ORIGINAL RESEARCH

Pulmonary function abnormalities in pulmonary tuberculosis patients who have successfully completed treatment for in the past

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ABSTRACT
Pulmonary TB leads to development of mucosal edema, hypertrophy and hyperplasia of mucosal glands, increased mucous hyper secretion and smooth muscle hypertrophy. These changes affects the caliber of airways, increases their thickness and decreases airflow, through the mechanism of cicatricial fibrosis. Patients with a history of pulmonary tuberculosis who have successfully completed treatment with complete microbiological cure and meeting the inclusion and exclusion criteria and who comes to Pulmonology outpatient department were enrolled for this study after obtaining the informed and written consent. Study was approved by the institutional ethical committee. Among the patients having pulmonary dysfunction on PFT, more than half of the patients had a severe or very severe dysfunction (61%).77.3% of the patients in the study group presented with dyspnoea as a symptom. Grade I dyspnea (32%) was the most common among study group. 22.7% patients did not have dyspnoea.
Key words: Pulmonary function abnormalities, pulmonary tuberculosis, dyspnea

Introduction

Tuberculosis (TB) is one of the oldest diseases know to affect human beings. *Mycobacterium tuberculosis* is causative organism of Tuberculosis. TB is one of the top 10 causes of death and the leading cause from a single infectious agent.[1]According to WHO Global TB report 2018.Globally, the best estimate is that 10.0 million people (range, 9.0–11.1 million) developed TB disease in 2017: 5.8 million men, 3.2 million women and 1.0 million children. There were cases in all countries and age groups, but overall 90% were adults (aged ≥15 years). [1]

Over the last two decades treatment of TB has significantly improved. However such successful treatment of TB based on either documentation of bacteriological clearance of *Mycobacterium tuberculosis* bacilli from the involved site or completion of the prescribed drug dose not assess structural and functional effects on the involved organ which is the hallmark of the pathology of TB [2].

Pulmonary TB leads to development of mucosal edema, hypertrophy and hyperplasia of mucosal glands, increased mucous hyper secretion and smooth muscle hypertrophy. These changes affects the caliber of airways, increases their thickness and decreases airflow, through the mechanism of cicatricial fibrosis.[3]

While any part of the body may be affected by TB, pulmonary TB is the most common site of disease primarily because the Mycobacterium tuberculosis bacilli is transmitted through the respiratory route. Thus TB is a major contributor to the overall burden

of lung disease in the world. It may be that in the majority of patients with pulmonary TB, the resulting structural and functional damage is small and does not pose any significant long term lung health risk, however, for some patients an episode of pulmonary TB may herald the beginning of chronic respiratory disease and pose a significant risk of reduced longevity despite the "successful" treatment of their disease [4]

Patients with treated TB may remain lifelong sufferers of disabling sequelae ofthe disease which subsequently impair their quality of life [5]. Studies with longer follow-up have revealed that a large percentage of patients with treated pulmonary tuberculosis show signs of permanent airflow obstruction or restrictive impairment. Post tuberculosis pulmonary impairment, therefore has emerged as a distinct clinical entity [6].

Functional impairment and morbidity in such tuberculosis survivors, which frequently represent the most economically productive section of the society, have substantial effect on world economy and growth. The magnitude of the effect appears to be in the range of a 0.2 to 0.4 percent increase in the rise of per capita income for a ten percent lower level of notified incidence of tuberculosis. This would amount to between US$ 1.8 and US$ 3.6 billion per annum in increased output, if this figure is representative of the whole world's population.[12] Thus efforts aimed at reducing morbidity in tuberculosis survivors may have a very significant impact on growth and productivity, globally.

India accounts for 26% of global TB burden. It is important to identify patients with pulmonary function deterioration after the completion of pulmonary TB treatment. However, little is known about the trends in the changes in pulmonary function associated with pulmonary function deterioration. Therefore, a study was undertaken to assess trends of pulmonary function deterioration in patients who had completed their course of anti-tubercular therapy.

Methodology

Study Population

Patients with a history of pulmonary tuberculosis who have successfully completed treatment with complete microbiological cure and meeting the inclusion and exclusion criteria and who comes to Pulmonology outpatient department were enrolled for this study after obtaining the informed and written consent. Study was approved by the institutional ethical committee.

Sample size: 75

Study design: Hospital based cross sectional study

Sampling technique: Convenience sampling

Inclusion criteria

1. Adult male/female (age >18 years)
2. History of pulmonary tuberculosis with complete treatment
3. Sputum AFB negative.

Exclusion criteria

1. Smoking
2. History of prior lung disease like Bronchial Asthma, COPD and Bronchiectasis
3. Occupation posing risk to lung function
4. Interstitial lung disease
5. HIV positive status
6. Pregnancy
7. Spirometry contraindicated such as recent eye or upper abdominal surgery
8. Ischaemic heart disease
9. Lung parenchymal involvement as evidenced by clinical examination, X ray or sputum AFB positivity
10. Kyphoscoliosis or congenital chest abnormality.

Investigations

Routine investigations were done for all cases and included

a) Hemoglobin % with ESR
b) Total WBC count, Differential WBC count.
c) Random blood sugar
d) Blood urea and Serum creatinine
e) ECG and Chest X-ray
f) Sputum for AFB
g) Pulmonary function tests
h) HIV ICTC

A detailed history was taken to rule out smoking, occupational predisposition to lung disease or underlying prior lung disorder. Asthma was ruled out on the basis of theHistory of variable respiratory symptomsas Wheeze, shortness of breath, chest tightness and cough.

Generally more than one type of respiratory symptom

- Symptoms occur variably over time and vary in intensity
- Symptoms are often worse at night or on waking
- Symptoms are often triggered by exercise, laughter, allergens, cold air
- Symptoms often appear or worsen with viral infections

Patients who fulfilled the above criteria were diagnosed as Asthma and were thus excluded from the study. Ischemic heart disease were excluded on the basis of history, clinical examination and electrocardiogram.

Results

Table 1: Age distribution in study group

Age groups(Years)	Frequency	Percent
≤30	24	32.0
31-45	20	26.7
46-60	15	20.0
> 60	16	21.3
Total	75	100.0

The above table and graph shows the age distribution of the study population.
The mean age of the population was 45.32 years with a minimum age of 18 years and maximum age of 85 years. Maximum number of patients were in the < 30 and in the 31-45 year age group.

Table 2: Gender distribution among study group

Gender	Frequency	Percent
Male	53	70.7
Female	22	29.3
Total	75	100.0

In this study, out of 75 patients, 53 were male (70.7%) and 22 were female (22.3%)

Table 3: distribution of study group as per interpretation

Interpretation	Frequency	Percent
Obstruction	10	13.3
Restriction	20	26.7
Mixed	29	38.7
Normal	16	21.3
Total	75	100.0

Above table shows the distribution of the pattern of Pulmonary Function Test (PFT) abnormalities in the study group.
Out of 75 patients, 59 patients (78.7%) had an abnormal PFT, while 16 patients (21.3%) had normal study. Among patients those having abnormal PFT, the most common patterns of abnormality observed were Mixed pattern and Restrictive pattern comprising 38.7% and 26.7%patients respectively, followed by Obstructive pattern, seen in 13.3% patients.

Table 4: distribution of bronchodilator reversibility (BDR)

BDR		Interpretation		Total
		Obstruction	Mixed	
Poor	Frequency %	8 (80%)	27 (93%)	35 (89.7%)
Good	Frequency %	2 (20%)	2 (7%)	4 (10.3%)
Total	Frequency %	10 (100%)	29 (100%)	39 (100%)

Out of 75 patients, 39 patients had obstructive component on PFT. Out of these, 10 patients had a pure obstructive abnormality while 29 showed mixed pattern.
Only 4 patients out of 39 (4.3%) showed good BDR.

Table 5: distribution of severity of pulmonary dysfunction

Degree of severity	Frequency	Valid Percent
Mild	4	6.8
Moderate	11	18.6
Moderately severe	8	13.6
Severe	16	27.1

Very severe	20	33.9
Total	59	100.0

Among the patients having pulmonary dysfunction on PFT, more than half of the patients had a severe or very severe dysfunction (61%).

Table 6: Distribution of dyspnoea among the study group

Dyspnoea	Frequency	Percent
Grade I	24	32.0
Grade II	21	28.0
Grade III	13	17.3
Absent	17	22.7
Total	75	100.0

77.3% of the patients in the study group presented with dyspnoea as a symptom. Grade I dyspnea (32%) was the most common among study group. 22.7% patients did not have dyspnoea.

Discussion

The results of study showed that a very high percentage of patients, 59 patients (78.7%) out of 75 were found to have respiratory impairment on PFT. Previous published studies also showed comparable results as Pasipanodya*et al.* [7] conducted a study in the United States which showed that 59% of patients treated for TB subsequently had abnormal pulmonary function,Manji*et al*.[8] conducted a study in Tanzania and observed the prevalence of abnormal lung functions in 74% of cases. This study confirms that pulmonary impairment after TB (PIAT) is an emerging and distinct clinical entity.

In the present study, spirometry assessment of post-TB cases, mixed pattern was observed in 38.7% cases. Studies by Ramos *et al*. [9] and Singla*et al*.[10] observed predominantly mixed pattern of spirometric abnormality in the study population and such a high prevalence of mixed pattern can be explained by the extensive fibrosis coexisting with airflow obstruction.

Other PFT impairment findings was restrictive pattern comprising 26.7%patients, followed by obstructive pattern, seen in 13.3% patients. While 16 patients (21.3%) had normal study.

The severity of pulmonary dysfunction seen on PFT showed marked variability ranging from mild involvement (7%) to very severe involvement (34.1%). Most of the patients in the study group had a moderate to severe pulmonary dysfunction. As evident in this study, pulmonary impairment after TB (PIAT) and its severity are directly related to the alteration of structure and function of the respiratory system caused by tuberculosis. Healing of tuberculosis with fibrosis and cicatrization causes alterations in the pulmonary parenchyma which in turn, leads to residual radiological changes and pulmonary dysfunction.

Pulmonary impairment after TB (PIAT) could potentially be prevented at three levels. Primary prevention could be achieved by preventing TB infection. Secondary prevention would focus on preventing persons with LTBI from developing tuberculosis. Tertiary prevention would rely on developing targeted treatments for persons with active tuberculosis to mitigate lung damage. It has been suggested that immune modulatory therapy for TB pericarditis, multidrug resistant tuberculosis and TB meningitis may reduce the severity of post disease sequelae.In the absence of an effective vaccine, immune modulatory or optimized therapy against TB, public health measures that prevent infection and progression to TB disease are the only currently available measures to reduce long-term disability from TB.

Structural changes in the lung resulting from aberrant tissue repair leads to fibrosis and calcification. Tracheal deviation as a result of fibrotic strands, atelectasis and collapse due to bronchial compression by external lymph nodes or endobronchial tuberculosis, pleural fibrosis are some of the factors responsible for a reduction in lung volumes thereby producing volume loss which is evident on PFT as a restrictive abnormality.

In this study, restrictive abnormality was diagnosed on PFT on the basis of reduction in the forced vital capacity. However, reduced FVC by itself does not prove a restrictive ventilatory defect. It is often caused by sub maximal inspiratory or expiratory efforts and/or patchy peripheral airflow obstruction. Thus for accurate assessment of restrictive defect a measurement of Total Lung Capacity (TLC) should be done using the gas dilution techniques. A restrictive ventilatory defect is characterized by a reduction in TLC below the 5th percentile of the predicted value.The above tests could not be performed in the present study due to technical difficulties.

Understanding of the mechanism that drive structural changes and associated of airway obstruction following pulmonary tuberculosis is poor. Possible mechanisms include bronchial stenosis and lung scarring secondary to parenchymal involvement. Endobronchial involvement may produce localized bronchial obstruction and fibrosis, while tuberculous lymphadenopathy can cause extrinsic bronchial compression. Parenchymal lung destruction can affect pulmonary compliance resulting in an increased tendency for peripheral airways collapse and

subsequent air trapping.In addition,destruction of elastic and muscular components of the bronchial walls resulting in bronchiectasis, which is associated with airflow obstruction and TB increases the activity of the matrix metalloproteinases, thus contributing to pulmonary damage.

Conclusion

- Among the patients having pulmonary impairment, mixed pattern having both restrictive and obstructive component was the most common abnormality seen in 38.7% of the patients. Restrictive defect was the second most common found in 26.7% cases while obstruction was seen in 21.3% cases.
- 39 patients out of 75 had an obstructive component on PFT out of which 29 had an associated restrictive defect while 10 had pure obstruction.Among these, 4 patients showed a good bronchodilator reversibility and were thus considered to have post tubercular bronchial asthma.

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