

Original Research Article

Serial pulmonary function test abnormality in tuberculous pleural effusion

Ayush Bansal^{1,2*}, Shekhar Trimbak Nabar²

¹Department of Medicine, Atal Bihari Vajpayee Institute of Medical Sciences and Dr. Ram Manohar Lohia Hospital, Connaught Place, New Delhi

²Department of Medicine, D.Y. Patil University, School of Medicine, Navi Mumbai, Maharashtra, India

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*Correspondence:

Dr. Ayush Bansal,

E-mail: drayushbansal@gmail.com

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ABSTRACT

Background: Pleural effusion is a common clinical problem that frequently causes dyspnoea and poor ventilatory function. In addition to fluid, pleural thickening, septations and calcifications can add to the functional deterioration of lungs. The drainage of pleural effusion is very effective in improving the functionality of lungs. Large volume pleural fluid tapping results in immediate hemodynamic improvement and relief from dyspnoea.

Methods: The aim of the present study was to estimate the impact of tubercular pleural effusion on the ventilatory function of the lungs and to find out the correlation between the effect of pleural tapping and functional effect on the lungs. The study comprised of thirty tubercular pleural effusion cases. They were observed for six months by doing serial chest X-rays and pulmonary function test.

Results: It was observed that tuberculous pleural effusion causes a restrictive abnormality and small airway obstruction. These abnormalities improve gradually over a period of six months when the patient is on anti-tubercular treatment. The role of any therapeutic intervention towards decreasing these lung function abnormalities will be subject of separate large-scale prospective study.

Conclusions: Functional defects and residual pleural thickening has no correlation with the initial severity of pleural effusion.

Keywords: Pulmonary function test, Residual pleural thickening, Restrictive abnormality, Tubercular pleural effusion

INTRODUCTION

The normal pleural space has only few milliliters of liquid, forming a film of about 10 mm thickness between the visceral and parietal pleural surfaces and it helps in lubricating the normal to and from motion of the lungs during breathing. Tuberculous pleural effusions are usually unilateral and can be of any size. The fluid is straw colored and at times hemorrhagic; it is an exudate with a protein concentration >50% of that in serum (usually ≈ four-six gm/dL), a normal to low glucose concentration, a pH of ≈

7.3 and detectable white blood cells (usually 500-6000/μl). Neutrophils may predominate in the early stage, but lymphocyte predominance is the typical finding later. Mesothelial cells are rare. Acid fast bacilli are seen on direct smear in only 10-25% of cases, but cultures may be positive for *Mycobacterium tuberculosis* in 25-75% of cases. The levels of Adenosine Deaminase (ADA), an enzyme found in most cells, are increased in tuberculous pleural effusions.

Different lung volumes and capacities which are helpful in understanding a pulmonary function test have been

depicted in Figure 1.¹ However, PFT in pleural effusion shows moderate restrictive abnormalities with mildly reduced diffusion capacity with mild hypoxemia and mild respiratory alkalosis, at presentation. The derangements in PFT are proportional to the severity of pleural effusion. After institution of Anti-Tubercular Therapy (ATT), radiological improvements occur much earlier, but the lung functions continue to improve for up to six months. Residual Pleural Thickening (RPT) has been found in about half of the patients treated in a number of studies.²⁻⁴ To help reduce the incidence of RPT and to facilitate recovery, therapeutic thoracentesis has been tried to obtain symptomatic improvement. In the present study, author proposed to assess, whether any restrictive PFT abnormality develops over a period of six months (i.e. their treatment period) and try to correlate such an abnormality with radiographic characteristics. The objectives of the present study were (i) to study the lung function abnormalities in diagnosed cases of tuberculous pleural effusion, (ii) to correlate the abnormalities if detected with the severity of pleural effusion and (iii) to correlate such abnormalities if detected with the radiological parameters and treatment.

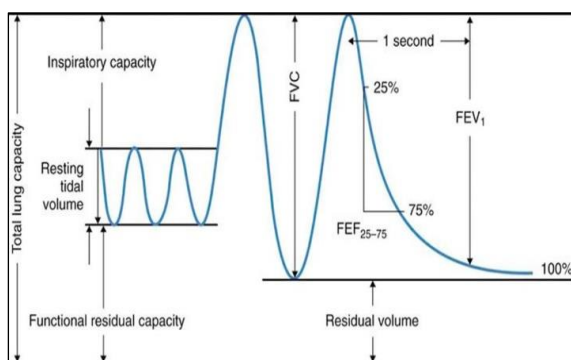


Figure 1: Spirogram with volumes and measurements; FEF_{25-75%}- forced expiratory flow at 25%-75% vital capacity, FEV₁- forced expiratory volume in one sec, FVC-forced vital capacity.

METHODS

The current study was a prospective observational study, where convenience sampling method was used. Ethical approval of the study was sought from ethical committee at D.Y. Patil University, School of Medicine, Navi Mumbai (Ethical Committee Approval No. PDDY PMC/ethics/dissent/8).

The inclusion or exclusion of tubercular patients in the study was based on different criterion defined below.

Inclusion criteria

- Age >12 years.
- A diagnosis of tuberculous pleural effusion based on clinical data, pleural fluid characteristics and radiological findings.

- Subjects willing to give consent for the study.

Exclusion criteria

- Age <12 years
- Patients already on ATT
- Smokers or any occupation which can cause restrictive diseases (farmers, coalmine workers)
- Those with chest deformity, heart diseases, gross obesity, diabetes mellitus, asthma, obstructive airway diseases, parenchymal pulmonary tuberculosis, non-tubercular pleural effusion.

Thirty patients, diagnosed as tuberculous pleural effusion, meeting the inclusion and exclusion criteria over a period from December 2013- March 2014 were followed up for a period of six months. A written informed consent was taken from all the participants before initiation of the study.

Study protocol

The patients selected for the study, were initially subjected to diagnostic and therapeutic pleural tap on admission. A post pleural tap chest X-ray was done. They were then started on 4 drugs ATT for two months (comprising of Isoniazid, Rifampicin, Ethambutol and Pyrazinamide), followed by a two-drug therapy for four more months (comprising of Isoniazid and Rifampicin). The patients were followed up with the serial chest X-rays, at completion of second and sixth months. The patients were also subjected to PFTs on admission (post-pleural tap) and then after sixth month. The pleural effusion was graded as follows,

- Mild- Just above the costophrenic angle till lower border of 5th rib
- Moderate- up to lower border of 3rd rib
- Severe- above the 3rd rib

RPT of >2 mm was considered to be radiologically abnormal.

Criteria for assessing the severity of abnormalities on PFT⁵

The abnormalities on PFT were characterized as obstructive and restrictive based on the following criterion.

Obstructive abnormality

This is interpreted when the FEV₁/FVC (Forced Expiratory Volume in 1st second/Forced Vital Capacity) ratio is below the normal range. The severity of the abnormality might be graded as follows:

"May be a physiological variant"	% Predicted FEV ₁ ≥100
"Mild"	% Predicted FEV ₁ <100 and ≥70
"Moderate"	% Predicted FEV ₁ <70 and ≥50

"Severe" % Predicted FEV₁ <50 and ≥34

Restrictive abnormality

This is most reliably interpreted on the basis of TLC (Total Lung Capacity). If this is not available, one may interpret a reduction in the VC (Vital Capacity) without a reduction of the FEV₁/FVC ratio. The severity of the abnormality might be graded as follows:

- "Mild" % Predicted FVC < lower limit of normal range but ≥70
- "Moderate" % Predicted FVC <70 and ≥50
- "Severe" % Predicted FVC <50 and ≥34

Statistical analysis

Comparison of different parameters in the study to establish statistical significance was done using ANOVA and Paired t-test.

RESULTS

In the present study, the severity of tubercular pleural effusion has been correlated with the lung function.

At the same time, the impact of therapeutic pleural fluid tapping, and ATT has been studied on the improvement of lung function.

Also, the restrictive abnormality in lung function has been correlated with RPT. The above-mentioned objectives have been discussed in detail in the following sections.

Lung function abnormalities in patients with tuberculous pleural effusion

In this study, author have found a significant restrictive abnormality in lung function. All the selected patients had an initial restrictive abnormality. They had an FVC% value of less than 80%.

The gradual improvement in the mean PFT parameters (restrictive abnormality and the small airway disease) over a period of 6 months of follow up. An interesting finding in this study was the presence of small airway disease. (Table 1)

This was manifested as an abnormal FEF_{25%-75%} (Forced Expiratory Flow from 25% to 75% of total expiration) (Table 1).

Table 1: Improvement in PFT parameters over time.

Visit	FVC	FVC%	FEV ₁	FEV ₁ %	FEV ₁ /FVC%	FEF _{25%-75%}
Reference value	3.35	-	2.70	-	79.93	3.89
Post- pleural tap	1.95	57.67	1.61	58.9	81.73	2.06
After 6 months	2.71	80.5	2.43	89.93	89.2	3.51

Table 2: Comparison of FVC (%) by chest X-ray findings at various intervals among patients.

Chest x-ray findings	Post-pleural tap FVC%		FVC% after 6-months	
	Mean	SD	Mean	SD
Severe effusion	-	-	-	-
Moderate effusion	61	-	-	-
Mild effusion	57.55	10.12	-	-
2-10 mm (RPT)	-	-	80.15	7.45
< 2 mm (RPT)	-	-	82.75	5.02
Total	57.67	9.97	80.5	7.22
ANOVA	F-value	1.3	F-value	0.42
	p-value	0.293	p-value	0.52
	Difference is not significant		Difference is not significant	

Correlation between restrictive abnormality with the severity of pleural effusion and the RPT was studied using analysis of variance (ANOVA) and the results for the same are tabulated in Table 2.

Since, p-values are >0.05, it meant that there is no statistical significance between FVC % and chest X-ray findings which implies that no relationship was observed between the initial severity of pleural effusion and the final restrictive abnormality (Table 2).

Correlation between PFT abnormalities (if detected) and severity of pleural effusion

Table 3 summarizes the severity of pleural effusion and the residual pleural thickening. 19 patients had severe pleural effusion on admission, while 11 had moderate pleural effusion. The serial chest x-rays showed that the RPT was radiologically significant in 26 of the 30 patients. Out of these 26 patients, 17 had severe effusion and nine had moderate effusion, initially. Also, out of the four patients who had RPT <2 mm after six months, two

had severe effusion and two had moderate effusion, initially. After two and six months, an incidence was found of 86% i.e., 26 of 30 patients had radiologically significant RPT (2 mm) (Table 3).

Significant improvement in PFT parameters has been seen in this study (p-values <0.05). Over a period of six months, FEV₁ improved from 58.9% to 89.9%, FVC from 57.6% to 80.5% and FEF_{25-75%} from 2.06 to 3.15 (Table 1, 4-6). The above tables show improvement in restrictive abnormality of the study population.

Table 3: Chest X-ray findings at follow-up visit.

Chest x-ray pa view		Pleural effusion			RPT		Total
		Severe	Moderate	Mild	2-10 mm	<2 mm	
Pre-pleural tap	No.	19	11	-	-	-	30
	%	63.33%	36.67%	-	-	-	100%
Post-pleural tap	No.		1	29	-	-	30
	%		3.33%	96.67%	-	-	100%
After 2 months	No.		-	-	26	4	30
	%		-	-	86.67%	13.33%	100%
After 6 months	No.		-	-	26	4	30
	%		-	-	86.67%	13.33%	100%

SD- standard deviation, ANOVA- Analysis of variance

Table 4: Comparison of FVC at different visits (paired 2-tailed t-test at 95% confidence interval; $\alpha=0.05$).

Comparison of FVC on follow up	Mean (n=30)	SD	t value	p value
Reference value	3.35	0.56	10.036	2.715 X 10 ⁻¹⁴
Post- pleural tap	1.96	0.493	Difference is significant	
Reference value	3.35	0.56	4.475	4.65 X 10 ⁻⁷
After 6 months	2.71	0.52	Difference is significant	
Post- pleural tap	1.96	0.493	-5.674	3.624 X 10 ⁻⁵
After 6 months	2.71	0.52	Difference is significant	

Table 5: Comparison of FEV₁ /FVC (%) at different visits (paired 2-tailed t-test at 95% confidence interval; $\alpha=0.05$).

Comparison of FEV ₁ /FVC (%) on follow up	Mean (n=30)	SD	t value	p value
Reference value	79.93	6.10	-0.94	0.35X10 ⁻³
Post- pleural tap	81.73	8.3	Difference is significant	
Reference value	79.93	6.10	6.018	1.27 X 10 ⁻⁷
After 6 months	89.2	5.61	Difference is significant	
Post- pleural tap	81.73	8.3	4.012	1.74 X 10 ⁻⁴
After 6 months	89.2	5.61	Difference is significant	

Table 6: Comparison of FEF_{25%-75%} at different visits (paired 2-tailed t-test at 95% confidence interval; $\alpha=0.05$).

Comparison of fef _{25%-75%} on follow up	Mean (n=30)	SD	T value	p value
Reference value	3.89	0.64	10.82	1.49 X 10 ⁻¹⁵
Post- pleural tap	2.06	0.65	Difference is significant	
Reference value	3.89	0.64	-4.23	8.36 X 10 ⁻⁵
After 6 months	3.15	0.75	Difference is significant	
Post- pleural tap	2.06	0.65	6.102	9.23 X 10 ⁻⁸
After 6 months	3.15	0.75	Difference is significant	

Correlation of lung function abnormalities (if detected) with radiological parameters and treatment

In this study, PFT done immediately after thoracentesis found a significant restrictive abnormality and it showed significant improvement on follow up. (Table 1). FEV₁% immediately after pleural tap was 58.9% and it improved to 89.93% after 6 months of ATT. Similarly, FVC% immediately after pleural tap was 57.67% and it improved to 80.5% after 6 months of ATT.

DISCUSSION

In patients with pleural effusion, studies have demonstrated restrictive lung functions and hypoxemia and their improvement after thoracentesis.⁶⁻⁸ But very few studies are available about the course of recovery of lung functions after institution of therapy. Yoo et al, studied only three patients; Altschule et al, studied eight patients and Estenne et al, studied nine patients.⁸⁻⁹ This study of 30 patients concluded that there is no effect of initial severity of pleural effusion on residual PFT abnormalities.

The incidence of RPT after ATT varies from one study to another. Lee et al, in his study had found a 10% incidence, Soler et al, had 72% and Barbas et al, had 52%.^{2,10,11} This wide variation in the incidence of RPT can be attributed to the lack of a uniform concept of RPT. We had decided on an RPT of more than 2 mm as radiologically significant (Table 3).

A study by Bhatia et al, has shown that pleural effusion has a ventilatory restrictive and small airway obstructive pattern on spirometry, as mean pre-treatment FEV₁, FVC and FEF_{25%-75%} were 63.14%, 51.06% and 50% respectively.¹³ After six months of treatment, FEV₁, FVC and FEF_{25%-75%} improved to 82%, 80.9% and 83.9% respectively. They had also found that the small airway disease improves while the restrictive abnormality persists, and the restriction had a relation with the severity of pleural effusion.

This study however differs from that of Bhatia et al in that, there was no relationship between severity of pleural effusion and restrictive abnormality (Table 2).¹² The small airway obstruction is a significant finding in the lung function tests. Endobronchial fibrosis in small airways as a result of tubercular parenchymal disease may be responsible for this. This suggests that tuberculous pleural effusion is no more a compartmentalized affection of the pleura, but also has some parenchymal component difficult to demonstrate clinically and radiologically.

A study done by Soler et al, had concluded that RPT is a consequence of an inflammatory mechanism.¹¹ Barbas et al, had also demonstrated that the presence of RPT was

not related to the chemotherapeutic regimen or the performance of a therapeutic thoracentesis.^{2,4,11} Also it was seen in the same study that approximately 50% of patients with tuberculous pleural effusion will have RPT when their therapy is completed, but one cannot predict which of the patients will have RPT from their clinical profile.⁴

Thus, it can be concluded that tuberculous pleural effusion causes a restrictive abnormality and small airway obstruction which showed tendency to improve over six months treatment period. These abnormalities have no relationship with the initial severity of pleural effusion or the RPT. The role of any therapeutic intervention towards decreasing RPT will be subject of separate large-scale prospective study.

CONCLUSION

The conclusions which could be drawn from our study are as follows:

- Tuberculous pleural effusion causes a restrictive abnormality and small airway obstruction.
- These abnormalities improve gradually over a period of six months when the patient is on ATT.
- These abnormalities also have no relationship with the initial severity of the pleural effusion or the RPT.

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Ethical approval: The study was approved by the Institutional Ethics Committee

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