PEER REVIEW HISTORY

ARTICLE DETAILS

TITLE (PROVISIONAL)	Clinical significance of low forced expiratory flow between 25% and 75% of vital capacity following treated pulmonary tuberculosis: a cross-sectional study
AUTHORS	Pefura-Yone, Eric Walter; Kengne, Andre; Kamdem-Tagne, Pierre Eugene; AFANE ZE, Emmanuel

VERSION 1 - REVIEW

REVIEWER	Ozkan Yetkin Inonu University Hospital Department of Pulmonery Medicine Malatya-TURKEY
REVIEW RETURNED	08-May-2014

GENERAL COMMENTS	FEF25-75% is marker of small-medium size airway functions. This parameter is depend on patient effort, age, smoking and .past medical contition. Tuberculosis is affected mainly alveolar spaces and can be caused impairment airway and parachimal function. This is not new. knowledge For this reason association between tuberculosis and airway functions especially FEF25-75% is not acceptible.

REVIEWER	Jotam Pasipanodya UT Southwestern
REVIEW RETURNED	14-Jun-2014

GENERAL COMMENTS	Summary The study assessed small airway obstruction in 177 TB patients treated at a referral health facility in Cameroon. ATS/ERS recommended methods were used. Logistic regression models were employed to determine independent risk factors (including pre-treatment delays and symptoms and clinical factors) associated with post-TB treatment airways obstruction. Because the study was based on data from a large reference TB hospital, measures of prevalence are likely to biased but reflective of pulmonary TB disease sequelae. Small airways obstruction was observed in 63% of patients and majority of these had persisting respiratory symptoms despite successful TB therapy. These finding underlie the importance of preventing TB as well as optimization of TB treatment with a view to mitigate TB disease sequelae. However, according to the authors early TB diagnosis can reduce post-TB airways obstruction. Minor revisions

	1. State exactly when the pulmonary function tests (PFT) were performed; is it immediately after completing treatment? 2. Report # patients that were drug resistant 3. Clearly definition of persisting respiratory signs should be explicitly stated in the methods 4. On page 7 last paragraph in the results, what do you mean by incorrect spirometry records? Do you mean PFT test that were not reproducible? 5. Given the association between smoking and smoking volume, i.e., pack-years and small airways obstruction, both should be accounted for in your regression model, if the collected data does allow for it. 6. Remove the fourth column in table 2 (p-value$), it does not add value. It only confuses the reader 7. Spirometric values in table 1 can be depicted better in a box plot because the variability in those values

VERSION 1 – AUTHOR RESPONSE

Reviewer: 1
Reviewer Name Ozkan Yetkin
Institution and Country Inonu University Hospital
Department of Pulmonery Medicine
Malatya-TURKEY
Please state any competing interests or state 'None declared': COPD,
Sleep Medicine

FEF25-75% is marker of small-medium size airway functions. This parameter is depend on patient effort, age, smoking and .past medical contition. Tuberculosis is affected mainly alveolar spaces and can be caused impairment airway and parachimal function. This is not new. knowledge For this reason association between tuberculosis and airway functions especially FEF25-75% is not acceptible.
Our answer: Thank you for this comment. It is possible that the findings from this study are not new but we are not aware of published studies on post-tuberculosis distal airflow obstruction (DAO) and the possible connection with persistence of respiratory signs following treatment for pulmonary tuberculosis.

Reviewer: 2
Reviewer Name Jotam Pasipanodya
Institution and Country UT Southwestern
Please state any competing interests or state 'None declared': None

Clinical significance of low forced expiratory flow between 25% and 75% of vitall capacity following treated pulmonary tuberculosis. Pefura-Yone, EW., Kengne, A., Kamden-Tagne, PE
Reviewer's comment
Summary
The study assessed small airway obstruction in 177 TB patients treated at a referral health facility in Cameroon. ATS/ERS recommended methods were used. Logistic regression models were employed to determine independent risk factors (including pre-treatment delays and symptoms and clinical factors) associated with post-TB treatment airways obstruction. Because the study was based on data from a large reference TB hospital, measures of prevalence are likely to biased but reflective of pulmonary TB disease sequelae. Small airways obstruction was observed in 63% of patients and

majority of these had persisting respiratory symptoms despite successful TB therapy. These finding underlie the importance of preventing TB as well as optimization of TB treatment with a view to mitigate TB disease sequelae. However, according to the authors early TB diagnosis can reduce post-TB airways obstruction.

Minor revisions
1. State exactly when the pulmonary function tests (PFT) were performed; is it immediately after completing treatment?

Our answer: The PFTs were performed in the month following the end of tuberculosis treatment. The corresponding sentence has been added at the beginning of spirometric measurements section where it reads: “The spirometric measurements were done in the month following the completion of TB treatment.”

2. Report # patients that were drug resistant

Our answer: Dug susceptibility tests (DST) are not routinely done for patient with new tuberculosis cases in this center. However, all patients with retreatment cases have DST. All 22 patients in retreatment group (previous TB) were susceptible to major anti-tuberculous drugs. We also excluded patients with failure (positive sputum examination at the end of 5th or 6th month of treatment), meaning that virtually our patients are probably susceptible to TB drugs. This has been added in the methodology section on page 5. It reads:
‘Sputum culture and drugs susceptibility test (DST) were done for all retreatment cases. Patients with any of the following conditions were excluded: patients with treatment failure, patients with resistance to at least one antituberculosis drug, on-going bacterial pneumonia or within the four weeks preceding inclusion, chronic respiratory condition before TB diagnosis, on-going treatment with beta blockers, physical or mental inability to perform spirometry test’

3. Clearly definition of persisting respiratory signs should be explicitly stated in the methods

Our answer: Fixed. It reads: “Patients whose symptoms continued at the end of TB treatment were considered having persistent respiratory symptoms”.

4. On page 7 last paragraph in the results, what do you mean by incorrect spirometry records? Do you mean PFT test that were not reproducible?

Our answer: Thank you to raise this question. This means that the spirometric maneuvers were not acceptable and/or not reproducible. It has been amended and now reads:
‘One refused to consent, ten had incorrect spirometry records (not acceptable and/or not reproducible manoeuvres) while one had a FEV1/FVC<0.70.’

5. Given the association between smoking and smoking volume, i.e., pack-years and small airways obstruction, both should be accounted for in your regression model, if the collected data does allow for it.

Our answer: Please, we have investigated the relationship between the smoking volume (pack-years) and the chronic respiratory symptoms. We didn’t find any association. This has been fixed in corresponding result section.

6. Remove the fourth column in table 2 (p-value$), it does not add value. It only confuses the reader

Our answer: fixed

7. Spirometric values in table 1 can be depicted better in a box plot because the variability in those values

Our answer: Fixed