

# An Analysis of the pH of Exhaled Breath Condensate and Its Correlation to Severity of Interstitial Lung Disease

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## 1. Introduction

The term *interstitial lung disease* (ILD), in general, implies the clinical manifestation of inflammatory-fibrotic infiltration of the alveolar walls resulting in detrimental effects on the capillary endothelium and the alveolar epithelial lining cells. A small numbers of interstitial macrophages, fibroblasts, and myofibroblasts reside within the interstitium. Other components of the interstitium include collagen-related macromolecules and the noncollagenous proteins such as fibronectin and laminin<sup>1</sup>.

Exhaled Breath Condensate (EBC) contains aerosolised airway lining fluid and volatile compounds that provide noninvasive indications of ongoing biochemical and inflammatory activities in the lung. EBC is a safe, non-invasive method that requires little or no processing. It is simpler than induced sputum collection, involving no more than tidal breathing into a collection device. Importantly it correlates well with other indices of airway inflammation, specifically induced sputum eosinophilia and neutrophilia. A low EBC pH is found during acute exacerbations of asthma, chronic obstructive pulmonary disease (COPD), and cystic fibrosis. Thus EBC pH holds promise in being used as a surrogate marker in place of invasive or more complicated attempts at assessment of airway inflammation, such as biopsy, bronchoalveolar lavage or induced sputum<sup>2</sup>.

Collection of EBC was first described in 1980 in the former Soviet Union, but has recently been revisited as a non-invasive means of analyzing properties of the lung<sup>3,4</sup> and the first article was published in 1980.

Exhaled breath condensate is now being used by centres throughout the world in an effort to gain insight into the airway environment in multiple lung diseases. It is a safe and simple procedure even in small children<sup>5</sup>.

## 2. Materials and methods

- This is a prospective observational study involving ILD patients subjected to Expiratory Breath Condensate Collection.
- Sample Size: 30 Cases of ILD and 30 controls (based on statistical records from the PFT lab)

- Material: Eco Screen Breath Condensate Machine, pH meter, ABG machine, Spirometer

Informed consent of all the participants of the study was obtained after the nature of the procedure and possible discomfort and risks which were fully explained.

Brief case history was taken. Any active infection was ruled out by ablood haemogram and chest radiograph. Exhaled breath condensate was collected using the Eco screen breath condensate machine. After exhaled breath condensate collection, pH was measured by an ABG machine within 5 minutes of collection without de-aeration. After exhaled breath condensate collection patients were asked to perform pulmonary function tests both pre and post bronchodilator. Values obtained for every age and sex group were cross-matched and analysed.



Eco-screen Breath Condensate machine

Figure 1: EBC machine

### 3. Results

- Of the 30 cases studied, 23 has a NSIP (nonspecific interstitial pneumonia) pattern on HRCT (high resolution computed tomography) [76.7%] and 7 had UIP (usual interstitial pneumonia) pattern [23.3%].

**Table 1:** Relation between FVC values as percent of predicted and pattern on HRCT

		HRCT Pattern		Total
		UIP	NSIP	
FVC [% of predicted]	>80	0	1	1
	60-80	5	12	17
	40-60	2	10	12
	<40	0	0	0
Total		7	23	30

- Out of 17 cases with FVC values above 60% of predicted, 11 had an EBC pH value of less than 7.45 [64.7%]. 9 cases out of 13 with FVC values of less than 60% predicted had an EBC pH value of greater than 7.45 [69.22%].

**Table 2:** Relation between EBC pH and FVC values as % of predicted

		FVC [% of predicted]				Total
		>80	60-80	40-60	<40	
EBC pH range	7.35-7.40	0	4	1	0	5
	7.40-7.45	0	7	3	0	10
	7.45-7.50	0	2	4	0	6
	>7.50	1	3	4	1	9
Total		1	16	12	1	30

- Of the 30 control subjects, 29 had an FVC value of greater than 80% of predicted [96.7%]. 22 of the 29 controls with FVC of greater than 80% predicted; had a pH value between 7.25 and 7.35 [75.8%].

**Table 3:** Correlation of EBC pH and FVC value as percent of predicted

		EBC pH grouping				Total
		<7.20	7.20-7.25	7.25-7.30	7.30-7.35	
FVC value [% of predicted]	>80	4	3	10	12	29
	60-80	1	0	0	0	1
Total		5	3	10	12	30

### 4. Discussion

Pulmonary function tests (PFTs) are used in conjunction with clinical, radiographic and histologic reports in assessing and assuring an accurate diagnosis of patients with ILD. On the other hand, in patients with appropriate symptoms, PFTs can serve as early diagnostic tools.

In a detailed analysis, Fulmer and colleagues provided a semiquantitative histologic description of 23 patients with IPF<sup>22</sup>. Although spirometry, lung volumes, and Diffusion lung capacity of Carbon Monoxide (DLCO) correlated poorly with histologic abnormality, exercise gas exchange (corrected for achieved Vo<sub>2</sub>), exhibited the best correlation with both fibrosis (on histology) and cellularity<sup>6</sup>.

There are three principal contributors to EBC<sup>7</sup>. First are variable-sized droplets that are aerosolized from the airway lining fluid. Second is distilled water that condenses from the gas phase out of the nearly water-saturated exhalate, which dilutes the aerosolized airway lining fluid. Third are water soluble volatile substances that are exhaled and absorbed into the condensing breath. The water-soluble volatile constituents are found in substantially higher concentrations and are therefore more readily assayed than the non-volatile compounds.

The study done by Alfredo Guillen-del Castillo et al<sup>8</sup> sought to demonstrate that systemic sclerosis (SSc)-related ILD might be mediated by an autoimmune inflammatory process in the lung, causing a release of cytokines and metabolites that could be measured noninvasively in EBC. In all the SSc patients studied, low EBC pH values were related to worse pulmonary function tests during 4 years of follow-up<sup>8</sup>.

In our study, of the cases with an FVC percentage of less than 60% of predicted value, only 1 case could perform the DLCO. It was found to be below normal value. This is in agreement with published literature and observations during daily practice as patients with lower FVC values are unable to perform the DLCO maneuver satisfactorily.

As demonstrated in this study, out of 17 cases with FVC values above 60% of predicted value, 11 had an EBC pH value of less than 7.45 [64.7%]. 9 cases out of 13 with FVC values of less than 60% predicted had an EBC pH value of greater than 7.45 [69.22%].

This shows that with a decrease in FVC value below 60% of predicted i.e. with progression of the ILD, the EBC pH value increased above 7.45.

This contradicts the findings of Alfredo Guillen-del Castillo, et al<sup>8</sup> who had found that with progression of ILD in SSc, the EBC pH decreased in value.

### 5. Conclusion

We found that with an increase in the severity of ILD on radiological investigations and symptomatology, the EBC pH increased in value.

This study was a pilot study with a small sample size and the methods used for measuring the pH of the EBC has to be considered as a confounding factor during interpreting the results.

Further detailed studies with a larger sample size are required for establishment of guidelines for the use of EBC pH as a prognostic factor in ILD patients.

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