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RESEARCH ARTICLE

A six-month follow-up study to evaluate changes of pulmonary function test in Category I pulmonary tuberculosis treatment completed patient

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ABSTRACT

Background: Tuberculosis (TB) is being a preventable and curable disease that it accounts the world-wide problem. India is one of the TB burden countries. Clinical manifestation of pulmonary TB leads pulmonary dysfunction with functional changes in the lung tissue. Treated patients are free from mycobacterium and considered cured, but the restoration of lungs function in these patients is also needed. **Aims and Objectives:** This study plans to evaluate and compare the pulmonary function test (PFT) parameters immediately, 3 months and 6 months after the completion of TB treatment and assess its severity. **Materials and Methods:** By convenient sampling, 118 voluntarily participated pulmonary TB-treated patients completing Category I regimen. PFT during three intervals after the completion of full course of antitubercular drugs was evaluated. Spirometry was done in sitting position according to the American Thoracic Society (ATS) recommendation and interpretation of the results was done. **Results:** Male-to-female proportion of the pulmonary TB patients was 56.8% versus 43.2%, respectively, within 22-65 years. Maximum patients, that is, 39% were within 31-40-year-age group. Immediate after completion of the treatment, 7.6% had symptoms of exertion dyspnea which were not on follow-up visits. The percent predictive values of the PFT were marginally above the impairment values. There was statistically significant difference mean forced vital capacity (FVC) ($P < 0.001$), forced expiratory volume at one second/FVC ratio percentage ($P < 0.01$), peak expiratory flow rate ($P < 0.05$), and maximal voluntary ventilation ($P < 0.01$) at the three intervals. Pulmonary function results were normal in 89.8% of patients immediately after the completion of TB treatment, in 91.5% at 3 months and 88.1% at 6 months. Impaired pulmonary function values were in 10.2% of patients at immediate, 8.5% at 3 months, and 11.9% patients at 6 months after completion of TB treatment. The 6-month PFT findings in 6.8% had obstructive changes, 3.4% had restrictive, and 1.7% with mixed PFT changes. **Conclusion:** There is the presence of pulmonary functional limitations in Category I TB-treated patients. Values for PFT were still lower in few patients even after completion of 6 months of treatment for Category I pulmonary TB.

KEY WORDS: Pulmonary Tuberculosis; Pulmonary Function Test; Category I Regimen; Spirometry; American Thoracic Society; Forced Expiratory Volume at One Second; Peak Expiratory Flow Rate; Forced Vital Capacity; Maximal Voluntary Ventilation

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INTRODUCTION

Tuberculosis (TB) is a chronic disease caused by *Mycobacterium* TB infection. The disease manifests all human body sites but most commonly as pulmonary TB. Although TB is a preventable and curable disease, it accounts the worldwide problem. India is one of the TB burden countries. From global incidence, India accounts for

one-fourth of TB cases annually. As per the WHO Global TB Report, 2015, out of the estimated global annual incidence of 9.6 million TB cases, 2.2 million were estimated to have occurred in India.[1,2]

TB management aims to ensure cure, minimize relapses, and cut the transmission chain of this communicable disease. The WHO has standardized the regimen for its management along with the individual countries' effort in controlling the disease transmission. India's efforts of continuous improvement in its National TB programs have led to the Revised National TB Control Program (RNTCP) to control the epidemic of TB.[2-4]

Pulmonary TB involves the airways, leading to mucosal edema, hypertrophy and hyperplasia of mucous glands, increased mucus secretion, and smooth muscle hypertrophy.[5] TB is in a catabolic state and experience weight loss due to reduced food intake due to loss of appetite, nausea and abdominal pain, nutrient losses from vomiting and diarrhea, and metabolic alterations caused by the disease.[6]

Pulmonary TB has its function sequelae also on asymptomatic-treated patients with its impairments.[5,7,8] The clinical manifestation leads pulmonary dysfunction with functional changes in the lung tissue by hyperinflation and restriction of the lungs and rise or decline of their elasticity.[9] Other than TB and infective cause, one of the environmental causes that lung functions are impaired is the air pollution as observed in traffic policeman affecting their health status.[10] Duration of smoking leads to chronic obstructive pulmonary diseases reciprocated in pulmonary function test (PFT) examination.[11] Treatment guidelines aim in chemotherapeutic management for preventing spread and cure to TB in the patients.

Treated patients of pulmonary TB have been recognized to be developing chronic obstructive pulmonary diseases. Treated pulmonary TB patients are free from *mycobacterium* infection but have variable presentation of lung function findings affecting the quality of patient's life.[9,12-16]

India strategic plans to work on chemoprophylaxis and also preventive measures in halting spread of TB. There is the need to know the extent of the impairment of lung function in pulmonary TB-treated patients in India, so that proper planning to ensure the functional restoration in lungs in treated patients can be done. Hence, this study aims to evaluate the pulmonary function status at different intervals in patients after been treated for pulmonary TB.

MATERIALS AND METHODS

A prospective observational study was conducted on 118 newly diagnosed pulmonary TB-treated patients referred to the Department of Respiratory Physiology of Shri Bhausaheb Hire Government Medical College and Hospital, Dhule, Maharashtra, during June 2015 to December 2016.

This study included adults diagnosed and referred by collaborating department of treated pulmonary TB patients having completed Category I full course of antitubercular treatment [$2(EHRZ)_3/4(RH)_3$] supervised as per the RNTCP guidelines of India.[3,4] Adult above 18 years, negative for sputum smear of acid-fast bacilli, and without radiological or systemic complication were the inclusion criteria of the patients. Extrapulmonary TB, pregnant, and moribund patients were excluded from the study. In the study, 146 patients agreed voluntarily to participate in the research and signed the written informed consent. A total of 118 patients were evaluated as they were having all three PFT findings of the follow-up period. 28 patients were excluded as they lost for follow-up PFT. This study was approved by the Institutional Ethical Committee.

Detailed information was collected through a standardized form with demographic data, clinical data, medications, and smoking habits. A spirometry assessment of pulmonary function was done for forced vital capacity (FVC), forced expiratory volume at one second (FEV1), peak expiratory flow (PEF), and maximum minute volume. The device used was the Medspiror, RMS Pvt., Ltd., portable spirometer. The test on patient was done in seating position with elbows bent and his mouth firmly attached to the mouthpiece and nose clip was also used to prevent air leakage. The patient was asked to perform maneuvers and the best of three results were considered as per the American Thoracic Society (ATS) guidelines[17] for PFT. Each patients were tested immediately after completion of antitubercular regime, after 3 months and 6 months. Out of 146 patients, 28 were excluded from analysis as they had lost on follow-up in 3 or by 6 months after completion of treatment. The reference equations were from an Indian predicted equation used adult normative population as per the manufacturer. Predicted values of corresponding pulmonary function parameters were compared to the calculated reference equation derived for the comparable standard participants in Indian population.

Data were analyzed using the statistical program software Statistical Package for the Social Sciences (SPSS) version 16.0 for Windows. Pearson's chi-square test and repetative measure ANOVA were used. The significance level of 5% ($P < 0.05$) was considered.

RESULTS

In this study, a total of 118 TB-treated patients were evaluated for PFT. Of the participants, 56.8% (67) were male and 43.2% (51) were female. Age of patients was within the range of 22-65 years. Mean age of the patients was 36.4 years with 9.6 years standard deviation (SD). Mean age of male patients

was 40.2 ± 7.6 years SD (range 21-65 years) and of female patients was 34.2 ± 8.9 years (range 24-56 years) which was statistically significant ($P < 0.001$).

Maximum patients, that is, 39% (46) were within 31-40 years age group (52.2% male; 47.8% female). TB-treated young adult male within 21-30 years age group in the study were 76% (19), whereas only 24% (6) were female out of 21.2% (25) total patients. 32.2% (38) were within 41-50 years age group, whereas only 7.6% (9) patients were more than 50 years old. There was statistically no significant ($P > 0.05$) difference of the gender in TB-treated patients.

Immediately after completion of the treatment, 7.6% (9) had symptoms of exertion dyspnea while none had any residual complaints. 34.7% (41) TB-treated patients perceived their health to be not as that of before getting infected by TB disease. After 3 months, all persons had no symptoms and all felt completely healthy now and were able to do regular physical activities as pre-disease state.

Mean body mass index (BMI) of patients immediately after TB treatment was 21.1 kg/m^2, after 3 months, it was 22.8 kg/m^2 and it was 21.6 kg/m^2 after 6 months. There was statistically no significant ($P > 0.05$) difference of BMI of patients at the follow-up of 6-month period. All patients were involved in active work before developing TB. Smoking history was noted in 31.3% (21) of male patients. In 35.6% (42) of patients, TB was diagnosed after more than 1-month duration. 59.3% (70) of patients in the study were urban dwellers while 40.7% (58) were from rural area.

Maximum patients were married, educated up to primary or secondary level, and were from low socioeconomic status. Occupational history revealed that maximum patients were domestic worker/homemakers or agricultural workers and loom industry workers. There was exposure to indoor smoke in 39.2% (20) of females (Table 1) Mean spirometry immediately after completion of the anti-TB treatment, at 3 months and at 6 months in all patients was low than the predictive values. The percent predictive values of the PFT were marginally above the impairment values (Tables 2-4). There was statistically significant difference mean FVC ($P < 0.001$), FEV1/FVC ratio percentage ($P < 0.01$), peak expiratory flow rate (PEFR) ($P < 0.05$), and maximal voluntary ventilation (MVV) ($P < 0.01$) while no significant difference of FEV1 in patients during follow-up evaluation (Table 2) In male patients, there was only significant difference of mean FVC ($P < 0.001$) while no significant ($P > 0.05$) difference of FEV1, FEV1/FVC, PEFR, and MVV at different interval (Table 3).

All PFT parameters of female patients had statistically insignificant ($P > 0.05$) difference for FVC, FEV1, FEV1/FVC, PEFR, and MVV at different interval (Table 4). PFT results were normal in 89.8% of patients immediately after completion of TB treatment, in 91.5% at 3 months and 88.1% at 6 months. Impaired pulmonary function values were interpreted during immediate PFT evaluation in 10.2% (12) patients, in 8.5% (10) at 3 months, and 11.9% (14) patients at 6 months after completion of the TB treatment.

Table 1: Sociodemographic history of TB-treated patients

Sociodemographic factors	Findings	*n* (%)
Marital status	Single	4 (3.4)
	Married	92 (78.0)
	Widowed/separated	22 (18.6)
Education	Primary	22 (18.6)
	Secondary	59 (50.0)
	Higher secondary and above	37 (31.4)
Occupation	Student	5 (4.2)
	Domestic/homemakers	41 (34.7)
	Agriculture	34 (28.8)
	Industry	27 (22.9)
	Laborer	11 (9.3)
Socioeconomic status	Lower class	98 (83.1)
	Middle class	20 (16.9)

TB: Tuberculosis

In immediate PFT examination, 5.9% (7) had obstructive changes, 3.4% (4) had restrictive, and 0.8% (1) had mixed changes in the PFT variables. The 3-month evaluation had 5.9% (7) having obstructive changes, 2.5% (3) patients with restrictive, and only one with mixed changes. The 6-month PFT findings in 6.8% (8) had obstructive changes, 3.4% (4) had restrictive, and 1.7% (2) with mixed PFT changes. There was higher proportion of PFT impairment noted in males than female TB-treated patients immediately after TB treatment, at 3- and 6-month duration. There was statistically no significant ($P > 0.05$) difference between males and females at different time intervals (Table 5).

DISCUSSION

In 118 TB patients after completion of regular treatment (TB-treated patients), PFT was evaluated. In the study, mean age of the TB-treated patients was 36.4 ± 9.6 years, having older males than female. However, there was no statistically significant ($P > 0.05$) difference of male-to-female proportion (Table 6). We found exposure to indoor smoke was seen in 39.2% of female patients of TB. Pulmonary TB-treated patients had altered presentation in lung function tests. In our study, lower but statistically significant difference of FVC, FEV1/FVC ratio, PEFR, and MVV was noted in between immediate, 3 months, and 6 months after TB-treatment duration (Table 2). There was mild impairment of the PFT parameters in this study. After immediate PFT examination, 5.9% had obstructive changes, 3.4% had restrictive, and 0.8% had mixed changes

Table 2: Actual and percent predicted (% predicted) values of PFT at different follow-up duration in TB-treated persons (*n*=118)

Post-TB duration	FVC (L)	FEV1 (L)	FEV1/FVC (%)	PEFR (L/s)	MVV (L/min)
Immediate					
Actual	2.32 (0.52)	1.96 (0.58)	84.5 (11.4)	4.54 (1.29)	94.85 (8.7)
% predicted	84.6	83.4	87.6	88.5	76.8
3 months					
Actual	2.51 (0.64)	1.99 (0.62)	80.3 (12.7)	5.03 (1.64)	93.4 (13.4)
% predicted	83.4	81.5	82.8	85.1	75.2
6 months					
Actual	2.79 (0.55)	2.02 (0.59)	85.4 (15.7)	4.89 (1.45)	97.9 (11.8)
% predicted	87.3	84.6	86.9	87.7	77.4
ANOVA					
P value	<0.001	0.742	<0.01	0.03	<0.01

PFT: Pulmonary function test, TB: Tuberculosis, FVC: Forced vital capacity, FEV1: Forced expiratory volume at one second, PEFR: Peak expiratory flow rate, MVV: Maximal voluntary ventilation

Table 3: Actual PFT at different follow-up duration in male TB-treated persons (*n*=67)

Post-TB duration	FVC (L)	FEV1 (L)	FEV1/FVC (%)	PEFR (L/s)	MVV (L/min)
Immediate	2.46 (0.78)	2.13 (0.64)	87.4 (19.8)	5.29 (1.66)	99.43 (12.5)
3 months	2.98 (0.51)	2.27 (0.84)	82.3 (14.6)	5.21 (1.38)	97.2 (10.9)
6 months	2.85 (0.84)	2.29 (0.76)	85.6 (17.3)	5.34 (1.71)	102.4 (16.3)
P value	<0.001	0.407	0.228	0.892	0.08

PFT: Pulmonary function test, TB: Tuberculosis, FVC: Forced vital capacity, FEV1: Forced expiratory volume at one second, PEFR: Peak expiratory flow rate, MVV: Maximal voluntary ventilation

Table 4: Actual values of PFT at different follow-up duration in female TB-treated persons (*n*=51)

Post-TB duration	FVC (L)	FEV1 (L)	FEV1/FVC (%)	PEFR (L/s)	MVV (L/min)
Immediate	2.11 (0.65)	1.91 (0.73)	83.9 (18.1)	4.15 (1.22)	87.21 (10.2)
3 month	2.19 (0.51)	2.05 (0.94)	80.1 (12.4)	4.36 (1.95)	89.47 (11.4)
6 month	2.34 (0.97)	1.98 (0.52)	80.3 (18.4)	4.18 (1.63)	92.42 (13.9)
ANOVA-*P* value	0.279	0.642	0.428	0.780	0.090

PFT: Pulmonary function test, TB: Tuberculosis, FVC: Forced vital capacity, FEV1: Forced expiratory volume at one second, PEFR: Peak expiratory flow rate, MVV: Maximal voluntary ventilation

Table 5: PFT status according to gender in post-TB patients at different study duration

Gender	PFT status	Immediate	3 months	6 months
Male (*n*=67)	Impaired	8 (11.9)	6 (9)	11 (16.4)
	Obstructive	4 (6)	4 (6)	6 (9)
	Restrictive	2 (3)	2 (3)	2 (3)
	Mixed	1 (1.5)	1 (1.5)	1 (1.5)
Female (*n*=51)	Impaired	4 (7.8)	4 (7.8)	3 (5.9)
	Obstructive	3 (5.9)	3 (5.9)	2 (3.9)
	Restrictive	2 (3.9)	1 (2)	2 (3.9)
	Mixed	00	00	1 (2)

PFT: Pulmonary function test, TB: Tuberculosis

Table 6: Distribution of age group according to gender of TB-treated patients

Age group (years)	Gender		Total
	Female (%)	Male (%)	
21-30	6 (24.0)	19 (76.0)	25 (100.0)
31-40	22 (47.8)	24 (52.2)	46 (100.0)
41-50	20 (52.6)	18 (47.4)	38 (100.0)
>50	3 (33.3)	6 (66.7)	9 (100.0)
Total	51 (43.2)	67 (56.8)	118 (100.0)

TB: Tuberculosis

in the PFT variables. In our study, symptoms of exertional dyspnea were noted immediate after completion of the antituberculor therapy in 7.6% of patients while none had any other residual complaints. However, 34.7% of patients felt their health not to be as pre-deceased state. Mean BMI was normal in patients of our study and there was statistically no significant ($P > 0.05$) difference of BMI of patients at the follow-up of 6-month-period.

As every disease management strategy plans to eliminate causative factors so relation of TB to functional impairment of tissue was evaluated after completion of specified treatment.

Similar to our finding, more male than female patients had pulmonary TB in a study.[6,13] In females, biomass gas inhalation and smoke from cooking fires or other sources are found to contribute risk in TB.[13] The pulmonary impairment was present in 45.6% of patients including airway obstruction in 32.3% of patients, restrictive pattern in 9.2% of patients, and 4.1% of patients had combined pattern.[14] Abnormal PFT findings were 5.4 times more likely in survivors of pulmonary TB patients.[13] Verma et al., in his study, found 16.3% of patients had obstructive airway disease and mixed obstructive with restrictive disorder was found in 22.8% patients.[13] Our study had much lower impairment findings as compared to other studies due to selection criteria of uncomplicated patients. Furthermore, variable pulmonary function impairment was noted by authors in their study on patients treated with short-course TB regimen.[13] Restrictive and combined obstructive and restrictive lung function patterns were the predominant abnormalities while some found restrictive abnormality to be more common.[9] In only one anti-TB treatment group, 20% of patients had no changes in lung function and 53.3% had mild disorder.[18] Similar to our findings, a study had also noted that 9.7% of participants as having mild impairment, but it also had 16.5% of participants with moderate impairment, and 9.7% of having severe lung impairment not matching to our findings.[12,13] Furthermore, 56% of the cases were found to have moderate to advanced residual damage to the lungs by Mohamad Saleh.[18]

All cases of treated pulmonary TB are prone to develop pulmonary function impairment. Even asymptomatic patients may have defective lung function; residual lung function impairment after treatment.[7] Symptoms of pulmonary impairment generally do not occur in persons with chronic lung disease until FEV1 has fallen to 50% of normal values.[9] Symptom screens alone are unlikely to detect pulmonary impairment after TB. In this study, previous history of smoking was present in 31.3% of male patients. Lung function and FEV1/FVC ratio were significantly lower in smokers than in non-smokers but statistically insignificant after adjusting for demographics and other risk factors.[13] Same as to the finding in our study, gender, smoking, and occupation had no significant effect on the prevalence of low pulmonary function.[5,12,13] Similarly, in our study, the BMI were lower in group with TB, indicating the possibility of a state of malnutrition, and muscle wasting in these patients.[5,6]

Delays in the identification and treatment of TB lead to the increase in lung damage and more frequent comorbidities and impairment of the quality of life.[5] As TB leads inflammatory changes, it may cause temporary or permanent parenchyma changes that reflect on lung function tests as stated by researchers.[9] The improvement observed in a study occurred only in the first few years (5 years or less) following treatment.[18] Similarly, in our study, there was improvement in PFT by 6 months in some patients having pulmonary impairment.

In our study, PFT was affected immediately in pulmonary TB-treated patients and had shown changes up to 6 months. Follow-up evaluation has given better understanding of the alteration of the PFT in the pulmonary TB-treated patients. This study has the limitation of identification of risk association for the PFT impairments. It had short-duration follow-up and needs correlation of the PFT findings with the past history of the patients and thus generate a prediction plan of pulmonary functional restoration.

CONCLUSION

In new TB treatment completed patients, there is microbiological cure but the study indicates the presence of pulmonary functional limitations in patients. Thus, disease affects the functional capability and has its own pathophysiological manifestation. Adequate and timely treatment of Category 1 TB has reduced the burden of pathophysiological of airflow limitation. Values for PFT were significantly lower in patients who had been treated for pulmonary TB. This phenomenon indicates the possibility that healing and recovery of the lungs are still going on even after stopping all anti-TB therapy as per the recommendation of the regimen. The PFT comparison shows improvement of lung function paramaters that may be the structural improvement and better lung function.

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