

TUBERCULOSIS AIRWAY DISEASE AND BRONCHIECTASIS – A DEBILITATING TRIO*R. Ramakrishna¹, P. V. Kalyan Kumar²**¹Professor and HOD, Department of Pulmonology, Katuri Medical College, Guntur.**²Associate Professor, Department of Pulmonology, Katuri Medical College, Guntur.***ABSTRACT****BACKGROUND**

We studied patients of COPD and analysed their past history of Pulmonary tuberculosis. Sixty patients of post tubercular bronchiectasis were analysed. In the third study we studied the association of bronchiectasis among patients diagnosed as COPD. The study was conducted in our tertiary care centre from 2011 to 2014.

METHODS

In the first study we analysed the history of Pulmonary Tuberculosis among the COPD patients above 30 years' age diagnosed with clinical, radiological, spirometric analysis along with routine sputum and haematological examination.

In the second study 60 cases of Post tubercular bronchiectasis were analysed for Male: Female ratio, comorbidities, type of bronchiectasis and symptoms.

In the third study we analysed 50 patients of COPD diagnosed with symptomatology and spirometry and subjected them to clinical, radiological (Chest X-ray, CT scan), serum albumin levels and microbiological examination by sending for sputum culture.

We correlated all the three studies and analysed the results.

RESULTS

In this study we found that 57% of patients diagnosed to have chronic obstructive pulmonary disease by clinical examination and spirometry were found to have a history of tuberculosis treatment. Post tubercular obstructive airway disease was more common in males (Male: female ratio 48:9). Among the males all but one were smokers. 36 of 47 male smokers had a smoking index of more than hundred. Among the 9 female patients only one was a limited smoker and all of them were passive smokers and exposed to biological fuel. Among sixty patients of post tubercular bronchiectasis Male: Female ratio was 58:42. More than 50% of these patients were smokers. Among these cases of post tubercular bronchiectasis 28% had chronic obstructive pulmonary disease as comorbidity. In our analysis of 50 cases of moderate to severe chronic obstructive airway disease we found 60% of them had associated bronchiectasis by HRCT. Mean age of these patients of bronchiectasis associated with COPD was 63±7 with male preponderance of 9:1. This combination of patients had more exacerbations, less serum albumin levels and more mortality.

CONCLUSIONS

Majority of patients diagnosed to have COPD gave history of Tuberculosis. Tuberculosis is an important cause of pulmonary fibrosis and COPD like illness. Tuberculosis induced pulmonary fibrosis and tubercular airway disease leads to bronchiectasis. COPD is associated with bronchiectasis in a number of patients. COPD patients are prone to develop Pulmonary tuberculosis because of smoking and poor respiratory defences. Bronchiectasis patients have associated with COPD and are prone to Tuberculosis infection. The three diseases present in variable proportion in patients and cause considerable morbidity and mortality and increase cost of treatment. Early treatment of Tuberculosis and Prevention of smoking can prevent these complications.

KEYWORDS

Airway Disease, Bronchiectasis, Pulmonary tuberculosis, COPD, FEV1/FVC, Smoking Index.

ABBREVIATIONS

PTBX-Post tubercular bronchiectasis, HRCT-High resolution computerized tomography, COPD-Chronic Obstructive Pulmonary disease.

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INTRODUCTION: The triad of Pulmonary Tuberculosis, obstructive airways disease and bronchiectasis is responsible for considerable morbidity and mortality in India. The specialty with this triad is Tuberculosis disease of the lungs leads to fibrosis and reactive airways and leads to crippling obstructive and restrictive lung disease similar to chronic obstructive pulmonary disease.

Chronic obstructive pulmonary disease is common in smokers and so is tuberculosis. Both Chronic obstructive lung disease and pulmonary tuberculosis may coexist. COPD patients are prone to secondary bacterial infections including mycobacterial disease. Pulmonary Tuberculosis leads to bronchiectasis. Bronchiectasis causes secondary infections and associated with airway disease. Chronic obstructive lung disease patients have associated bronchiectasis. The triad leads to crippling secondary infections, increased morbidity and mortality and increase in hospital expenditure. The problem is magnified if there is coexisting diabetes mellitus and or HIV disease which increases the suffering further.

MATERIALS AND METHODS: We studied patients of chronic obstructive pulmonary disease above 30 years of age and studied the history of Tuberculosis. Studied 50 cases of Post tubercular bronchiectasis with history of Pulmonary Tuberculosis. We looked for bronchiectasis by chest X Ray and HRCT among patients admitted for moderate to severe COPD.

STUDY DETAILS AND RESULTS: We have included the summary of three studies done in our tertiary care centre. Study one is the enumeration of patients of COPD with history of Tuberculosis. Second study is the study of post tubercular bronchiectasis and third a study of association of bronchiectasis in moderate to severe COPD patients. We analysed our results and compared with authenticated studies.

Study I: We have studied 100 cases of COPD diagnosed with FEV1/FVC 0.7 or less presenting with symptoms of cough with expectoration and breathlessness in our tertiary care centre. Among them 57(57%) gave the history of tuberculosis. 48 were male and 9 were females. Among the 48 male smokers 36 gave a smoking index of >100. 11 patients had a smoking index of <100 and one was a non-smoker. Among the female patients only one was a smoker and all the female patients gave the history of passive smoking and exposure to biological fuel. Age range of the patients was 41 to 81. Average age of post tubercular airway disease was 58.2.

Study II¹: Post Tubercular Bronchiectasis: We did a 2-year study on the prevalence and clinical profile of post tubercular bronchiectasis in our tertiary care Centre. We included the following patients.

1. Those who completed successful Anti-TB Treatment (ATT) with symptoms cough with expectoration and dyspnoea, fever and haemoptysis.
2. Thorough clinical examination eliciting the signs of bronchiectasis, consolidation and coarse crepitations.
3. Sputum for acid fast bacilli (AFB) -spot and overnight specimen done and only sputum AFB negative cases were included in the study.

Exclusion Criteria:

1. Sputum positive for AFB status. 2. Extremely moribund conditions. 3. Unwilling and non-cooperative patients
Sample size was 60 subjects (n=60) with male-female ratio of 35:25 (58%:42%), with in the age range of 17–69 years, of which majority were in the 31–50 years' group (43.3%). Initial presenting symptoms were productive cough (95%), dyspnoea (90%) and haemoptysis (35%). History of smoking was noted in 53% of total sample. It is worth noting that minority of the females were also smokers.

Chronic obstructive pulmonary disease (COPD) (28%) is the major co morbid condition associated with PTBX¹ followed by hypertension (12%), type 2 diabetes (5%) and coronary artery disease (5%) (Fig. 1).

Majority of patients had bronchiectatic changes which were identifiable on chest X-ray (53%). One-fourth patients had fibrosis (25%). Features of extensive pleura-pulmonary fibrosis were evident in 9 cases (15%). Fungal ball was seen in 4 cases (7%). Bilateral involvement was seen in 25 cases (42%) followed by right predominance (33%).

HRCT Thorax revealed the following types: 1. Traction bronchiectasis: 25 cases (42%). 2. Mixed bronchiectasis: 15 cases (25%). 3. Saccular bronchiectasis: 9 cases (15%). 4. Cystic bronchiectasis: 7 cases (12%). 5. Central bronchiectasis: 4 cases (6%).

Secondary bacterial infections in our study included staphylococcal, klebsiella and pseudomonas species. Our study of Post tubercular bronchiectasis has associated COPD in 28% of patients. Two patients in our study of sixty patients showed active tuberculosis in the bronchial washings.

Study III²: Bronchiectasis in COPD Patients: In our own study of association of bronchiectasis in COPD patients. 50 patients of COPD having moderate to severe COPD were analysed with clinical, chest X-ray, CT scan, serum c reactive protein and albumin levels and microbiological study by sputum microscopy for culture and sensitivity and gram stain. Mean age of the patients was 63±7.87 years. Out of 50 Patients 45 were men (90%) and the remaining were women (10%). Bronchiectasis was present in 30 patients (60%). H. influenza was the commonest organism isolated from sputum. Patients with bronchiectasis had significantly more exacerbations (p=0.0001), severe airway obstruction (p=0.037), higher CRP levels (p=0.0001) and low albumin levels (p=0.007). Nine patients (30%) died in bronchiectasis group and only one patient (3.33%) died in patients without bronchiectasis. Our study showed an elevated prevalence of bronchiectasis in patients with moderate to severe COPD and was associated with severe airway obstruction. Increased exacerbations, inflammation, malnutrition and mortality in Indian patients.²

DISCUSSION: Bronchiectasis in Post Tuberculosis patients We have studied the association of bronchiectasis in COPD patients and Post Tubercular bronchiectasis in our tertiary care centre and analysed the results of post tubercular airway disease from authenticated studies.

In a Chinese study³ the main causes of bronchiectasis were pulmonary TB (31.17%), bacterial infection and pertussis. The peak age ranges of post-TB bronchiectasis were 30 to 39 and 60 to 69. Patients with post-TB bronchiectasis were prone to have haemoptysis but less sputum. The chest radiography of patients with post-TB bronchiectasis represented upper lobes injury of the lung. Less pseudomonas aeruginosa culture positive and less acute exacerbation were recorded in post-TB bronchiectasis patients from the data of available follow-up patients.³

Tuberculosis of the bronchi and bronchioles can cause destruction of the airways. Endobronchial and peribronchial obstruction of airways because of lymph nodes can cause obstruction and pooling of secretions with secondary infection and further destruction of the airways and can cause bronchiectasis. Bronchiectasis is associated with reactive airways because of secondary infection leading to obstructive and restrictive airway disease. Bronchiectasis patients are prone to secondary infections including mycobacterial disease. An association between chronic obstructive pulmonary disease (COPD) and tuberculosis (TB) has been described, mainly due to smoking and corticosteroid use. Whether inhaled corticosteroid (ICS) therapy is associated with an increased risk of TB remains unclear.⁴

Tuberculosis and Airway Disease: Tuberculosis (TB) is a major cause of death worldwide. The World Health Organization estimated that there were 9 million new cases of TB in 2013.⁵ The risk factors for TB included age, male gender, low socioeconomic status, malnutrition, substance abuse, silicosis, human immunodeficiency virus infection, malignancy, diabetes, renal disease, celiac disease, gastrectomy, transplant, and receiving corticosteroids and tumor necrosis factor inhibitors. In addition, an association between obstructive pulmonary disorders (i.e. chronic obstructive pulmonary disease [COPD] and asthma) and active TB has been described, mainly due to smoking and corticosteroid use. Keeping a high suspicion and regularly monitoring for the development of pulmonary TB in COPD patients are necessary, especially for those receiving higher doses of oral corticosteroids and other COPD medications. Although ICS therapy has been shown to predispose COPD patients to pneumonia in large randomized clinical trials, it does not increase the risk of TB in real world practice.^{4,5}

COPD and Tuberculosis: COPD patients are at high risk of developing pulmonary TB, especially those frequently receiving oral corticosteroids and oral β -agonists. Although ICS therapy has been shown to predispose COPD patients to pneumonia in large randomized clinical trials, it does not increase the risk of TB in real world practice.⁴

The study done by chih-HsinLee et al⁴ showed that COPD patients were more likely to develop pulmonary TB than non-COPD subjects under a wide variety of diagnostic scenarios for COPD. ICS was not a risk factor for developing active pulmonary TB among COPD patients after considering important clinical characteristics and other prescriptions.

COPD patients who received higher doses of oral corticosteroids and oral β -agonists were more likely to develop active pulmonary TB.⁴ Age, male gender, diabetes, and receiving oral corticosteroids were risk factors for TB. Use of Inhalation corticosteroid ICS does not lead to increased risk of developing TB.⁴ COPD patients are at risk of serious bacterial infections including tuberculosis.^{4,6} In the executive summary of the 2006 update of the Global initiative for chronic obstructive lung disease (GOLD) guidelines, the role of tuberculosis in the development of chronic airways obstruction has been recognized. According to the GOLD Workshop summary, chronic bronchitis or bronchiolitis and emphysema can occur as complications of pulmonary tuberculosis.⁵

A Pakistani study⁷ found that 55.3% of treated pulmonary tuberculosis patients presenting with dyspnoea, had an obstructive ventilatory defect. Post tubercular impairment can manifest as reversible or irreversible obstructive airway disease, mixed defect or as pure restrictive defects. Immunological mechanisms have been postulated as a cause of Post tubercular asthma. Cavitation, extensive fibrosis, bulla formation and bronchiectasis implicated in the genesis of COPD caused by the destroyed lung due to pulmonary tuberculosis. Only a few studies have been done to identify this entity, but all the studies have definitely concluded that such an entity exists. However, the exact abnormality that results from tuberculosis infection has to be considered in detail with future studies and a better understanding of the pathophysiology of airflow limitation may point the way to therapeutic strategies for control of symptoms in these patients.⁷

Pulmonary tuberculosis can lead to obstructive and restrictive lung disease resembling COPD. It can result in both reversible and irreversible airway obstruction. It is unclear whether there is a similarity in the pathology but clinically we see a post-tubercular disease which is more or less similar to COPD.

In the Platino study⁸ the overall prevalence of airflow obstruction (forced expiratory volume in one second/forced vital capacity post-bronchodilator <0.7) was 30.7% among those with a history of tuberculosis, compared with 13.9% among those without a history. Males with a medical history of tuberculosis were 4.1 times more likely to present airflow obstruction than those without such a diagnosis.

In the HnizdoeE et al. study⁹ in post tubercular obstructive airway disease the risk factors associated with pulmonary function deterioration included smear-positive disease, extensive pulmonary involvement prior to anti-tuberculosis treatment, prolonged anti-tuberculosis treatment, and reduced radiographic improvement after treatment.⁹

Bronchiectasis and Secondary Infections: Mycobacterium tuberculosis can cause and complicate bronchiectasis.

Bronchiectasis may result from pulmonary Mycobacterium tuberculosis infection, with the incidence reflecting the prevalence of tuberculosis in the population. It

is also increasingly recognized that opportunist mycobacteria are associated with localized or widespread bronchiectasis. Bronchiectasis, like other forms of lung damage, makes patients prone to picking up environmental mycobacterial species and bronchial damage may occur as a result of opportunist mycobacterial infection. Opportunist mycobacteria have been isolated in 2% and 10% of random sputum specimens from patients with bronchiectasis, but the clinical significance is unclear. Patients with *Mycobacterium avium* complex infection may develop bronchiectasis over years.⁶

The scenario can be different in a populous country like India where tuberculosis is rampant. Tuberculosis can be a secondary complication in a case of post tuberculosis bronchiectasis patient because of endogenous reactivation secondary to poor nutrition and destroyed lung or exogenous reinfection.

Airway diseases, bronchiectasis and bronchial asthma present with similar symptoms.¹⁰ The differentiation between asthma, chronic obstructive pulmonary disease and bronchiectasis in the early stage of disease is extremely important for the adoption of appropriate therapeutic measures. Because of the high prevalence of these diseases and the common pathophysiological pathways, some patients with different diseases may present with similar symptoms.¹⁰

Bronchiectasis is often accompanied by airway disease. In our study of post tubercular bronchiectasis 28% of patients showed symptoms of COPD. Bronchiectasis is often accompanied by obstructive disease.¹

Airflow obstruction in bronchiectasis is primarily linked to evidence of intrinsic disease of small and medium airways on CT scanning and not to bronchiectatic abnormalities in large airways, emphysema, or retained endobronchial secretions.¹¹

Persistent airflow obstruction is a recognized feature of some patients with bronchiectasis. CT scan in COPD patients helps in recognition of previously unrecognized bronchiectasis.¹² COPD associated with bronchiectasis has longer exacerbations and increased morbidity.

Bronchiectasis develops with recurrent damage to the airways, which generally occurs in individuals with mucociliary clearance that is altered by genetic susceptibility, thus leading to inflammation and destruction of the muscular and elastic components of the bronchial walls. Respiratory infections are the leading causes of bronchiectasis; however, other pro-inflammatory attacks can trigger or accelerate the process, such as a toxin inhalation, environmental exposure, smoking, aspiration of gastric contents or changes in immune responses.

SUMMARY AND CONCLUSION: Tuberculosis is very rampant in countries like India China, Bangladesh, Pakistan, Brazil, Indonesia and South Africa.⁵ Despite the successful national tuberculosis programme there is considerable pool of Tuberculosis both pulmonary and extra pulmonary disease in these countries. Rapid urbanization crowded living condition, smoking and malnutrition contributes to the

spread of the disease. The agony of a person suffering from tuberculosis does not end with treatment of the disease with specific drugs. Pulmonary function deterioration occurs after a variable interval after anti tuberculosis therapy. The risk factors associated with pulmonary function deterioration included smear-positive disease, extensive pulmonary involvement prior to anti-tuberculosis treatment, prolonged anti-tuberculosis treatment, and reduced radiographic improvement after treatment.⁸

Pulmonary Tuberculosis associated fibrosis leads to Restrictive lung disease, obstructive lung disease similar to COPD and reactive airways with Bronchial asthma like symptoms. The exact pathology of Post tubercular COPD like illness has not been studied though it clinically resembles chronic obstructive pulmonary disease.

Post tubercular complications like Bronchiectasis, and COPD increase the morbidity and mortality and makes a person with this trio a respiratory cripple interfering with the daily living. Further Tuberculosis occurs predominantly in men of working age group and can influence the financial status of the respective families. As per the studies in China prevalence of bronchiectasis in patients with history of tuberculosis was around 30%. In our study of treated cases of tuberculosis prevalence of bronchiectasis was 53%. Prevalence of COPD in post tubercular bronchiectasis patients in our study was 28%. The Chinese study showed that post tubercular bronchiectasis is associated with more complications like haemoptysis³ Secondary infections in Post tubercular bronchiectasis is from organisms like staphylococcus aureus, H. influenzae and Pseudomonas aeruginosa which are responsible for resistant infections, complications and increase in cost of therapy.

Thus Tuberculosis can cause bronchiectasis and airway disease. Smoking is an aetiological factor for both Tuberculosis and COPD. Bronchiectasis patients have susceptibility to bacterial infections including *Mycobacterium tuberculosis* and *M. avium-intracellulare*. Bronchiectasis is associated with airway disease and COPD patients have high prevalence of Bronchiectasis in nearly 60% of our patients. COPD patients can have secondary infections and mycobacterial disease.

Tuberculosis, Bronchiectasis and COPD is a deadly triad responsible for increase in hospital admissions, increased health care expenditure and financial burden for the individual families.

The problem becomes much complicated in the event of coexistent Diabetes mellitus and or HIV disease both of which can be facilitating factors for development of Pulmonary Tuberculosis and complications thereon.

High degree of awareness on the part of the physician, early treatment of Tuberculosis with proper drugs, implementation of RNTCP programme, prevention of smoking and explanation of the hazards of smoking at an early age by means of awareness programs can decrease this problem of third world countries.

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