



Functional Evaluation In Pulmonary Tuberculosis Sequelae Patients In Relation With Type Of Pattern Of Lung Damage And Lag Time In Starting Treatment

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Abstract

Introduction: Pulmonary Tuberculosis can cause chronic impairment of lung function even after completion of anti-TB treatment. Several factors predict the deterioration of pulmonary function in treated cases. The time course for change in pulmonary function and risk factors have not been well studied so far as we have limited resources for the management of restrictive and mixed pattern of impairment it is essential that for patients with significant respiratory symptoms and multiple risk factors, periodical assessment of pulmonary function should be done to monitor the progress of lung function. Aim of our study is to analyze the pattern of lung damage – obstructive / restrictive / mixed whichever is commonly occurring in Pulmonary Tuberculosis sequelae patients. Also to find the association between Lag Time (time interval between onset of symptoms and diagnosis of the disease) and extent of destruction of lung tissue

Method: This study was done as a cross – sectional study in 120 patients both male & female (male-81 and female – 39) attending Thoracic Medicine outpatient department at chengalpattu Medical College were selected for the study. Easy On PC Spirometry was used for analysing. Percentage of the Predicted values of FEV₁, FVC, FEV₁ / FVC, FEF_{25%} -75% were taken for analysis.

Conclusion: The present study shows that because of the marked residual changes in the Lung caused by Tuberculosis infection, there occurs a considerable and significant decline in Lung function in post treatment period. In this study the pattern of impairment of lung function noticed was restrictive pattern, mixed pattern and the extent of impairment increases as lag time, number of episodes of treatment and duration after treatment increases.

Keywords: Tuberculosis, Spirometry, Lag time

Introduction

Tuberculosis among much other chronic illness is still one of the major causes of morbidity and mortality affecting human beings since immemorial time. Pulmonary TB seems to have never disappeared in India since Robert Koch identified the causative agent in 1882.¹ Even today, we get patients affected by Pulmonary TB with all the effective control and preventive measures taken over the years. Not only

the medical implication but also the social and economic impact of TB has been enormous.

According to Global Tuberculosis report 2014 the prevalence of Pulmonary TB worldwide is around 9 million and in India the incidence is 2.2 million and prevalence is 2.8 million cases.²

There are many studies which focused on the pathophysiology, diagnosis, and treatment of

Pulmonary TB but only a few studies were done so far on the after effects of PT infection in lungs.

In the few studies that are being done on evaluation of Lung functions in PT Sequelae patients there are concrete evidences stating that there is permanent functional deterioration in these patients.

Many studies say that the obstructive pattern of lung damage is the commonest finding. But recent studies say that there are more number of patients with restrictive and mixed pattern of damage.³

According to previous studies the changes are more pronounced during 13- 18 months after completion of anti-TB treatment In our area where people seek medical help at a very late stage, there is involvement of both bronchi & parenchyma leading to extensive damage of both. It is important to identify patients with deterioration of pulmonary function after the completion of treatment because it affects the quality of life of the patients to a great extent. This evaluation can be done by an easy and accessible technique called spirometry. Hence based on this aim of our study is to analyze the pattern of lung damage – obstructive / restrictive / mixed whichever is commonly occurring in Pulmonary Tuberculosis sequelae patients. Also to find the association between Lag Time (time interval between onset of symptoms and diagnosis of the disease) and extent of destruction of lung tissue.

Material & Methodology

This study was done as a cross – sectional study in 120 patients both male & female (male-81 and female – 39) attending Thoracic Medicine outpatient department at chengalpattu Medical College were selected for the study. Both male & female aged 30 - 60 years, released from treatment 18 months prior to the study and within 5 years after completion of treatment and there was cessation of smoking after diagnosis of Pulmonary TB were included in study, whereas patients with active pulmonary TB, extra pulmonary TB, MDR TB, HIV positive, with Severe respiratory distress, bed ridden, pregnancy, Diabetes mellitus, Recent myocardial infarction , Cardiac disease like unstable angina , were excluded from study.

Easy On PC Spirometry was used for analysing , Institutional Ethics committee approval was obtained before starting of study, Informed consent was obtained on the day of recording Subject was advised to avoid full meals 2 hours prior to the test , Alcohol consumption 4 hours prior to the test. , Short acting bronchodilators 6 hours prior to the test Long acting bronchodilators 12 hours prior to the test. Percentage of the Predicted values of FEV₁, FVC, FEV₁ / FVC, FEF_{25%} -75% were taken for analysis.

The pattern of lung function impairment was assessed from spirometry results using percentage of the predicted values of FEV₁/FVC, FVC.⁴ Severity of restrictive impairment of lung function was assessed using percentage of predicted values of FVC.⁵ Mild restriction – 60 to 80%, Moderate restriction – 45 to 59%, Severe restriction - <45% Statistical analysis was done by using SPSS 22.0 version. Anthropometric measurements and lung function parameters were analysed by arithmetic mean and standard deviation. The mean value of lung function parameters in each pattern of lung function impairment was analysed by ANOVA and Chi square test.

The mean value of lung function parameters were correlated with number of episodes of TB treatment, time duration after treatment (months) and lag time in days (time duration between onset of symptom and diagnosis) by Spearman's rho analysis.

Results

In our study 120 subjects (male -81, female – 39) who had completed tuberculosis treatment 18 months before the study and within 5 years of completion of treatment were participated in the study.

In our study population maximum number of patients belongs to age group 51 – 60 (n=53). Minimum number of patients belongs to age group 30 – 40. (n=32). Among the 120 subjects participated in this study 67.5% were male subjects, and 32.5% were female subjects. Male : female ratio in this study was around 2:1. The below table 1 shows the distribution of pattern of Lung Function Impairment among the study group.

TABLE 1: Frequency distribution of different patterns of Lung Function Impairment.

Diagnosis	Frequency (n=120)	Percent (100)
Mild restriction	40	33.3
Moderate restriction	32	26.7
Severe restriction	14	11.7
Mixed pattern	21	17.5
Normal study	13	10.8

Mean ± S.D value of FVC varies significantly in different patterns of lung function study (**P < 0.01**). FVC value decreases as severity of lung impairment increases. Statistical analysis was done by ANOVA. Significant difference in mean value of FVC between normal study and restrictive pattern was observed. There is significant decrease in mean FVC value between mild restriction and severe restriction pattern of lung damage. There is not much difference between mean value of FVC in mixed pattern and mean value of FVC in severe restriction.

TABLE 2: FVC in various patterns of Lung Function Impairment

Parameters	Pattern of damage	N	Mean ± S.D	Minimum	Maximum	Sig
FVC (Percentage of predicted value)	Normal study	13	89 ± 6.04	80	99	0.000*
	Mild restriction	40	66.28 ± 5.27	60	80	
	Moderate restriction	32	51.03 ± 5.91	26	59	
	Severe restriction	14	38.71 ± 3.81	34	45	
	Mixed pattern	21	41.67 ± 9.90	25	62	
	Total	120	57.15 ± 16.47	25	99	

Statistical analysis by ANOVA shows that the Mean ± S.D value of FEV₁ varies significantly in different patterns of lung function study (**P < 0.01**). FEV₁ value decreases as severity of restrictive pattern increases, but mean value of FEV₁ is higher compared to FVC in restrictive patterns of lung impairment except in mixed pattern. The difference in mean value of FEV₁ between normal study and restrictive pattern is much less compared to difference in mean value of FVC between normal study and restrictive pattern. Significant decrease in FEV₁ Value was observed as severity of lung damage increases. Significant difference in mean value of FEV₁ between restrictive pattern and mixed pattern was observed

TABLE 3: FEV₁ in various patterns of Lung Function Impairment

Pattern	of						

Parameter	damage	N	Mean ± S.D	Minimum	Maximum	F	Sig
FEV ₁ (Percentage of predicted value)	Normal study	13	88.69 ± 5.00	81	96	326.78	0.000*
	Mild restriction	40	69.72 ± 4.52	60	83		
	Moderate restriction	32	54.5 ± 6.79	43	66		
	Severe restriction	14	44.64 ± 4.10	35	51		
	Mixed pattern	21	26.71 ± 6.61	16	37		
	Total	120	57.27 ± 19.40	16	96		

Also statistically significant (**P < 0.01**) variation was noted in FEV₁ / FVC values depending up on the severity of lung damage. As severity increases the mean value of FEV₁ / FVC decreases. But in all range of severity value of FEV₁ / FVC is >70% suggesting that the pattern of damage was restrictive in nature. In mixed pattern mean FEV₁/FVC is less than 70% ANOVA test was used for analysis. Mean FEV₁/FVC value is more than 70% indicating the pattern of damage is restrictive, but significant decrease in mean value was observed as severity increases. In mixed pattern the FEV₁/FVC is below 70%.

Significant difference (**P < 0.01**) in FEF_{25-75%} value between different pattern of Lung Function Impairment was noted. Mean value of FEF_{25-75%} in various patterns of Lung Function Impairment is well below 65% in restrictive and mixed pattern. As severity of lung impairment increases mean value of FEF_{25-75%} decreases significantly. Significant difference in mean value of FEF_{25-75%} between restrictive and mixed pattern was observed.

TABLE 4: Relationship between Lag time and pattern of Lung Function Impairment

Parameter	Pattern of damage	N	Mean ± S.D	Minimum	Maximum	F	Sig
Lag time (days)	Normal study	13	49.62 ± 15.47	30	75	39.22	0.000*
	Mild restriction	40	60.75 ± 29.41	30	120		
	Moderate restriction	32	171.72 ± 95.34	30	365		
	Severe restriction	14	195 ± 72.30	60	330		
	Mixed pattern	21	254.76 ± 81.51	60	365		

Total	120	138.75 ± 101.57	30	365		
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ANOVA shows significant variation between each pattern of Lung Function Impairment and lag time ($P < 0.01$). As lag time increases the lung function impairment is more severe.

Discussion

Tuberculosis is a worldwide public health problem with higher morbidity and mortality among all chronic infections. India alone accounts for 24% of global burden of Tuberculosis.²

Pulmonary Tuberculosis affects almost all parts of the respiratory system including bronchi, bronchioles, lung parenchyma and lymph nodes. The pathogenesis involved is an inflammatory process causing upregulation of several proteases like matrix metalloproteinases and dysregulation of protease control which causes lung remodeling³

Histopathological abnormalities occur even after successful treatment of the disease causing sequelae changes in the lungs which can be in the form of fibrosis, cavity formation, bronchial and bronchiolar obstruction, bronchiectasis etc. These sequelae changes in the respiratory tract can cause obstructive, restrictive or mixed pattern of lung function impairment.³

Many studies have shown that the common pattern of lung function impairment in pulmonary TB sequelae patients was obstructive in nature. But the recent studies have shown that restrictive pattern and mixed pattern are most commonly observed rather than obstructive pattern in these patients.

All these factors have a negative effect on quality of life of a patient who had been treated for tuberculosis with successful therapy, so it is essential to assess the impairment of lung function as early as possible for an early intervention.^{6,7}

In the present study the age group of selected subjects was between 30 – 60 years but it was observed that more number of patients fall in the age group of 51 - 60 years (44%) compared to 26% who belonged to age group 30-40 years. This may be because normally there is gradual decline in pulmonary function after the age of 30 years.⁴ In Tuberculosis affected elderly individual there is an accelerated decline of lung function noticed especially over the age of 40.⁽⁵⁴⁾

More number of male patients participated in the present study compared to female patients (Male-81, Female-39). There is evidence in global TB report 2014 which states that 60% of new cases reported every year belong to male gender. The gender difference is may be due to the fact that less number of women approaches for medical aid compared to men. The other factors contributing to increased susceptibility to TB infection in male gender are the habit of tobacco use either by smoking, tobacco quid is common among them and also the risk of exposure to the infection and passive smoking in working environment is more for men compared to women.

Pattern Of Lung Function Impairment

The pattern of lung function impairment observed in the study were restrictive pattern and mixed pattern only. The probable reason for this may be the increase in lag time period i.e. the time duration between onset of respiratory symptoms and the time of diagnosis as Tuberculosis.

There is concrete evidence that as the lag time increases the extent of damage to lung also increases.⁸ The Lag time in this study varies from a minimum of 30 days to maximum of 365 days. This may be because most of the patients are asymptomatic or may experience minimal symptoms like fever and malaise ordinarily until disease is far advanced especially during primary Tuberculosis.⁹ Another cause may be the subjects participated in the study were from rural areas with poor health education and poor socioeconomic status which hampers them to access medical aid as early as they experienced symptoms. This increased Lag time might have been the cause for extensive damage resulting in restrictive or mixed pattern.

Few subjects in the study (13 out of 120) had a normal pattern in spirometry. This may be due to different factors such as they might have had better pulmonary function prior to attack of tuberculosis compared to subjects who showed restrictive/mixed pattern. The occupational and environmental exposure might have been less compared to other

subjects. According to Mohammed Saleh Al- Hajjaj a continuous healing process is taking place in the lungs even after completion of treatment. This may also be the cause for normal study in these patients.¹⁰

FEV₁/FVC RATIO

The ratio in all types of impairment is well above 70% suggesting the pattern of damage is restrictive in nature. The severity of restrictive pattern of damage was assessed based on FVC value.⁴ Accordingly, the severity varied from mild to moderate to severe restriction in the present study

And also it was observed that there is decline in FVC & FEV₁ values depending upon the severity of lung impairment. This is in consistent with a study by Luiz Carlos D'Aquino et al who says that interpretation of restrictive pattern identified by Spirometry can be made more accurate by incorporating the magnitude of reduction in FVC and elevated FEV₁/FVC ratio.¹¹

FVC & FEV₁

In the present study a significant decrease in FVC & FEV₁ was noted as severity of restriction increases. Decline in FVC value was more compared to decline in FEV₁. This is in consistent with a study by Eun Jo Lee et al who found that there is negative correlation between FVC and FEV₁ values and extent of Lung damage.¹² Venkateshiah et al in their study had also stated the usefulness of both FVC & FEV₁ values in evaluating the extent of destruction of lung. According to them the FVC and FEV₁ decline as severity of damage increase.⁹

In mixed pattern where both obstructive and restrictive damage occurs and there is significant decrease in FVC and FEV₁, and the value of FEV₁/FVC is around 63% which is well below 70%.⁴

FEF 25-75%

The decline in value of FEF_{25-75%} below 65% in both restrictive and mixed pattern of damage in this study indicates there was significant smaller airway obstruction in these subjects. This is consistent with finding of Eric Walter Pefura- Yone et al who suggest that FEF_{25-75%} <65% is a useful criterion for diagnosis of small airway obstruction in treated pulmonary TB patients who had restrictive /mixed pattern. They also suggested that decrease in FEF_{25-75%} is associated with poor profile of other spirometry

indices like FVC & FEV₁. This was also observed in the present study.¹³

The pathogenesis of small airway obstruction is due to destruction of parenchyma surrounding the distal small airways by fibrosis causes the loss of radial traction on the airways thereby causing distortion and narrowing of these small airways.¹³

Lag Time And Lung Function Impairment

In the present study a negative correlation between lag time and values of pulmonary function parameters was observed. This is similar to the study by Eric Walter who states that long duration prior to TB diagnosis is an important predictive factor for persisting respiratory signs following successful treatment. Delay in diagnosis of TB has shown a direct relationship with severity of pulmonary damage.¹³

Conclusion

The present study shows that because of the marked residual changes in the Lung caused by Tuberculosis infection, there occurs a considerable and significant decline in Lung function in post treatment period. In this study the pattern of impairment of lung function noticed was restrictive pattern, mixed pattern and the extent of impairment increases as lag time, number of episodes of treatment and duration after treatment increases.

As we have limited resources for the management of restrictive and mixed pattern of impairment it is essential that an early and effective intervention is necessary for detection, diagnosis and compliance of treatment in pulmonary tuberculosis affected individuals.

This study again like many other studies stresses that even after successful completion of anti-Tuberculosis treatment, a regular periodical assessment of pulmonary functions with simple and feasible method like Spirometry and addition of Pulmonary Rehabilitation Program along with Anti Tuberculosis treatment is necessary to improve the Quality of Life of the individuals affected by Pulmonary Tuberculosis to a greater extent which helps them to lead a symptomless, comfortable and fruitful life in future.

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