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Impact of lag time on lung function impairment in pulmonary tuberculosis sequelae patients – A cross-sectional study

Sreekaanth S[1], Ragulan Rajalingam[2], Jereen Varghese[3], Viswambhar V[4], Vidhya Priya[5]

[1]Post Graduate III Year, [2]Associate Professor, [3]Assistant Professor, [4]Professor and Head, [5]Post Graduate II Year, Department of Respiratory Medicine, Shri Sathya Sai Medical College and Research Institute, Chennai, Tamil Nadu, India

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ABSTRACT

Background: Treatment completed pulmonary tuberculosis (PTB) patients are often left with permanent pulmonary function impairment. Lag time remains a major factor in determining the severity of the sequelae. **Aims and Objectives:** This study aims to assess the impact of lag time on PTB sequelae. **Materials and Methods:** A cross-sectional study was conducted during July 2019–December 2020. A total of 85 patients presenting with clinicoradiological features of PTB sequelae were recruited for the study and spirometry and diffusion capacity of lungs (DLCO) were done. They were divided into study groups based on lag time. The lag time (in days) was considered as primary explanatory variable. One-way ANOVA and Chi-square tests were used. coGuide V.1.0 was used for statistical analysis. **Results:** The mean lag time was 52.94 days in the study population. The mean duration of after treatment was 15.45 years in the study population. There was a statistically significant difference across study groups (classified based on the lag time) in lung function such as FVC%, FEV1, FEVI/FVC, MEF, DLCO, and duration of after treatment ($P<0.05$). **Conclusion:** The lag time from the development of symptom to the diagnosis of the disease has a significant impact on lung function impairment in PTB sequelae patients since the increase in lag time increases the severity of lung function impairment. Early identification and treatment may help in reducing the progression of lung function impairment.

Key words: Pulmonary tuberculosis; Chronic disease spirometry; Respiratory function test; Antitubercular agents

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INTRODUCTION

The morbidity and mortality caused by the disease are high in developing countries, caused due to associated HIV infection, poverty, and low socioeconomic standards.[1,2] Lag time in pulmonary tuberculosis (PTB) is the interval between onset of symptoms and diagnosis of disease. Assessment of the relationship between lung function impairment and factors associated with lag time in PTB sequelae patients will help prevent an early diagnosis of lung function decline, which in turn improves the quality of life in these patients. Hence, this study was planned to determine the impact of lag time on the severity and type of lung function impairment in PTB sequelae patients.

Aims and objectives

This study aims to assess the impact of lag time on pulmonary tuberculosis sequelae.

MATERIALS AND METHODS

A cross-sectional study was conducted in a rural tertiary care hospital. The study was conducted from July 2019 to December 2020. Patients presenting in respiratory medicine outpatient department with clinical-radiological features of PTB sequelae were recruited as study participants. Both male and female patients, patients who have completed treatment at least 18 months prior to the study, age >18 years, patients who have stopped

Address for Correspondence:
Dr. Viswambhar V, Professor and Head, Department of Respiratory Medicine, Shri Sathya Sai Medical College and Research Institute, Chennai - 600 130, Tamil Nadu, India. **Mobile:** +91-7401295666. **E-mail:** narain.vneni@gmail.com

smoking after a diagnosis of pulmonary TB and X-ray chest showing features suggestive of fibrosis, cavity, calcifications, and bronchiectasis were included in this study. Patients with features suggestive of active PTB, extra-PTB, severe respiratory distress, any pre-existing airway, parenchymal, or interstitial lung diseases, and not fit for spirometry were excluded from the study. A detailed pre-structured questionnaire was used for data collection. A total of 85 patients were recruited for the study by convenience sampling technique. Complete physical examination, chest radiographs, spirometry, and diffusing capacity of the lungs for carbon monoxide diffusion capacity of lungs (DLCO) were done. The pre-structured questionnaire contained details on age, lag time, and post-treatment duration. Lag time is considered as the time from the development of the first symptoms of TB to the actual diagnosis of TB. Post-treatment duration is regarded as the time after the completed full course of anti-tuberculosis treatment (ATT).

Sample size calculation

The sample size was calculated assuming the proportion of pulmonary impairment as 47.7% as per the study by Chushkin and Ots.[3] The other parameters considered for sample size calculation were 11% absolute precision and a 95% confidence level. The required sample size as per the above-mentioned parameters was 80. To account for a non-participation rate of 5%, another four subjects were added to the sample size. Hence, the final required sample size was 84.

Statistical methods

Spirometry parameter such as FVC, FEV1, FEVI/FVC, and MEF and DLCO was considered as the primary outcome variable. Lag time (in days) was considered the primary explanatory variable. ANOVA was used to assess statistical significance. The association between explanatory variables and categorical outcomes was assessed by cross-tabulation and comparison of percentages. The Chi-square test was used to test statistical significance. $P<0.05$ was considered statistically significant. coGuide version V.1.0 was used for statistical analysis.[4]

RESULTS

A total of 85 subjects were included in the final analysis.

Among the study population, the mean age was 49.44 years. Among the participants, the DLCO severity showed that 35 (41.18%) had mild, 23 (27.06%) moderate, 12 (14.12%) had normal, and 15 (17.65%) had severe DLCO, respectively. The mean lag time was 52.94 days in the study population. The mean duration of after treatment was 15.45 years in the study population (Table 1).

There was a statistically significant difference across study groups (classified based on lag time) in lung function such as FVC%, FEV1, FEVI/FVC, MEF, DLCO, and duration of after treatment ($P<0.05$). Out of 15 people with lag time 15–30 days, 26.67% had obstruction spirometry pattern. Out of 17 people with lag time 31–45 days, majority 52.94% had obstruction spirometry pattern. Out of 53 people with lag time >45 days, majority 62.26% had mixed pattern, followed by 24.53% had restriction spirometry pattern. The difference in small airway obstruction across the study groups was found to be significant with $P<0.001$ (Table 2).

DISCUSSION

In this study, there was a statistically significant difference across study groups (classified based on lag time) in spirometry values such as FVC%, FEV1, FEVI/FVC, MEF, DLCO, and duration of after treatment ($P<0.05$), indicating that increase in the lag time leads onto more impairment in the lung function. With high prevalence, the TB cure is also high, indicating a substantial population is cured of acute disease. The cured pulmonary TB survivors have residual structural and functional lung sequelae.[5-8] These sequelae have been recently identified and described in

Table 1: Summary of baseline parameters (n=85)

Parameter	Summary
Age (in years) (Mean±SD)	49.44±13.73 range (23–75)
Gender	
Male	53 (62.35%)
Female	32 (37.65%)
Spirometry parameter (Mean±SD)	
FVC% (n=76)	74.18±19.02 range (45–117)
FEV1% (n=76)	69.5±19.17 range (33–114)
FEVI/FVC (n=76)	72.07±9.28 range (48–86)
MEF 25–75% (n=76)	44.17±21.38 range (11–87)
Spirometry pattern	
Mixed pattern	33 (38.82%)
Obstruction	20 (23.53%)
Restriction	19 (22.35%)
Normal	13 (15.29%)
Small airway obstruction	66 (77.65%)
DLCO % (Mean±SD)	60.22±16.84 range (62–34)
DLCO severity	
Normal	12 (14.12%)
Mild	35 (41.18%)
Moderate	23 (27.06%)
Severe	15 (17.65%)
Lag time (days) (Mean±SD)	52.94±17.72 range (50–20)
LAG time (in days)	
15–30	15 (17.65%)
30–45	17 (20.00%)
>45	53 (62.35%)
Duration after treatment (years) (Mean±SD)	15.45±7.49 range (14–2)

DLCO: Diffusion capacity of lungs

Table 2: Comparison of baseline parameters across different lag time (in days) (n=85)

Parameter	Lag times (in days)			P-value
	15–30 (n=15)	31–45 (n=17)	>45 (n=53)	
Lung function (Mean±SD)				
FVC% (n=76)	94.5±26.62	83.4±13.97	67.49±14.38	<0.001†
FEV1% (n=76)	95.8±15.75	82.33±9.87	60.57±14.49	<0.001†
FEVI/FVC (n=76)	77.8±4.59	79.2±6.11	68.84±9.08	<0.001†
MEF 25–75% (n=76)	63.6±11.03	58±15.82	36.29±19.95	<0.001†
Spirometry pattern				
Mixed pattern	0 (0%)	0 (0%)	33 (62.26%)	*
Normal	9 (60%)	4 (23.53%)	0 (0%)	
Obstruction	4 (26.67%)	9 (52.94%)	7 (13.21%)	
Restriction	2 (13.33%)	4 (23.53%)	13 (24.53%)	
Small airway obstruction	6 (40%)	11 (64.71%)	49 (92.45%)	<0.001‡
DLCO % (Mean±SD)	75.8±20.65	68.12±15.36	53.28±11.46	<0.001†
DLCO severity				
Normal	8 (53.33%)	4 (23.53%)	0 (0%)	*
Mild	4 (26.67%)	8 (47.06%)	23 (43.4%)	
Moderate	2 (13.33%)	5 (29.41%)	16 (30.19%)	
Severe	1 (6.67%)	0 (0%)	14 (26.42%)	
Duration after treatment (years) (Mean±SD)	12.13±5.05	11.24±6.42	17.74±7.53	<0.001†

*No statistical test was applied – due to o subjects in the cells, †One-way ANOVA, ‡Chi-square test, DLCO: Diffusion capacity of lungs

the literature.[9,10] The detrimental effects caused due to the post-cure sequelae also add to the morbidity caused due to TB.[11-13] Determining the negative health impacts of the disease play an important role in the planning of control actions.

This study aimed to determine the impact of lag time on PTB sequelae patients. Among the 85 PTB sequelae patients, the duration after ATT was 15.45±7.49 years. The abnormalities and the derangement in lung function can be identified by pulmonary function tests (PFTs). PFTs show altered patterns of abnormalities, which are useful in the diagnosis of various respiratory diseases. The most commonly used lung function measurement is spirometry. It measures lung volumes against time.[14] The spirometry values of the study participants showed that 33 (38.82%) had a mixed pattern, 23.53% had an obstruction, and 22.35% had restriction. The destruction of lung parenchyma caused due to PTB is by the mechanism up-regulating several processes and also by deregulating protease control. Histopathological abnormalities after completion of treatment for PTB include cavitation, fibrosis, bronchiectasis, and calcification. Lung function impairment is related to long-term respiratory symptoms, in turn affecting the quality of life.[15] A study by Lee et al., showed that the increase in the severity of the PTB sequelae leads to falling in the FEV1 and FVC, indicating impaired lung functions.[16] The obstructive features in this present study may be due to the loss of elasticity of the bronchial wall components. A similar observation was made by Roberts et al., who the study compared the computer tomography findings with spirometry.[17] Patients of PTB, after completion of the full course of ATT, have chest radiographs revealing inactive lesions. These lesions are responsible for respiratory disability by causing impairment and decline in pulmonary function.

The mean lag time between the onset of symptoms and diagnosis of TB among the participants was 52.94±17.72 days. The shortest lag time is 20 days and the longest is 50 days. A study by Ngahane et al.,[18] showed that the median duration of symptoms before TB diagnosis was greater in patients who were found to have lung function impairment than in patients without impairment. The cause for the delay in our study may be that majority of the participants had poor health education and belonged to rural villages with poor socioeconomic status, which decreased their health-seeking behavior. This increased lag time may be the cause of extensive pulmonary function derangement resulting in a restrictive or mixed pattern. The limitation of this present study is that it was done on small sample size and a single rural center experience. In a study on the long term, a larger sample from different socioeconomic strata is recommended to study the various other factors that affect the lag time.

CONCLUSION

PTB infection causes long-term post-treatment sequelae. The lag time between the development of symptoms and diagnosis of the disease plays a significant role in the post-treatment sequelae. Hence, an early clinical diagnosis which reduces the lag time should be made to reduce the morbidity caused due to the disease.

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ETHICS STATEMENT

The study was approved by the Institutional Human Ethics Committee and Institutional Review Board. Data confidentiality was maintained. Written informed consent was obtained from the patients.

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Authors Contribution:
VV- Conceptualized the study and played primary role in compiling, analysis and interpretation of the data; **SS, RR, JV, VV, VP-** All the drafts were prepared, reviewed and final draft was approved; **SS, RR, JV, VV, VP-** Contributed in fine tuning of the proposal, contributed in data collection and entry. Reviewed the results and contributed to preparation and review of drafts. All the authors have read and approved final version of the manuscript. All the authors take complete responsibility for the content of the manuscript.

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Shri Sathya Sai Medical College and Research Institute, India.

Orcid ID:
Sreekaanth S - https://orcid.org/0000-0002-5591-0701
Ragulan Rajalingam - https://orcid.org/0000-0003-2926-6673
Jereen Varghese - https://orcid.org/0000-0003-1151-9492
Viswambhar V - https://orcid.org/0000-0002-9154-9626
Vidhya Priya - https://orcid.org/0000-0002-9303-5063

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