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A Review on Clinicoradiological and Spirometry Patterns in Post-Tb Sequlae

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ABSTRACT:
Mycobacterium tuberculosis is the infectious illness that causes tuberculosis (TB). Incidence of tuberculosis is extremely high in India. Even when TB therapy is over, lung damage is still caused by TB. TB survivors have abnormal radiological imaging patterns and spirometry patterns. The majority of national tuberculosis initiatives do not take post-TB impacts into account. Greater contributions to the global health burden are caused by pulmonary tuberculosis sequelae- associated morbidity. Spirometry and radiological imaging, such as chest X-rays and CT scans, were employed to evaluate post-TB patients in a majority of the article. This review endorses the results that abnormal spirometric values persist even after successful completion of tuberculosis treatment, that the type of defect varies depending on the extent of the disease, with obstructive pattern being the most common, and that a variety of radiological changes have been identified as complications and sequelae to tuberculosis healings that have an impact on the quality of life of the patient.
Key words:post-TB impacts, spirometry, radiological imaging, obstructive pattern.

I. INTRODUCTION:

Mycobacterium Tuberculosis, an aerobic, non-motile, non-spore forming rod, is the culprit behind tuberculosis (TB). They have a thickness of 0.3 µm and a length of 2-4 µm. The lungs remain the primary location of the illness TB, despite the fact that TB may impact various areas of the body. When it attacks the lungs, tuberculosis is referred to as pulmonary tuberculosis (PTB). Extrapulmonary TB refers to TB which impacts tissues or organs besides the lung, such as the bronchi, lymph glands, abdomen, urogenital system, epidermis, articulation, and bones, or dura mater. It can also be categorized as being either active TB or latent TB [1].

Differentiation between active TB and latent TB (Table-1)

ACTIVE TB INFECTION	LATENT TB INFECTION
The bacterial infection has proliferated, outlasted the body's defenses, and migrated to other bodily regions.	The immune system cannot kill the bacterial infection but has managed to prevent its spread throughout other parts of the body.
Symptoms will appear within a month or a few weeks.	Mycobacterium tuberculosis may never cause TB disease, and it may lie dormant for a lifetime.
Typically, symptoms consist of: A cough that lasts for at least three weeks. Coughing up blood. Sweating at night. Feels ill.	Present no symptoms.

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The patient is contagious and can expose others to TB.	The patient is not infectious.
Possessing a positive sputum test or having an abnormal chest X-ray (the mucous secreted by cells in the lower airways of the respiratory tract) or culture.	A sputum smear will come back negative and a chest X-ray will seem normal.
Usually indicates the presence of TB through a beneficial cutaneous or blood screening.	Frequently uses a beneficial cutaneous or blood screening to detect an infection with TB.
Will require treatment for active TB.	To keep TB from becoming active, the latent infection must be treated.

Tuberculosis is a persistent illness with extraordinarily substantial levels of death and disability. Research shows that on an annual basis there are nearly eight million illness and nearly one million fatalities [2].

The World Health Organization (WHO) a worldwide approach to eradicate tuberculosis, which led to a 1.6% annual drop in the diseases incidence, during the period 2000-2018 as well as the estimated death rates reduced between the years 2005 and 2019. In recent years, global estimates for both 2020 and 2021 showed increased death rates than the preceding years. This increased number of deaths is due to an upsurge of undiagnosed and untreated cases (reduced access to treatment) [3][4].

Only India's national TB prevalence study was finished globally in 2021[3]. The percentage of TB incidence in India was higher for the year 2021 when compared to 2020. According to estimates of one-fifth of the worldwide load, India is among the countries with the highest impact of TB [5].

The majority of the highest impact countries report cure rates exceeding 80% for the illness most common type, pulmonary TB. Pulmonary TB is treatable with a multi-drug regimen. However, mounting evidence suggests that lung injury may contribute to the emergence of long-lasting pulmonary sequelae along with impairment after TB treatment. The pulmonary effects of tuberculosis may be resistant to microbiological treatment [6].

For a substantial majority of patients, these morphological sequelae serve as a lifelong reason for pulmonary pain along with deteriorated pulmonary function. Due to the severity of their breathing difficulties, hemorrhage, either persistent subsequent infections or lung stenosis, these patients typically require repeated antitubercular treatment. Therefore, pulmonary TB sequelae place a significant strain on the public health system [7].

History of national programs for tuberculosis in India:

▪Before 1955: no survey for TB
▪1955-1958: National sample survey by Govt of India (incidence, prevalence)
▪1959-1962: plan for National TB Programme (NTP)
▪1993: WHO labeled TB as a global emergency
▪1993-1997: RNTCP (pilot study)
▪1997: RNTCP was launched based on WHO DOTS strategy
▪1997-2005: RNTCP phase 1
▪March 2006: RNTCP covered entire India
▪October 2006 – March 2012: RNTCP phase 2
▪April 2012 – March 2017: (National Strategic Plan phase 3)

▪**Mono resistant TB**: Is characterized by bacilli that are rifampicin-insensitive yet opposition to a single initial line ATD.
▪**Poly drug resistant TB**: As opposed to rifampicin and isoniazid resistance, the patients' bacilli are a barrier to using more than one initial line Anti-tubercular drug (ATD).
▪**Extensive drug resistant TB**: A case of Multi drug resistant tuberculosis (MDRTB) with bacilli that are also resistance to one second -line

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injectable ATD and a fluroquinolone is considered to have extensive drug resistance.

POST TB SEQUELAE:

Even after finishing therapy and being completely bacteriologically cured, the morphological and physiological changes in the chest brought on by pulmonary TB issues [7]. In PTB, the airways are affected causing mucosal oedema, cellular adaptations in the mucosal glands like hypertrophy/hyperplasia, excess production of mucus and hypertrophy of smooth muscles. The caliber of airway is disturbed with increased resistance and decreased airflow. Total lung capacity is decreased with fibrotic scarring. The severity of damage to the lungs is directly correlated with the timing of the TB diagnosis [10].

It is an issue because post- tuberculosis pulmonary disease is not well known [11]. Most national TB programme does not consider the after effects of TB. It can be difficult to distinguish between post-TB sequelae and recurrent TB. The criteria of Post- Tuberculosis Lung Disease (PTLD) provided by the debut global congress on post-TB disease, which is assurance of a persistent pulmonary deviation, regardless of their signs and symptoms preferably somewhat related to prior TB [12]. The research and medical communities have been more interested in PTLD recently. Up to 50 % of TB patients develop health problems that are similar to PTLD after completing their therapy, according to multiple studies. The likelihood that PTLD will contribute significantly to the global illness burden raises the possibility of preventative and management strategies. In 2020, there will be between 138 and 171 million TB survivors alive, with about one-fifth of them having received treatments in the previous five years.

An estimated 50 percent of incident TB-related lifetime disability-adjusted life years (DALYs) are attributed to PTLD. Patients with post-tuberculosis may have a low tolerance for exercise and a serious impairment that can interfere with daily activities [12]. A previous study has shown that even after complete microbial eradication, a considerable residual decrease in ventilatory function exists in individuals with pulmonary TB, who typically present with abnormal lung spirometry values when they initially arrive [13]. The post-TB obstructive syndrome, a range of ailments that are similar to those of chronic lung disease, pertains to those people [14].

The confluence of TB and Chronic Obstructive Pulmonary Disease (COPD) poses a serious danger to lung health worldwide, especially in India. With an estimated 3 million new cases of TB and COPD every year and 55.3 million common causes in 2016, India possesses the greatest burden of these illness in the world. Among all causes of mortality in the year 2019, lung illness that is chronically obstructive was still the third most popular [3]. Among the growing burden of COPD, a significant contribution is by the treated TB patients [15]. TB survivors present with lower Forced Vital Capacity (FVC) and post-bronchodilators Forced Expiratory Volume in one second (FEV1) than COPD patients [16].

There is two-to- four-timesa greater chance of lung function changes compared to non-tuberculosis patients and have a short life expectancy [11][17]. Bronchodilatory effects is achieved with short-acting as well as long-acting agents along with inhaled corticosteroids [6][16] (Table 2,3). It has been demonstrated that pulmonary rehabilitation therapies enhance patient quality of life, lung function, andsymptomatology [16]. Approaches to address pulmonary impairment after medical cure of TB is warranted [15].

Drugs for the management of post PTB (Table-2)

Short - acting β_2 agonist (SABA)	**Long – acting β_2 agonist (LABA)**	**Short- acting muscarinic antagonist (SAMA)**
• Salbutamol • Terbutaline • Levosalbutamol • Fenoterol	• Formoterol • Salmeterol • Indacterol • Vilanterol • Olodaterol	• Ipratropium bromide

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Drugs for the management of post PTB (Table-3)

Long – acting muscarinic antagonist (LAMA)	Inhaled corticosteroids	Methyl xanthines
• Tiotropium bromide • Glycopyrrolate	• Beclomethasone dipropionate • Budesonide • Fluticasone • Flunisolide • Ciclesonide • Mometasone furoate	• Theophylline • Aminophylline • Cholinetheophyllinate • Hydroxyethyl theophylline • Doxophylline • Acebrophylline

Radiological manifestations:

▪Different radiological signs of post-TB sequelae may involve the pleura, mediastinum, pulmonary parenchyma, airways, and vasculature. The spectrum of these manifestations is shown in (Table 4)[1][2][8][14][19].

PARENCHYMAL	AIRWAY	PLEURAL/ CHEST WALL	VASCULAR	MEDIASTINAL
• Tuberculoma • Residual cavitation • Thin – walled cavity • Cicatrization collapse • Aspergilloma • Bronchogenic carcinoma • Fibrotic bands • Emphysema • Destroyed lung syndrome • Calcifications	• Bronchiectasis • Tracheobronchial stenosis • Broncholithiasis	• Empyema • Fibrothorax • Bronchopleural fistula • pneumothorax	• Rasmussens aneurysm • Arteries and thrombosis • Dilated bronchial arteries	• calcified lymph nodes • Fibrosing mediastinitis • Pericardial TBs

PARENCHYMAL COMPLICATIONS:

▪**Tuberculoma** – A well -defined nodule or mass in the lungs caused by Mycobacterium tuberculosis is known as pulmonary tuberculoma.

▪**Thin-walled cavity**- Any round circumscribed by an epithelial or fibrous wall of variable thickness. (<2mm).

▪**Cicatrization collapse**- A cicatrization collapse results from both parenchymal and tracheal involvement. A portion or the entire lung totally disintegrates, causing cavitation that might culminate in crippling fibrosis, which is the end result of primary or secondary TB.

▪**Aspergilloma** – is a mass caused by a fungal infection.

▪**Emphysema** – is one the illness that make up COPD. Emphysema is a progressive lung condition that results in the slow deterioration of lung tissue, especially the alveoli (tiny air sacs).

▪**Fibrotic bands (pulmonary fibrosis)-** Fibrosis means thickening or scarring of the Tissue.

▪**Residual cavitation**- Is a central nodule or area of accumulation that is filled with gas in the lung.

▪**Calcifications** – Deposition of calcium in the pulmonary parenchyma.

▪**Destroyed lung syndrome**- The term destroyed lung syndrome refers to the extensive deterioration of the lung that results from pulmonary and primarily infectious diseases.

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▪**Bronchogenic carcinoma**- Bronchogenic carcinomas are cancers that start in the bronchi or the parenchyma of the lung.

AIRWAY COMPLICATIONS:

. Bronchiectasis – is a constant illness in which the airways of the lungs widen, resulting in a collection of surplus mucus that may make the lungs more prone to infection.

▪**Tracheobronchial stenosis**- Both trachea (windpipe) and bronchial tubes are Constricted.

▪**Broncholithiasis** – When calcified debris erodes into the tracheobronchial tree or Lung parenchyma, it can cause irritation and blockage.

PLEURAL/CHESTWALL COMPLICATIONS:

▪**Fibrothorax** – This disorder is characterized by a buildup of fibrous tissue within the pleural space, as a result of pleural fluid that has not been adequately drained.

▪**Chronic pneumothorax**- When air seeps into the area between your chest wall and lungs.

▪**Bronchopleural fistula**- An abnormal passageway or connection between the pleural cavity and the airways in the lungs.

▪**Empyema** – A pus-filled collection in the pleural cavity.

VASCULAR COMPLICATIONS:

▪**Rasmussen aneurysm**-A pulmonary artery branch's inflamed pseudo aneurysmal dilation next to a tuberculous cavity.

▪**Thrombosis** – A blood clot that prevents and inhibits blood flow to a pulmonary Artery.

▪**Arteritis** – Inflammation of an artery or arteries.

▪**Dilated bronchial arteries**- It increase the likelihood of clinically severe hemoptysis and can be identified when the bronchial artery's caliber is greater than 2 mm.

MEDIASTINAL COMPLICATIONS:

▪**Calcified lymph node**- Most often results from prior granulomatous infections, especially tuberculosis, and histoplasmosis.

▪**Mediastinal fibrosis**- A small percentage of all mediastinal disorders are mediastinal fibrosis, commonly known as chronic or sclerosing mediastinitis.

▪**Pericardial tuberculosis**- Chronic granulomatous reaction, significant fibrotic thickening, and widespread pericardial calcification are the hallmarks of pericardial tuberculosis.

SPIROMETRY:

The method most frequently used to evaluate lung function is spirometry, which plots volume against time. Following are some examples of measurements:

▪The forced vital capacity (FVC) is the highest possible amount of air that can be forcibly exhaled after an individual has fully inspired.

▪The forced expiratory volume in one second (FEV1) assessment evaluates how much air an individual can forcefully exhale in one second.

▪FEV1: FVC. Obstructive or restricted breathing issues can be identified using these measurements.

▪If the ratio of FEV1 to FEV is less than 80% of the expected norm, there may be an airflow obstruction, such as COPD.

▪Over 80 percent of the predicted standard for FEV1: FVC suggests restricted volume, such as abnormalities of the chest wall. Reduction in the FVC than FEV1 implies confined capacity [20].

IMPAIRMENT IN LUNG FUNCTION SEVERITY:

▪Using FEV1 (includes obstruction or restriction into account).

▪Mild = expected FEV1>70%

▪Moderate = expected 60-69%

▪Moderate – severe = expected 50-59%

▪Severe = 35-49% expected

▪Very severe = <35% expected

II. DISCUSSION:

Gupta et al., observed that patients with tuberculosis who successfully finished treatment had a higher burden of pulmonary function impairments and COPD [6]. In accordance to research by Dinaso et al., individuals suffering from multidrug-resistant tuberculosis primarily suffer from a mixed condition [2]. The obstruction pattern is more common (39%) according to Godoy et al's., study, although mixed ventilatory defects are more common (34%) according to Ramos et al's., research, with obstructive, normal, and restrictive patterns following [18].

Though the obstructive defect is most common, according to Maguire et al., Pasipanodya et al., observed a pattern of restriction as the most frequent (31%) cause [21].

Panda et al., discovered that 77.2% of individuals had impaired pulmonary function test, with restrict defect being the most common (39.6%), then mixed defect (34.7%), and obstructive defect found in only 2.8% of cases. In addition, they noticed that fibrosis and

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bronchiectasis, the two most prevalent pulmonary tuberculosis sequelae, were the most common imaging findings [13].

Peculiar PFT was detected in 94% of the participants with restrictive defect in 42%, mixed defect in 39%, and obstructive defect in 12% of patients in an investigation by de Valliere and Barker that assessed remaining lung damage following the ending of therapy for multidrug-resistant tuberculosis [22].

After MDR-TB patients completed their tubercular medication, Singla et al., examined their PFTs and discovered aberrant spirometric values in 96% of the patients, who primarily had mixed types of defects (66%) while only 19% possessed complete restrictions and 11% had pure obstruction [23].

In studies by Akkara et al., and Menezes et al., obstructive flaws were more prevalent. In an investigation by Plit et al., evaluated the change in PFT throughout TB treatment and residual disease after treatment, 46% of the patients had abnormal Spirometry after treatment completion; 28% of these patients had obstructive defects, while 24% had restrictive defects [24][25].

Following restrictive and obstructive patterns and normal patterns, Khara et al., discovered that the mixed ventilatory deficit is more common in post-TB patients. These findings are consistent with those of Lucia Maria et al., who also observed that the combined ventilatory defect is more prevalent [10][28].

The most prevalent abnormality, according to research by K. Sailaja et al., and Gowthami et al., is obstructive, which is followed by mixed and restrictive patterns. The degree of impairment also increases with the number of treatment episodes [27][28].

Pulmonary obstruction constitutes one of the complications of diminished lung function in post-pulmonary tuberculosis, according to Tarigan et al., However, Nagahane et al., found that restrictive pattern disorders had been the most common in 45.4% of the individuals who had previous episodes of treated pulmonary tuberculosis [14][19].

The illness of the obstructive airway is widespread in previously treated TB cases and reported between 1–10 years of follow-up, in accordance with research conducted in India, researchers Verma et al., Rajasekaran et al., Krishna et al., and Salvi and Barness [29-32].

As a result of pulmonary tuberculosis, Kajal et al., discovered that fibrosis and calcification are consistently observed in every patient [8].

Menon et al. discovered that parenchymal consequences are more prevalent in patients who have had TB, however Ali MG, Muhammad zs et al., reported in their study that 91% of their patients experienced pleural and parenchymal sequelae following therapy [33][34].

After taking antitubercular drugs for pleural effusion, Kwon et al. found that 68.3% of patients still had residual pleural opacity on CT [35].

Pulmonary parenchymal problems ranged from 40 to 65% in the study by Harada et al. This is in line with the findings of Naik et al., who found that parenchymal complications were present in 65% of the cases.Bacterial infection of the wall of the bronchi and consequent fibrosis can lead to the development of bronchiectasis. Comparing the results of the Naik et al., study with the findings of the Hyae Young Kim et al., study, which found that 40.1% of patients with active post-primary TB had bronchiectasis [1][36][37].

Most of the cases were obstructive, followed by restrictive patterns, according to Gali et al [38]. They also found that pulmonary fibrosis and bronchiectasis accounted for the bulk of the cases. Verma SK et al., revealed results that were comparable [29].

Deshpande and colleagues found that post-tb patients have a higher incidence of parenchymal and airway problems [39].The effect of tuberculosis (TB) on patients' quality of life was documented by Dhuria et al., who found that the patients' scores were clearly lower than those of the control group. The primary categories ofimpairment, according to the authors, were the psychological and physical domains. The physical domain deals with the capacity to carry out daily tasks [40].

Despite the microbiological cure, TB significantly lowers a patient's quality of life, as demonstrated by a systematic review done by Guo et al.78% of the patients indicated that their quality of life had been harmed, according to Godoy et al., and 46% of the subjects reported having a reduced quality of life in accordance to Singla et al [18][23][41].

According to Cruz RCS et al., and Ramos LM et al., TB patients continue to have radiographically detectable pulmonary complications even after their condition has healed, endangering their quality of life and ability to breathe [42][43].

Males predominate, according to Patil et al.'s findings (64%). When symptomatic and

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asymptomatic post-TB cases were assessed using spirometry, the most common type found in 40% of cases was an obstructive pattern, which was followed by a mixed pattern (18%) and a restrictive pattern (10%) [44].

Males dominated the study, according to Tiwari et al.61.1% of the COPD patients had a history of TB, according to Munda MK et al. Furthermore, they reported that males experienced PTLDs at a higher rate than females [45][46].In their investigation, Pal et al., identified a 57% male prevalence as well as the most frequentcomplications—COPD—following tuberculosis, whereas BPF—which was observed in 2.5% of cases—was the least prevalent [47].

III. CONCLUSION:

This review endorses the results that abnormal spirometric values persist even after successful completion of tuberculosis treatment, that the type of defect varies depending on the extent of the disease, with obstructive pattern being the most common, and that a variety of radiological changes have been identified as complications and sequelae to tuberculosis healings that have an impact on the quality of life of the patient. Long-term follow up is essential even after the TB therapy has been completed from the microbiological infection. To meet this challenge, the National Tuberculosis Elimination Program needs to implement a pulmonary rehabilitation program.

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