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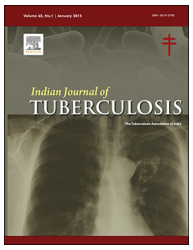

Original Article

Initial airflow obstruction in new cases of pulmonary tuberculosis: Complication, comorbidity or missed?

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ABSTRACT

Tuberculosis (TB) may have a similar spirometry findings as a chronic obstructive pulmonary disease but the prevalence of TB-induced airflow obstruction (AO) is still unknown.
Objectives: To measure frequency of AO in new TB cases at the beginning of treatment and to evaluate factors associated with obstructive abnormalities following TB diagnosis.
Materials and Methods: 317 patients that have no history of prior AO were recruited into the study with a median age of 39.0 years (IQR, 30.0–49.0). AO was defined using the $FEV_1/F(VC) <$ LLN.
Results: AO was detected in 29.97% (95/317) new TB cases. These patients had a more severe clinical manifestation of TB with a greater likelihood of cough, OR = 5.47 (95%CI 1.90–15.70) and wheezing, OR = 10.51 (95%CI 5.72–19.27), $p < 0.001$. The frequency of AO was positively associated with bronchoscopic evidence of narrowing of the main airways. Furthermore, from multiple logistic regression analysis we would assume that higher FEV_1 value in TB patients with AO was related to greater BMI and inversely associated with older age, female sex and radiographic extent ($p < 0.05$).
Conclusions: Obstructive pattern on spirometry frequently occurs in new TB cases without previously detected AO. This category of patients should be targeted for detailed follow-up, particularly, in high TB burden countries.

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1. Introduction

Tuberculosis (TB) is a growing problem in Ukraine because existing military conflict adds to the pre-existing challenges, such as a high rate of drug resistance and human immunodeficiency virus (HIV) co-infection.[1] However, TB case detection based on annual chest radiology rather than sputum smear microscopy (in 2015 there were only 2.6% TB cases identified by finding acid-fast bacilli (AFB) in primary health care)[27] leads to a delay in diagnosis with extensive lung lesions. Unfortunately, pulmonary dysfunction is a significant obstacle in achieving a desirable treatment outcome among TB patients.[12–14]

Airflow obstruction (AO) associated with active TB is often missed in routine practice.[3,7,33] AO may prolong sputum conversion time and delay healing of lung cavities,[9,14,35] despite effective TB treatment usually minimizes a restrictive ventilatory defect.[31] The prevalence of an obstructive abnormality (heterogeneous definitions) varies between 12.5 and 88.2% among different categories of TB patients.[2,35] Some authors considered airflow limitation as a ''red flag'' diagnostic tool for chronic obstructive pulmonary disease (COPD),[9,19] although others highlight active TB as an independent etiology of this phenomenon.[10,20,22,35] Nevertheless, discrepancies in study design and characteristics of selected participants, including sequelae of previous treatment[16] as well as coexistence of other diseases (HIV,[33] bronchial asthma (BA),[12] bronchiectasis[18] etc.), complicate estimates of the rate of AO among newly diagnosed TB patients.

Thus, the aim of the present study was to determine the frequency of initial AO among patients with new cases of pulmonary TB and to evaluate factors associated with obstructive abnormalities following TB diagnosis.

2. Study population and methods

2.1. Study design and participants

The present prospective cross-sectional study was carried out at the Regional Tuberculosis Dispensary in Vinnytsia from August 2007 to March 2012. Out of 2226 consecutively admitted patients aged 18 years or older with new cases of pulmonary tuberculosis, 352 (15.8%) were randomly selected and invited to participate in this study.

Inclusion criteria: 1) patients above 17 years of age with confirmed (culture positive) new case of pulmonary tuberculosis (a case never having previously received drug treatment for active TB or having received anti-TB drugs for less than one month); 2) at the time of spirometry test all participants could take anti-tuberculosis treatment, but not longer than one week.

Patients with any of the following conditions were *excluded*: 1) ever diagnosed with COPD, BA, bronchiectasis; 2) non-consenting patients; 3) ongoing treatment with β-blockers or corticosteroids; 4) pregnancy; 5) radiological evidence of lung pathology other than TB; 6) lack of cooperation; 7) technical difficulties; 8) mental or physical inability to perform the pulmonary function testing; 9) experience of smoking ≥10 pack/years; 10) intense/prolonged occupational exposure to noxious particles or gases; 11) exacerbation of allergic diseases; 12) HIV-positive patients.

Post-randomization exclusion of non-eligible patients ($n = 35$) was performed due to the following reasons: study personnel errors, $n = 4$; COPD, $n = 10$; bronchiectasis, $n = 1$; BA, $n = 3$; lung cancer/metastases, $n = 2$; ongoing treatment with corticosteroids, $n = 1$; allergy, $n = 2$; poor efforts during spirometry, $n = 4$; informed refusal patients, $n = 5$; HIV-positive individuals, $n = 3$.

The median age of the subjects ($n = 317$) was 39.0 years (IQR, 30.0–49.0). Comparative analysis of demographic characteristics between participants and adult population with new cases of pulmonary TB is shown in Table 1. Population data from 2010 was preferred for comparison as a midpoint of our study duration (2007–2013).

This study was approved by the Bioethics Committee at the National Pirogov Memorial Medical University of Vinnytsia and all participants gave written informed consent.

2.2. Methods

All patients underwent a standard evaluation that included complains, history, physical examination, chest radiography (CXR), laboratory investigations and lung function study.

2.3. Pulmonary function tests (PFTs)

Spirometry was performed and interpreted according to American Thoracic Society (ATS)/European Respiratory Society (ERS) Task Force on pulmonary function standards.[26,30] Measurements of forced expiratory volume in one second (FEV_1), vital capacity (VC), forced vital capacity (FVC) and forced expiratory flow between 25% and 75% of the FVC ($FEF_{25–75\%}$) were made using a portable Microlab Spiro (version 1.32, Rochester, UK) following the valid reference values of the European Community for Steel and Coal (ECCS). Pulmonary function tests (PFTs) were done in sitting position by qualified technologist under the direct supervision of the principal investigator.

Airflow obstruction was defined using the FEV_1/F(VC) ratio of less than the lower limit of normal (LLN) for relevant healthy population. The baseline VC or FVC has been chosen as a preferred parameter for diagnostic ratio calculating whichever was larger.[23] We analyzed flow-volume loop configurations to suspect predominant occurrence of the airway obstruction. Post-bronchodilator testing was performed if baseline spirometry showed an obstructive pattern. Significant reversibility was determined if after inhalation of 400 mcg salbutamol (four separate doses with 30-s intervals) and 15 min re-measurement - per cent/absolute changes in FEV_1 and/or FVC ≥12% and 200 ml compared with baseline values.[26]

Mouthpiece and transducer were cleaned and disinfected between patients to prevent the transmission of infection via direct contact with biological fluids.

2.4. Flexible fiberoptic bronchoscopy

Flexible fiberoptic bronchoscopy (FB) was performed in the procedure room via the oral route (Olympus; BF-PE2 or BF-TE2; Japan). There were standard indications: cough or

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