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Original Research Article

A Study on Clinical Profile and Risk of Exacerbation in Patients With obstructive Airway Disease Due to Post Tuberculosis Destroyed Lung

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Abstract

Treatment history of tuberculosis (TB) is a risk factor for obstructive airway disease in lung. However, it is not clear whether this clinical feature of patients with post TB destroyed lung has any difference according to the presence or absence of obstructive airflow limitation in lungs. The objective of the study was to evaluate differences in acute exacerbation of disease in patients with post TB destroyed lung according to the presence or absence of obstructive airflow limitation. We performed a retrospective cohort study and included patients with post TB destroyed lung. The presence of obstructive airflow limitation was defined as FEV1/forced vital capacity (FVC) < 0.7. One hundred and fifty-three patients were studied after applying exclusion criteria, and 122 (79.73%) was found to have obstructive airflow limitation. The percentage of patients with acute exacerbation was significantly higher in patients with obstructive airflow limitation compared to those without obstructive airflow limitation (89.3 v/s 67.7%; *P* value = 0.009) The rate of acute exacerbation of disease was higher in patients with obstructive airflow limitation (IRR, 1.19; 95% CI, 1.10-1.26). Lower body mass index (X vs. X + 1; HR, 0.955; 95% CI, 0.806-0.907) in addition to obstructive airflow limitation (HR, 1.525; 95% CI, 1.011-2.624), was found as an independent risk factor for acute exacerbation of disease. In conclusion, the presence of obstructive airflow limitation is an independent risk factor for acute exacerbation in patients with the post TB destroyed lung.

Keywords: Acute Exacerbation of Disease, Obstructive Airflow Limitation, Spirometry, Tuberculosis

Introduction

Tuberculosis (TB) is one of the common causes of death globally [1]. The complication after cure from the disease are many. These changes can be

characterized by either parenchymal, pleural, bronchial or mixed, including fibrosis in lung parenchyma, airway abnormalities like obstruction, bronchiectasis sicca, air trapping, lung volume loss etc. [2]. These changes are collectively known as post TB destroyed lung, which is one of the common causes for compromised lung function. Clinically this complication can be divided into obstructive, restrictive, or mixed types. The prevalence of these changes varies among studies. The study done by Plit et al. [3] found that obstructive airflow limitation in 28 % and restrictive disease in 24% of patients. On the other hand, Lee et al. [4] stated obstructive defects and mixed airflow limitation, in 86% of patients with post TB destroyed lung. However, in various studies the prevalence of airflow limitation differs significantly in patients with post TB destroyed lung [3-6]. The pathogenesis of obstructive airflow limitation in these patients is probably because of history of smoking itself [7], also airway collapse can cause air trapping and hyperinflation due to parenchymal destruction by TB [8]. This results in increase dyspnea in patients. The clinical manifestations in these patients with obstructive airflow limitation is nearly similar with chronic obstructive pulmonary disease (COPD) patients. The study conducted by Lee and Chang [9] found that in patients with post TB destroyed lung bronchodilator response was observed commonly, similar to the patients with COPD. Another study done by Gunen [10] reported that patients with post TB destroyed lung showed decreased pulmonary function than patients with COPD. Although, whether this clinical complication has any effects to the patients with post TB destroyed lung is still not clear. The objective of this study was to evaluate the impact of obstructive airway disease on the rate of acute exacerbation in patients with post TB destroyed lung.

Materials and Methods

The present study was approved by the institutional ethical committee. This was a retrospective cohort study done between January 2020 to January 2021to patients with pulmonary TB who were followed up at tertiary care centre for Tuberculosis patients at Bhopal Madhya Pradesh. Post TB destroyed lung was defined as: any previous history of pulmonary tuberculosis, negative sputum smear microscopy and no growth after 8 weeks on solid and liquid culture for Mycobacterium tuberculosis on the sputum sample, and lung parenchymal destruction in at least one fourth of a hemithorax on chest radiograph posterior-anterior view.

Exclusion criteria -: those patients who has active TB, active nontuberculous mycobacteria infection, or other lung disease— like pneumoconiosis, interstitial lung disease, and lung cancer.

Demographic, radiological, and clinical parameters were compared between patients with and without obstructive airflow limitation. The obstructive airflow limitation was defined as FEV1/ forced vital capacity (FVC) less than 70%.

Three categories were defined on the basis on lung parenchymal involvement on chest radiograph:

Grade I- Involvement up to one third of the hemithorax on chest radiograph,

Grade II- involvement between one third and two third of the hemithorax on chest radiograph,

Grade III- Involvement of more than two third of the hemithorax on chest radiograph.

Acute exacerbation of disease was defined as either an increase in or new onset of cough, sputum production and/or shortness of breath, along with these symptoms following should also needed systemic antibiotics, systemic steroids, or both and/or hospitalization.

Frequent exacerbators were also defined as patients who had two or more episodes of previously defined acute exacerbations in one year. All exacerbations were separated by at least or equal to 1 month.

Statistical analysis:

Chi-square test or Student's t-test were used to evaluate differences in parameters between two groups. Poisson regression model were used to calculate the rate of acute exacerbation. Various risk factors for acute exacerbation with 95% confidences interval (CI) were calculated by Cox regression analysis, with BMI as a continuous variable. The Lung function was studied by using a mixed linear

regression model.

Results:

Demographic data: - Total 193 patients were screened for the study, and among them 153 were enrolled in this study (Fig. 1). The baseline characteristics of patient, their lung function, and grade of lung parenchymal involvement are shown in Tables 1 and 2.

Table 1: Demographics variables of patients with post TB destroyed lung.

Variables	Number of patients (n= 153)
Female gender	72 (47.05)
Age (in years)	54.57 ± 9.67
Smoker	49/120 (40.83)
Smoking Pack-years	11.20 ± 16.25 (n= 108)
BMI (kg/m^2)	19.42 ± 3.50
Comorbidities:	
Diabetes Mellitus (type II)	14 (9.1)
Hypertension	46 (30)
Renal failure	2 (1.3)
Coronary artery disease	5 (3.2)
Congestive cardiac failure	10 (6.5)

Data - shown as Number. (%) or mean ± SD. SD= standard deviation, BMI = Body Mass Index

Table 2: Parameters of Lung function and categories for Lung parenchymal involvement

Variables	Number of patients (n= 153)
Parameters of Lung function	
FVC (L)	2.19 ± 0.62
FVC (% predicted)	61.7 ± 15.6
FEV_1 (L)	1.22 ± 0.48
FEV_1(% predicted)	43.3 ± 20.1
FEV_1/FVC ratio (%)	55.9 ± 15.5
DLCO (%predicted)	71.6± 17.0 (n = 34)
Lung parenchymal involvement	
Grade I	67 (43.7)
Grade II	44 (29.4)
Grade III	42 (27.4)

Data- shown as No. (%) or mean ± SD. SD= standard deviation, FVC= forced vital capacity, FEV1= forced expiratory volume in first second, DLCO= Diffusing capacity for carbon monoxide.

Table 3: Demographic variables in patients with or without obstructive airflow limitation

Variables	Obstructive Airflow limitation (present) (n = 122)	Obstructive Airflow limitation (absent) (n = 31)	*P* value
Female gender	58 (47.54)	14 (45.16)	0.557
Age (in years)	57.57 ± 8.89	54.43	0.976
Smoker	40/92 (43.47)	9/28 (32.14)	0.536
Smoking Pack-years	12.23 ± 15.35 (n= 94)	18.87 ± 10.34 (n=14)	0.865
BMI (kg/m^2)	20.65 ± 4.53	19.52 ± 4.53	0.017
Comorbidities: - Diabetes Mellitus (type II) Hypertension Renal failure Coronary artery disease Congestive cardiac failure	 11 (9.0) 37 (30.32) 2 (1.6) 5 (4.0) 8 (6.5)	 3 (9.6) 9 (29.03) 0 0 2 (6.4)	 1.000 0.431 1.000 1.000 1.000

Data - shown as Number. (%) or mean ± SD. SD= standard deviation, BMI= Body Mass Index

After applying exclusion criteria, among the 153 patients enrolled for the study, 122 (79.73%) had obstructive airflow limitation at the time of diagnosis of post TB destroyed lung. 58 patients were diagnosed as pure obstructive pattern among patients with obstructive airflow limitation. Among the remaining 64 patients, TLC was calculated only in 10 patients. Among them four patients showed obstructive pattern and 6 patients showed mixed pattern. In patients without any obstructive airflow limitation, 26 patients have restrictive type of pattern and 5 patients showed normal spirometry. Except for a higher body mass index (BMI) in patients with obstructive air flow limitation (20.65 ± 4.53 vs. 19.52 ± 4.53; P = 0.017) (Table 3), the baseline characteristics of patients with and without obstructive airflow limitation were not significantly different statistically. On the measurement of baseline lung function, the percent predicted values, and not the absolute values, of FVC was higher significantly, and both the percent predicted and absolute values of FEV1 was lower significantly in patients with obstructive airflow limitation in comparison to those without obstructive airflow limitation. Subgroup analysis was calculated between 58 patients with pure obstructive pattern and 6 patients with mixed pattern, FVC as well as FEV_1 were higher in patients with pure obstructive pattern in spirometry whether expressed as absolute (1.37± 0.37 vs. 0.89 ± 0.15 L, P < 0.001; 2.54 ± 0.79 vs. 1.77 ± 0.29 L, P < 0.001, respectively) or percent predicted values (49.12 ± 16.42 vs. 34.87% ± 7.86%, P < 0.001; 74.54 ± 17.22 vs. 48.23% ± 9.61%, P < 0.001, respectively). There was no statistically significant difference in the lung parenchymal involvement between the two groups analysed (Table 4).

Table 4: Parameters of Lung function and Lung parenchymal involvement

Variables	Obstructive Airflow limitation (present) (n = 122)	Obstructive Airflow limitation (absent) (n = 31)	*P* value

Parameters of Lung function			
FVC (L)	2.18 ± 0.79	2.05 ± 0.67	0.061
FVC (% predicted)	62.5 ± 13.6	53.2 ± 17.3	0.006
FEV_1 (L)	1.34 ± 0.33	1.59 ± 0.58	< 0.001
FEV_1(% predicted)	42.65 ± 18.5	61.6 ± 21.6	< 0.001
FEV_1/FVC ratio (%)	52.4 ± 10.7	81.6 ± 8.1	< 0.001
DLCO (%predicted)	73.16 ± 17.9 (n = 29)	63.24 ± 17.5 (n = 5)	0.431
Lung parenchymal involvement			0.103
Grade I	60 (49.18)	7 (22.58)	
Grade II	33 (27.04)	11 (35.48)	
Grade III	30 (24.59)	12 (38.70)	

Data- shown as No. (%) or mean ± SD. SD= standard deviation, FVC= forced vital capacity, FEV1= forced expiratory volume in first second, DLCO= Diffusing capacity for carbon monoxide.

Table 5: Frequency of acute exacerbation in patients with or without airflow limitation

Acute Exacerbation of disease	Obstructive Airflow limitation (present) (n = 122)	Obstructive Airflow limitation (absent) (n = 31)	*P* value
Incidence of acute exacerbation	109 (89.3)	21 (67.7)	0.009
Incidence rate (No. of exacerbation/person-year)	0.40 (0-8)	0.35 (0- 1.25)	0.001[#]
Frequent acute exacerbator	8/109 (7.3)	0/21 (0)	0.357
Need of mechanical ventilation during treatment	11 (10.8)	4 (19.0)	0.276

Data - shown Number (%) or median [range]. [#] Poisson regression, IRR, 1.19; 95% CI, 1.10-1.26, adjusted with age in years, gender, BMI, history of smoking, extent of lung destruction by TB, and FEV1. Abbreviations – IRR= incidence rate ratio, CI= confidence interval, BMI= Body Mass Index, FEV1= forced expiratory volume in first second.

Table 6: Factors predicting acute exacerbation of disease in post TB destroyed lung.

Variables	HR (95% CI)	*P* value
Obstructive Airflow limitation	1.525 (1.011-2.624)	0.043
Age in years	1.004 (0.967-1.030)	0.707
Gender predisposition (male vs. female)	1.573 (0.957-2.171)	0.061
BMI, kg/m2 (X v/s X+1)	0.955 (0.806-0.907)	0.046
Categories of lung involvement		0.079
Grade I vs. Grade II	0.626 (0.308-0.962)	0.032
Grade I vs. Grade III	0.769 (0.445-1.323)	0.268

Abbreviations – HR= hazard ratio, CI= confidence interval, BMI= Body Mass Index. Acute exacerbation of disease in post TB destroyed lung: -

The percentage of patients who was diagnosed as acute exacerbation of disease at least one time during the study period was significantly higher in patients with obstructive airflow limitation in comparison to those without obstructive airflow limitation (89.3 v/s 67.7%; *P* value = 0.009) (Table 5). When 58 non-smokers with obstructive airflow limitation were compared with those without obstructive airflow limitation, the percentage of patients who experienced acute exacerbation of disease was higher in patients with obstructive airflow limitation than in those without obstructive airflow limitation (89.3 vs. 67.7%; P = 0.015). The proportion of patients who experienced acute exacerbation of disease was not associated with the lung parenchymal involvement (88.6% vs. 70.5% vs. 91.5%; P = 0.857). Once adjusted for age in years, gender predisposition, Body Mass Index, history of smoking, and lung parenchymal involvement, the rate of acute exacerbation of disease (number of exacerbation/person-year) was higher in patients with obstructive airflow limitation than in those without obstructive airflow limitation (incidence rate ratio [IRR], 1.45; 95% CI, 1.27-1.45). For the incidence rate of acute exacerbation of disease, when FEV1 was adjusted, remained high in patients with obstructive airflow limitation (IRR, 1.19; 95% CI, 1.10-1.26; Table 5). Among patients with acute exacerbation of disease, 8/109 (7.3%) of those with obstructive airflow limitation were frequent acute exacerbators. No frequent acute exacerbator found among patients without obstructive airflow limitation; although, it was not statistically significant. Cox regression analysis was used for Predictive factors for acute exacerbation of disease. After adjusting for age in years, gender predisposition, and lung parenchymal involvement, the hazard ratio (HR) for acute exacerbation of disease in patients with obstructive airflow limitation was 1.525. The HR of BMI (X vs. X + 1) was 0.955 (Table 6).

Discussion:

Data from this study indicated that obstructive airflow limitation is an important risk factor for acute exacerbation of disease in post TB destroyed lung. Obstructive airflow limitation is one of the most important physiological complications of post TB destroyed lung. Although, the occurrence of obstructive airflow limitation in these individuals is variable from 28 to 86.4% in different studies [3,4]. In our study, the prevalence of obstructive airflow limitation was 79.73%. The huge difference observed in prevalence of obstructive airflow limitation between various studies could be because of different definitions of post TB destroyed lung. However, our study enrolled patients with lung parenchymal involvement in greater than one fourth of hemithorax, in comparison other studies did not define the lung parenchymal involvement [3] or defined a different value of parenchymal involvement [4]. However obstructive airflow limitation was reported in various studies as high as 85.9% of patients with post TB destroyed lung, its pathogenesis is not fully explained in any of the report. Till date the best-known cause of obstructive airflow limitation is exposure to smoke [7]; hence, this could also play very important role in pathogenesis of post TB destroyed lung, but on the other hand, more than half of patients with obstructive airflow limitation in this study were non-smokers, and we did not found any statistically significant difference between smoker and non-smoker groups. Therefore, the pathogenesis of obstructive airflow limitation in patients with post TB destroyed lung could not be explained only by exposure to smoke. This observation we discussed is also supported by other

studies that obstructive airflow limitation developed after pulmonary TB is not dependent only on smoking history [11-13].

A cross-sectional study done on causes of airways obstruction observed that airway obstruction was associated with TB in non-smokers [12]. Also, association between history of TB and airflow obstruction was established by the PREPOCOL study that obstructive airway disease was higher in post TB destroyed lung than that with smoking alone, the association was found to very strong [13].

In this study, the incidence of acute exacerbation of disease was significantly higher in patients with obstructive airflow limitation than in those without obstructive airflow limitation, this finding suggests that obstructive airflow limitation is an important risk factor for acute exacerbation of disease due to post TB destroyed lung. Cox regression analysis also supports this observation. The frequency of acute exacerbation of disease is already known to correlate with FEV1 and FEV1/FVC ratio in COPD patients [14-17], after adjusting the value of FEV1 and FEV1/FVC we calculated the incidence of acute exacerbation of disease. The incidence of acute exacerbation of disease was found to be higher in patients with obstructive airflow limitation. The extent of parenchymal destruction was not found to be associated with the incidence of acute exacerbation of disease in our study. As a whole, more than two third of patients suffered with acute exacerbation of disease. Patients with grade III of lung parenchymal involvement had more propensity to suffer with acute exacerbation of disease than those with grade II lung parenchymal involvement (table 6). These observations suggest that lung parenchymal involvement can be a cause of acute exacerbation of disease, however it may not be directly related to the grade of parenchymal involvement. Hence, it is possible that the impact TB on airflow limitation is far more important than lung parenchymal involvement alone with respect to the incidence of acute exacerbations.

In this study, we observed BMI as another risk factor for acute exacerbation of disease in post TB destroyed lung. low BMI was found as a significant factor associated with failure rate of non-invasive ventilation and the need of invasive ventilation in acute exacerbation of post TB destroyed lung [18].

There is a large lacuna in the knowledge regarding the post TB destroyed lung. Specially about obstructive airflow limitation. This is the one of the few studies in Indian context to compare the clinical features of post TB destroyed lung, particularly acute exacerbation of disease, and of patients with post TB destroyed lung with and without obstructive airflow limitation. Our study had few limitations. Firstly, it's design was retrospective. Patients with mixed airways disease could not be evaluated separately as the initial data for total lung capacity were not available. Second, the coexistence of COPD was not excluded in this study because we included patients with a history of smoking. Although, excluding ever smokers with obstructive airflow limitation, acute exacerbation of disease also occurred more in patients with obstructive airflow limitation. Third, treatment with pharmacological agents was not considered. Similar to the COPD, the efficacy of pharmacotherapy in post TB destroyed lung with obstructive airflow limitation should be evaluated in future study. A large multicentric well-designed prospective study without these limitations should be conducted to confirm the results of the present study and to formulate future guidelines in this field of pulmonary medicine. [19]

In conclusion, the presence of obstructive airflow limitation is an independent risk factor for acute exacerbation of disease in patients with the post TB destroyed lung.

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