Lung Function Impairment In Patients Treated For Pulmonary Tuberculosis and Associated Factors in Puducherry, South India

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Abstract

Context: After completion of treatment, a proportion of pulmonary tuberculosis (TB) (PTB) patients experience lung function impairment (LFI) which can influence their quality of life. Aim: This study was aimed to determine the prevalence of LFI in patients treated for PTB and the associated factors. Settings and Design: A cross-sectional study was conducted among patients treated for PTB in eight primary health centers in Puducherry. Subjects and Methods: The study was carried out among 118 patients. Those aged 18 and above whose PTB treatment outcomes were declared as cured or completed between 2018 and 2019 were included. Demographic data, respiratory symptoms before TB diagnosis, comorbidities, and chest radiography findings before TB treatment were collected. All participants underwent spirometric tests before and after dilatation with salbutamol nebulization. Statistical Analysis: Multivariable analysis identified smear-negative TB and indoor exposure to biomass for cooking as significant independent risk factors for LFI. Results: Of 118 participants interviewed, 70.3% were male and the median age of the participants was 47.7 years. The prevalence of LFI was 62.7% (95% confidence interval: 53.3–71.4). Conclusion: LFI was frequent in patients treated previously for TB. Creating awareness about the possible LFI among these patients along with the awareness for seeking health care for this condition is the need of the hour.

Keywords: Lung function impairment, pulmonary tuberculosis, spirometer

INTRODUCTION

Pulmonary tuberculosis (TB) (PTB) is one of the top ten causes of mortality worldwide killing about five thousand people daily. Among 30 high TB burden countries, India ranks first followed by Russia and South Africa. Lung function impairment (LFI) following PTB is reported in more than half of microbiologically cured patients, with approximately 10% having already lost half of their lung function. Very little is known about the prevalence of LFI among the patients treated for TB, in particular from countries like India where the incidence of the disease is more. Hence, this study was conducted to know the prevalence of LFI and to determine these associated factors in “previously treated” and “cured” patients (PTB) because completion of Anti-tubercular Treatment (ATT) is just initiation but not an end of their illness.

SUBJECTS AND METHODS

A cross-sectional analytical study was done among adults aged 18 years and above from January–December 2019 in primary health centers (PHCs) at Puducherry, South India. There are 27 PHCs in Puducherry and about 10% of the TB patients are availing treatment from the eight PHCs around Jawaharlal Institute of Postgraduate Medical Education and Research (JIPMER). The remaining 90% of the patients are receiving treatment, either from the remaining 19 PHCs or the government hospitals and medical colleges in Puducherry. The PHCs were selected around JIPMER based on convenience.

All adults with PTB (new or previously treated) from the eight PHCs, who were declared as “cured” or “treatment completed” were included. The study was conducted to know the prevalence of LFI and to determine these associated factors in “previously treated” and “cured” patients (PTB) because completion of Anti-tubercular Treatment (ATT) is just initiation but not an end of their illness.

Access this article online

Quick Response Code:  
Website:  
www.ijcm.org.in  
DOI:  
10.4103/ijcm.ijcm_564_21

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How to cite this article: Pydipalli M, Chinnakali P, Rajaram M, Sundaram SP, Roy G. Lung function impairment in patients treated for pulmonary tuberculosis and associated factors in Puducherry, South India. Indian J Community Med 2022;47:111-5.

Received: 11-03-21, Accepted: 14-09-21, Published: 16-03-22
completed” under the National TB Program, and whose
treatment outcomes were declared within 12 months before
the date of interview (September 2019 to October 2019) were
included. Multidrug-resistant TB patients, patients who
were declared cured or treatment completed and again diagnosed
as “smear-positive TB” during the study period, and patients
with a history of asthma and chronic obstructive pulmonary
disease were excluded from the study.

Assuming the expected proportion of PTB patients with LFI
as 45.4%,[3] by using OpenEpi software version 3.03, a sample
size of 185 was arrived. Eight primary health centers near to the
hospital were selected conveniently, and a total of 200 patients
who were declared as “cured” or “treatment completed” under
these eight PHCs were approached for the study. However,
results of 118 patients were taken as they only had performed
the complete spirometry procedure [Figure 1].

A list of eligible study participants was prepared from the
TB registers/NIKSHAY database maintained at the State TB
Office.

Information on morbidity and treatment characteristics was
extracted from the TB register and individual patient card.

Participant general information and respiratory symptoms
present before diagnosis of TB and at present, biomass exposure
for cooking or heating, and dust exposure (workplace) were
also obtained through interviews after obtaining the consent.

Lung function tests were performed with the patient in a sitting
position using a portable spirometer (RMS Helios 401) at a
place convenient to the patient (home or PHC) as per standard
guidelines for performing spirometry. To prevent air leakage,
a nose clip was used. About 7–8 spirometry tests were performed
for every subject. The values within 5% of the three tests were
acceptable. Forced expiratory volume in 1 s (FEV1), forced
vital capacity (FVC), and FEV1/FVC ratio were recorded.

A bronchodilation test was conducted by using salbutamol
nebulisation by positioning the patient in a sitting posture.
Nebulization was given for 10–15 min with a mixture of 1
ml of salbutamol (100 mg) and 3 ml of normal saline. Three
additional acceptable tests were recorded 15 min later. Before
the study, the investigator was trained for a 1-week duration
at the department of pulmonary medicine in performing lung
function tests using the portable spirometer. Those who were
found to have impaired lung function test during spirometric
measurements were referred to the department of pulmonary
medicine for further evaluation and management.

**Operational definitions**

Airflow obstruction was defined as FEV1/FVC <70% with
FVC >80% predicted. Restrictive defects were defined as
an FEV1/FVC ratio of >70% with an FVC <80% predicted.
Mixed defects were defined as FVC of <80% predicted and
an FEV1/FVC ratio of <70%. LFI is defined as the presence
of at least any one of these three abnormalities.[4]

**Statistical analysis**

Data were entered using EpiData version 4.4.2.1 and data
analysis was done using SPSS version 22. SPSS software name
originally stood for Statistical Package for the Social Sciences
(SPSS) but later changed to Statistical Product and Service
Solutions. Its manufacturer is SPSS Inc, IBM and has its
headquarter at Chicago, USA. LFI and pattern are expressed as
percentages with a 95% confidence interval (CI). Multivariable
regression analysis was done to identify the independent risk
factors and adjusted prevalence ratios (aPRs) with 95% CI were
calculated. P < 0.05 was considered statistically significant.

**Results**

Of the 185 participants invited to participate, 67 were excluded
(22 – not eligible, 28 – migrated, 15 – contraindication for
performing spirometry, and 17 – unacceptable spirometry
curves). The mean age of the participants was 48 (±15) and
the male-to-female ratio was found to be 3:1.

The overall proportion of patients with LFI (n = 74) was
62.7% (95% CI: 53.3–71.4). The restrictive pattern was more
predominant (60.1%) followed by a mixed (2.6%). Based on
FEV1 values, about half (48.6%) had severe LFI, followed
by mild and moderate with 25.7% each. More than half of the
participants with restrictive form had moderate LFI (51%). Participants, who were previously treated, smear-negative and those with dyspnea and tobacco use had significantly severe LFI [Tables 1 and 2].

In adjusted analysis, smear-negative patients (aPR = 1.2 [95% CI: 1.2–2.0]; P = 0.002) and indoor exposure to biomass (aPR = 1.4 [95% CI: 1.1–1.8]; P = 0.02) were found significant [Table 3].

**Discussion**

The study found that close to two-thirds of treated TB patients had LFI. Studies across the globe had reported varied prevalence ranging from 30.7% to 76.8%.[2,3,5-8] Even though a standard diagnostic definition was used by all other studies similar to this study, the observed difference could be due to difference in study setting as most of the studies were facility based. Furthermore, the present study included recurrent TB patients, which could have resulted in a higher prevalence.

The pattern of impairment in the present study was restrictive (60.1%), followed by the mixed type. This result is consistent with the other studies conducted across the globe.[2,3] The restrictive pattern is explained by the fact that there will be the destruction of lung parenchyma following TB infection. It could either be due to bronchial stenosis as a result of pressure from the peribronchial lymph nodes or may be due to increased metalloproteinase activity which contributes to pulmonary damage. However, these are not as common as a restrictive type of damage. Gothi et al.[9] demonstrated in one of their studies that the airflow obstruction could be a consequence of obliteratorive bronchiolitis.

The moderate form of LFI was observed in most of the patients with LFI in our study both among the patients with restrictive and overall functional impairment. It could be argued that the degree of lung damage varies proportionately with the duration of the disease manifestation, which could not be established in our study. A study conducted in the USA had shown that the severity of impairment ranges from moderate to severe.[10] LFI was found to be significantly higher among PTB participants who had dyspnea (71.2%) (51.9%; PR – 1.3 [95% CI: 1.0–1.8]) at the time of diagnosis. A few studies showed a similar significant association of dyspnea with LFI.[6,11] However, a study conducted by Ngahane et al.[3] had contradictory results. Dyspnea occurs mainly due to parenchymal lung disease which reduces gas exchange. Other major respiratory symptoms in lung dysfunction such as cough, hemoptysis, and chest pain were not significantly associated with LFI. The Fiogbe[6] study showed a significant association

| Table 1: Association of sociodemographic, morbidity, and behavioral characteristics with lung function impairment among post pulmonary tuberculosis participants in selected primary health centers, Puducherry, 2019 (n=118) |
|-----------------|-----------------|-----------------|-----------------|-----------------|
| Variables       | Total (n=118)   | LFI (n=74; 63%), n (%) | Crude PR (95% CI) | P       |
| Age group (years) |                 |                 |                 |         |
| <45             | 51              | 28 (54.9)       | 1               | 0.2     |
| 45-60           | 49              | 35 (71.4)       | 1.3 (0.9-1.7)   | 0.002   |
| >60             | 18              | 11 (61.1)       | 1.1 (0.7-1.7)   | 0.002   |
| Gender          |                 |                 |                 |         |
| Male            | 87              | 59 (67.8)       | 1.4 (0.9-2.0)   | 0.05    |
| Female          | 31              | 15 (48.4)       | 1               |         |
| Occupation      |                 |                 |                 |         |
| Unemployed      | 45              | 24 (53.3)       | 1               |         |
| Employed        | 73              | 50 (68.4)       | 0.7 (0.5-1.0)   | 0.06    |
| Diabetes        | 59              | 40 (67.7)       | 1.1 (0.8-1.5)   | 0.25    |
| Hypertension    | 30              | 22 (73.3)       | 0.9 (0.7-1.2)   | 0.8     |
| Type of treatment category* |         |                 |                 |         |
| New             | 90              | 53 (58.8)       | 1               | 0.03    |
| Previously      | 28              | 21 (75.0)       | 1.4 (1.1-1.8)   |         |
| Type of pulmonary TB† |         |                 |                 |         |
| Smear positive  | 106             | 63 (59.4)       | 1               | 0.02    |
| Smear negative  | 12              | 11 (91.6)       | 1.5 (1.2-1.3)   |         |
| Cavitations in X-ray (diagnosis) |         |                 |                 |         |
| Yes             | 25              | 16 (64.0)       | 1.02 (0.7-1.4)  | 0.89    |
| No              | 72              | 45 (62.5)       | 1               |         |
| Lung infiltrates at the time of diagnosis |         |                 |                 |         |
| Yes             | 55              | 35 (63.6)       | 1.02 (0.7-1.3)  | 0.84    |
| No              | 63              | 39 (70)         | 1               |         |
| The extent of lung infiltrates at the time of diagnosis (n=55) |         |                 |                 |         |
| Unilateral      | 28              | 15 (53.5)       | 1               | 0.1     |
| Bilateral       | 27              | 20 (74.0)       | 1.3 (0.9-2.0)   |         |

*Fisher’s exact, †Statistically significant with P<0.05. LFI: Lung function impairment, CI: Confidence interval, PR: Prevalence ratio, TB: Tuberculosis
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Indian Journal of Community Medicine ¦ Volume 47 ¦ Issue 1 ¦ January-March 2022

Ngahane et al.[3] also reported an insignificant association with these variables. There is a possibility of recall bias which could have resulted in inconsistent findings across the studies.

Similarly, LFI was significantly higher among the previously treated patients (PR – 1.4 [95% CI: 1.1–1.8]) as compared to newly diagnosed patients. This could be attributed to the fact that the increase in the number of episodes of TB increases lung damage and this finding was consistent with the studies conducted by Verma et al.[12] and Manji.[5]

The present study found that the prevalence of LFI was significantly higher among smear-negative PTB participants when compared with smear-positive cases. There is always a higher chance of delayed diagnosis and, in turn, delayed initiation of treatment in patients with smear-negative PTB. Moreover, the probability of recurrence is higher when compared to the smear-positive TB patients and hence this could explain the significant association. Regarding the highest sputum smear grading at the time of diagnosis, smear-negative PTB patients had more LFI (PR – 1.7 [95% CI: 1.2–2.3]). A study by Chung found that smear-positive cases were significantly associated with LFI.[13] The presence of a higher microbiological load increases lung damage in multiple ways, but the present study did not reveal such association with smear-positive TB and LFI. Again, this may be due to a smaller sample size of the present study compared to other studies.

Table 2: Association of respiratory symptoms and behavioral characteristics with lung function impairment among post pulmonary tuberculosis participants in selected primary health centers, Puducherry, 2019 (n=118)

| Variables                          | Total (n=118) | LFI (n=74; 63%), n (%) | Crude PR (95% CI) | P     |
|-----------------------------------|---------------|------------------------|-------------------|-------|
| Respiratory symptoms              |               |                        |                   |       |
| Chest pain                        |               |                        |                   |       |
| Yes                               | 33            | 19 (57.6)              | 1.12 (0.8-1.5)    | 0.47  |
| No                                | 85            | 55 (64.7)              | 1                 |       |
| Cough                             |               |                        |                   |       |
| Yes                               | 109           | 70 (64.2)              | 1.4 (0.6-3.0)     | 0.2   |
| No                                | 9             | 4 (44.4)               | 1                 |       |
| Hemoptysis                        |               |                        |                   |       |
| Yes                               | 53            | 35 (66.0)              | 1.1 (0.8-1.4)     | 0.49  |
| No                                | 65            | 39 (60)                | 1                 |       |
| Dyspnea†                          |               |                        |                   |       |
| Yes                               | 65            | 47 (71.2)              | 1.3 (1.01-1.85)   | 0.03  |
| No                                | 53            | 27 (51.9)              | 1                 |       |
| Ever-smoked tobacco†              |               |                        |                   |       |
| Yes                               | 72            | 51 (70.8)              | 1.4 (1.0-1.9)     | 0.02  |
| No                                | 46            | 23 (50)                | 1                 |       |
| Alcohol use‡                      |               |                        |                   |       |
| Yes                               | 53            | 31 (58.4)              | 0.8 (0.6-1.1)     | 0.39  |
| No                                | 65            | 43 (66.1)              | 1                 |       |
| Indoor exposure to biomass for cooking or heating | | | | |
| Yes                               | 15            | 12 (80.0)              | 1.3 (0.9-1.7)     | 0.13  |
| No                                | 103           | 62 (60)                | 1                 |       |
| Exposure to dust at the workplace |               |                        |                   |       |
| Yes                               | 39            | 22 (56.4)              | (0.7-1.2)         | 0.8   |
| No                                | 79            | 52 (65.8)              | 1                 |       |

†Statistically significant with P<0.05, ‡History of alcohol use in the past year. LFI: Lung function impairment, CI: Confidence interval, PR: Prevalence ratio

Table 3: Multivariable analysis showing association between lung function impairment and morbidity and behavioral characteristics among post pulmonary tuberculosis participants in selected primary health centers, Puducherry, 2019 (n=118)

| Variables                          | Unadjusted PR (95%CI) | Adjusted PR (95%CI) | P     |
|-----------------------------------|-----------------------|---------------------|-------|
| Type of treatment category        |                       |                     |       |
| Previously treated TB             | 1.4 (1.1-1.8)         | 1.12 (0.8-1.4)     | 0.3   |
| New diagnosed                     | 1                     | 1                   |       |
| Type of pulmonary TB              |                       |                     |       |
| Smear negative                    | 1.5 (1.2-1.9)         | 1.2 (1.2-2.0)       | 0.002 |
| Smear positive                    | 1                     | 1                   |       |
| Dyspnea                           |                       |                     |       |
| Yes                               | 1.3 (1.01-1.85)       | 1.2 (0.9-1.6)       | 0.1   |
| No                                | 1                     | 1                   |       |
| Indoor exposure to biomass        |                       |                     |       |
| Yes                               | 1.3 (0.9-1.7)         | 1.4 (1.1-1.8)       | 0.02  |
| No                                | 1                     | 1                   |       |
| Ever smoked tobacco               |                       |                     |       |
| Yes                               | 1.4 (1.0-1.9)         | 1.3 (0.9-1.8)       | 0.06  |
| No                                | 1                     | 1                   |       |

CI: Confidence interval, PR: Prevalence ratio, TB: Tuberculosis

of cough and expectoration at the time of diagnosis with LFI. Ngahane et al.[3] also reported an insignificant association with these variables. There is a possibility of recall bias which could have resulted in inconsistent findings across the studies.
Our study reported a significant difference in the prevalence of LFI among tobacco users when compared with nonsmokers. Smoking causes changes in metalloproteinase enzymes and lung scarring which leads to lung function damage. A few other studies also showed a significant association with smoking and LFI.[7,8]

To date, very few studies had documented LFI among post TB patients, that too in the community setting. The study was conducted among the patients enrolled from a district TB center, which in turn makes the study more generalizable. The spirometer was used to measure the LFI which added more objectiveness to the study. A pretested questionnaire and dedicated software for statistical analysis were used which reduced the chances of error. Total lung capacity, which is the best method to measure LFI, could not be carried out and the information about the patient’s lung function before the diagnosis was not available and hence the chance of bias in classification could not be ruled out.

According to the National TB Program, after treatment completion the patient should be followed up in every 6 months, up to 2 years to see for appearance of any clinical symptoms. This is done for early detection of recurrent TB by doing cough and sputum microscopy.[19] These follow-up visits shall include screening for lung function by spirometry to detect LFI. Further research is required to assess the utility of spirometry at the end of TB treatment when TB patients are still under TB care.

**Conclusion**

Two in three post TB persons were suffering from LFI. In India, almost half of the individuals who have a history of PTB are at a risk of developing LFI and these changes are increasing day by day. The risk factors such as smoking, air pollution, and indoor exposure to biomass further deteriorate lung function. Hence, there is a need for assessment of lung function in post PTB participants.

**Acknowledgments**

We thank Dr. Pritam and Dr. Sneha masters of Public Health Scholar, JIPMER, and eight primary health center staff, Puducherry, for their support in the conduct of the study.

**Financial support and sponsorship**

This study was financially supported by JIPMER intramural funding.

**Conflicts of interest**

There are no conflicts of interest.

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