAP $\geq$ 35 mm Hg) with mortality, a logistic regression was performed. Drug abuse and PAP $\geq$ 35 mm Hg were the factors that remained independently associated with mortality in the final model (Table 2).