THE VALUE OF BRONCHOALVEOLAR LAVAGE IN THE DIAGNOSIS AND MANAGEMENT OF SPECIFIC ILD IDIOPATHIC PULMONARY FIBROSIS

Methuku Narender¹, Laxmi Kumari Somishetty², Matta Bhashini³, Vavilala Satish Kumar Rao⁴, Auzumeedi Sai Kumar⁵, Subhakar Kandi⁶

HOW TO CITE THIS ARTICLE:
Methuku Narender, Laxmi Kumari Somishetty, Matta Bhashini, Vavilala Satish Kumar Rao, Auzumeedi Sai Kumar, Subhakar Kandi. “The Value of Bronchoalveolar Lavage in the Diagnosis and Management of Specific Ild Idiopathic Pulmonary Fibrosis”. Journal of Evolution of Medical and Dental Sciences 2015; Vol. 4, Issue 68, August 24; Page: 11813-11819, DOI: 10.14260/jemds/2015/1703

ABSTRACT: Diffuse parenchymal lung diseases (DPLD) encompasses a heterogeneous group of disorders, characterized by a spectrum of inflammatory and fibrotic changes affecting alveolar walls and air spaces. The onset, rate of progression and duration of symptoms are extremely variable, and presentations range from asymptomatic with long standing radiological changes to an acute onset of breathlessness. MATERIALS AND METHODS: Prospective study conducted on 30 patients admitted in Government general and chest hospital Hyderabad, All patients with clinical features and HRCT diagnostic of Idiopathic pulmonary fibrosis are included in the study. Study was done between February 2013 to December 2014. BAL was done based on ATS guidelines. RESULTS: Out of 30 patients, 19 were females and 11 were males. Out of 30 patients, 21 patients were having neutrophils as predominant cell type in BAL fluid, 6 patients were having lymphocytes as predominant cell type and 2 were having eosinophils and 1 patient was having macrophages as predominant cell type in BAL fluid. In patients with neutrophil predominant BAL fluid, 8 patients found to be having exclusively neutrophils and other cells were within normal limits and 5 were having raised lymphocytes, 5 were having raised eosinophils along with neutrophils and 3 patients were having both lymphocytes and eosinophils along with neutrophils. In patients with lymphocyte predominant BAL fluid, 1 patient is having exclusively raised lymphocytes and 5 patients were having raised neutrophils along with lymphocytes in BAL fluid. 2 patients were having exclusively raised eosinophils in BAL fluid. 1 Patient was found to be having macrophages as predominant cell type in BAL fluid along with raised neutrophils. CONCLUSIONS: BAL with fiber optic bronchoscopy is a safe procedure with a few minor complications. BAL cellularity in IPF patients shows neutrophil predominance. Lone Eosinophil predominance is seen only in patients with HRCT showing predominant honey comb pattern. KEYWORDS: Broncho Alveolar Lavage (BAL), Idiopathic Pulmonary Fibrosis (IPF), Interstitial Lung Disease (ILD).

INTRODUCTION: Diffuse parenchymal lung diseases (DPLD) encompasses a heterogeneous group of disorders, characterized by a spectrum of inflammatory and fibrotic changes affecting alveolar walls and air spaces. They comprise over 200 entities and include a wide spectrum of diseases, many uncommon and many of unknown etiology. The onset, rate of progression and duration of symptoms are extremely variable, and presentations range from asymptomatic with long standing radiological changes to an acute onset of breathlessness.

MATERIALS AND METHODS: It was a Prospective study conducted on 30 patients admitted in Government general and chest hospital Hyderabad, tertiary care center for pulmonary medicine from December 2014 to February 2015.
All patients of age >20 years with clinical features and HRCT diagnostic of Idiopathic pulmonary fibrosis are included in the study population. Patients who are unfit for diagnostic FOB and BAL, Seropositive HIV cases, Connective tissue diseases, Occupational diseases, Familial interstitial diseases are excluded from the study. 30 consecutive patients with HRCT chest picture diagnostic of IPF namely reticular, reticulo nodular and honeycombing pattern who attended outpatient department of pulmonary medicine, government general and chest hospital, Hyderabad between December 2011 and February 2013.

Approval from the institution’s ethical committee was obtained before commencement of study. All cases reported were thoroughly screened clinically, hematologically, biochemically and ECG wise a prebronchoscope work up was done. Olympus Company FOB with camera and monitor. BAL was done based on ATS guidelines Informed consent. Nil by mouth for at least 6 hours.

Reviewed radiographic images to determine ideal site of alveolar lavage Bronchoscope, collection trap, and tubing were well prepared before the procedure. Supplemental oxygen and monitoring equipment kept ready before the procedure. ECG, pulse-oximetry, BP cuff. Conscious sedation with a midazolam was given. Topical anesthesia with lidocaine with maximum limit of 5 mg/kg of bodyweight of 4% lidocaine was given.

Bronchoscope was advanced until wedged in a desired subsegmental bronchus at the desired location. 20mL of saline was infused with a syringe, observing the flow of saline at the distal tip of the bronchoscope. Maintaining wedge position, gentle suction (50-80mmHg) was applied collecting the lavage specimen in the collection trap. Up to total of 100-120 mL of normal saline was instilled and adequate specimen 40-60 mL - usually 40-70% of instillate was obtained. BAL specimen was sent for cellular and microbiological analysis. Patient was observed for a minimum of 1 hour after the procedure, with continued monitoring.

RESULTS: Total 30 consecutive patients with HRCT chest diagnostic of Idiopathic pulmonary fibrosis were taken in to present study. Out of 30 patients, 19 were females and 11 were males contributing, 63% and 37% of study population. Predominant age group in present study is 50 to 60 years contributing 40% of study population. Mean age of presentation is 54.03 years. Out of 30 patients, as majority were females, majority of patients were house wives contributing 40% of study population.

Out of 30 patients, 11 patients were exposed to smoke, contributing 36.66% of study population. Out of 30 patients 15 patients were having moderately severe restrictive disease contributing 50% of study population. Majority of patients in study population are having reticular and honey comb patterns as predominant pattern on chest x-ray, each pattern contributing 33.33%.

Out of 30 cases Reticular and reticulo nodular pattern seen in 18 patients contributing 60%, and honeycombing in 12 patients contributing remaining 40%. Out of 30 patients, 21 patients were having neutrophils as predominant cell type in BAL fluid, 6 patients were having lymphocytes as predominant cell type and 2 were having eosinophils and 1 patient was having macrophages as predominant cell type in BAL fluid.

Out of 21 patients, with neutrophil predominant BAL fluid, 8 patients found to be having exclusively neutrophils and other cells were within normal limits and 5 were having raised lymphocytes, 5 were having raised eosinophils along with neutrophils and 3 patients were having both lymphocytes and eosinophils along with neutrophils. Out of 6 patients, with lymphocyte predominant BAL fluid, 1 patient is having exclusively raised lymphocytes and 5 patients were having raised neutrophils along with lymphocytes in BAL fluid.
2 patients were having exclusively raised eosinophils in BAL fluid. 1 Patient was found to be having macrophages as predominant cell type in BAL fluid along with raised neutrophils. Out of 18 patients with predominant reticular and reticulonodular pattern, 14 were having neutrophils as predominant cells in BAL fluid and 3 were having lymphocytes as predominant cells and 1 patient is having macrophage as predominant cells in BAL fluid. Out of 12 patients with predominant honeycomb pattern, 7 were having neutrophils as predominant cells, 3 were having lymphocytes as predominant cells and 2 were having eosinophils as predominant cells in BAL fluid.

**DISCUSSION:** Bronchoalveolar lavage with Fiberoptic bronchoscopy is a safe technique which is useful in the diagnosis of certain forms of ILDs. Cellular pattern of BAL fluid in IPF patients helps in excluding other diagnoses and helps in prognostication of patients. Cytological pattern in BAL fluid may play a role in deciding treatment strategy. So every case of IPF should be subjected for BAL.

Idiopathic pulmonary fibrosis is a progressive fibrosing inflammatory disease of the lungs of unknown etiology. It affects males more than females, which is approximately twice common in males. The mean age in the largest survey reported being 67 years. However it may occur in either sex at any age. In the present study incidence regarding gender is reverse (F>M) and the disease occurred at much earlier age i.e. 5th decade instead of 7th decade as in western world and mean age being 54 years. These variations of findings could be due to geographical, racial distribution and increased median survival in the developed countries.

Though in the present study both sexes presented earlier compared to the west, yet it is similar to the study published by Maheshwar IU et al and Rasul et al. Study done by Rasul et al also got similar results with female predominance. However study population is small to draw any conclusions regarding gender prevalence. 36% of study group were exposed to smoke, which is a risk factor for IPF. As studies have stated welding and farming are risk factors for IPF, In our study, we found 6.66% of study population consisting of welders and 13.33% consisting of farmers. But sample size is small to make any conclusions. In Chest x-ray 94% of patients were having abnormalities. HRCT is a gold standard for diagnosing IPF and it obviates need for surgical lung biopsy. In present study group reticular and reticulonodular pattern is predominantly seen involving both lungs. PFT is showing restrictive disease in all patients of IPF. According to Schwartz DA et al and other studies neutrophils and eosinophils were predominant cell types in IPF.

In present study neutrophil followed by lymphocyte predominance is seen in BAL fluid. Majority of patients i.e., more than 50% of patients BAL fluid showing neutrophil predominance. All patients with neutrophil predominant BAL fluid were detected to be negative for microorganisms. Neutrophil count being >5%. Greater than 90% of patients with BAL fluid lymphocyte predominant cell type, were having lymphocyte count <15%. Exclusive eosinophil predominance was found to be seen only in patients with honeycomb pattern. Mixed pattern is seen in patients with both reticular, reticulonodular and honeycomb patterns on HRCT.

Several retrospective longitudinal studies suggest a median survival time from 2 to 3 years from the time of diagnosis. As study was conducted for 1 year 10 months, it is difficult to conclude regarding prognosis of patients of IPF based on BAL cellularity. But Haslam PL et al and Rudd RM et al showed that BAL fluid neutrophils and eosinophils carry a poor prognosis.

So further follow up of patients is required. BAL procedure is a safe procedure with few minor complications like transient fever, cough. In present study procedure was uneventful in almost all patients.
CONCLUSIONS: BAL with fiber optic bronchoscopy is a safe procedure with a few minor complications. There is an early presentation in both genders, almost a decade earlier compared to the West. Smoking is a risk factor for IPF. PFT shows Restrictive pattern in all patients of IPF. HRCT is a gold standard for the diagnosis of IPF. BAL cellularity in IPF patients shows neutrophil predominance. Lone Eosinophil predominance is seen only in patients with HRCT showing predominant honey comb pattern.

| Sl. No. | Sex  | Total | Percentage |
|--------|------|-------|------------|
| 1.     | Female | 19    | 63.3%      |
| 2.     | Male   | 11    | 36.66%     |
|        | **Grand Total** | **30** |          |

Table 1: Sex Distribution of Patients

| Age   | MALE | FEMALE | Grand Total and Percentage |
|-------|------|--------|---------------------------|
| 20 to 30 | 1    | 1      | 2 (6.66%)                 |
| 30 to 40 | 2    | 1      | 3 (10%)                   |
| 40 to 50 | 2    | 2      | 4 (13.33%)                |
| 50 to 60 | 3    | 9      | 12 (40%)                  |
| 60 to 70 | 2    | 4      | 6 (20%)                   |
| 70 to 80 | 1    | 2      | 3 (10%)                   |
| **Grand Total** | **11** | **19** | **30**                   |

Table 2: Demographic Data of Subjects

| Sl. No. | Occupation                        | No. of Patients |
|--------|-----------------------------------|-----------------|
| 1.     | Daily labourer                     | 10              |
| 2.     | House wife                         | 12              |
| 3.     | Business men                       | 2               |
| 4.     | Welding (Exposure to toxic fumes) | 2               |
| 5.     | Farmer                             | 4               |

Table 3: Occupation

| Sl. No. | Exposure to Smoke | Total | Percentage |
|--------|-------------------|-------|------------|
| 1.     | No                | 19    | 63.33%     |
| 2.     | Yes               | 11    | 36.66%     |
| **Grand Total** | **30**          |       |            |

Table 4: Exposure To Smoke
### Table 5: PFT

| Sl. No. | PFT Pattern                          | No. of Patients and Percentage |
|---------|--------------------------------------|-------------------------------|
| 1.      | Mild (70 to 80% of FVC) restriction   | 4 (13.33%)                    |
| 2.      | Moderate (60–69% of FVC) restriction  | 7 (23.33%)                    |
| 3.      | Moderate severe (50 to 59% of FVC) restriction | 15 (50%)                        |
| 4.      | Severe (35 to 50% of FVC) restriction | 2 (6.66%)                      |
| 5.      | Mixed                                | 2 (6.66%)                      |

### Table 6: Chest X-Ray

| Sl. No. | Chest X-ray pattern   | Number of patients and percentage |
|---------|-----------------------|----------------------------------|
| 1.      | Normal                | 2 (6.66%)                        |
| 2.      | Reticular             | 10 (33.33%)                      |
| 3.      | Reticulo nodular      | 4 (13.33%)                       |
| 4.      | Micronodular          | 4 (13.33%)                       |
| 5.      | Honeycombing          | 10 (33.33%)                      |

### Table 7: HRCT Chest

| Sl. No. | HRCT pattern                        | No. Of Patients and Percentage |
|---------|-------------------------------------|-------------------------------|
| 1.      | Reticular and Reticulonodular       | 18 (60%)                      |
| 2.      | Honeycombing                        | 12 (40%)                      |
|         | **Grand Total**                     | **30**                        |

### Table 8: BAL Cellularity

| Sl. No. | Cellular Pattern  | No. of Patients and Percentage |
|---------|-------------------|-------------------------------|
| 1.      | Neutrophils       | 21 (70%)                      |
| 2.      | Lymphocytes       | 6 (20%)                       |
| 3.      | Eosinophils       | 2 (6.67%)                     |
| 4.      | Macrophages       | 1 (3.34%)                     |
|         | **Total**         | **30**                        |

### Table 9: Correlation of HRCT Features With BAL Cellularity

| Sl. No. | HRCT features                         | Neutrophils | Lymphocytes | Eosinophils | Macrophages |
|---------|---------------------------------------|-------------|-------------|-------------|-------------|
| 1.      | Reticular and reticulonodular         | 14          | 3           | 0           | 1           |
| 2.      | honeycombing                          | 7           | 3           | 2           | 0           |

---

**TOTAL**: 30
REFERENCES:

1. American Thoracic society/European Respiratory Society (ERS) International Multidisciplinary Consensus Classification of the idiopathic interstitial pneumonias: Am J Respir Crit Care Med 2002; 165:277-304.

2. British Thoracic Society: The diagnosis, assessment and treatment of diffuse parenchymal lung disease in adults. Thorax 1999; 54 (suppl 1):S1-S28.

3. Collard HR, King TE, Jr., Bartelson BB, Vourlekis JS, Schwarz MI, Brown KK. Changes in clinical and physiologic variables predict survival in idiopathic pulmonary fibrosis. Am J Respir Crit Care Med 2003; 168:538-542.

4. Green FH. Overview of pulmonary fibrosis. Chest. 2002; 122:334S-339S.

5. Schwartz DA, Van Fossa DS, Davis CS, Helmer RA, Dayton CS, et al. Determinants of progression in idiopathic pulmonary fibrosis. Am J Respir Crit Care Med 1994; 149: 444 – 449.

6. Johnston IDA, Procott RJ, Ehalmes JE, Rudd RM, British Thoracic Society study of Cryptogenic Fibrosing Alveolitus, Current presentation and initial management. Thorax 1997; 52: 38.

7. Maheshwari U, Gupta D, Aggarwal AN, Jindal SK. Spectrum and Diagnosis of Idiopathic Pulmonary Fibrosis. Indian J Chest Dis Allied Sci 2004; 46:23-6.

8. Gender Differences in Clinical Presentation of Idiopathic Pulmonary Fibrosis at Lahore, Pakistan Rasul S.,1 Khalid M.C.,2 Imran N.,3 Khan S.U.,4 Younus M.

9. Hunninghake GW, Zimmerman MB, Schwartz DA, King TE Jr; Lynch JP III, Hegele R, Waldron J, Colby T, Muller N, Lynch D, et al. Utility of a lung biopsy for the diagnosis of idiopathic pulmonary Fibrosis. Am J Respir Crit Care Med 2001; 164:193–196.

10. Kathy B. Baumgartner,1 Jonathan M. Samet,2 David B. Coultas,1 Christine A. Stidley,3 William C. Hunt,1 Thomas V. Colby,4 James A. Waldron,5 and Collaborating Centers. Occupational and Environmental Risk Factors for Idiopathic Pulmonary Fibrosis: A Multicenter Case-Control; American Journal of Epidemiology 2000: Vol. 152, No. 4

11. Hansell DM, Bankier AA, Macmahon H, mcloud TC, Muller NL, Remy J. Fleischner Society: Glossary of terms for thoracic imaging. Radiology 2008; 246:697–722.

12. Schwartz DA, Helmers RA, Dayton CS, Merchant RK, Hunninghake GW. Determinants of bronchoalveolar lavage cellularity in idiopathic pulmonary fibrosis. J Appl Physiol (1985). 1991 Nov; 71(5):1688-93.

13. Nicholson AG, Colby TV, Dubois RM, Hansell DM, Wells AU. The prognostic significance of the histologic pattern of interstitial pneumonia in patients presenting with the clinical entity of cryptogenic Fibrosingalveolitis. Am J Respir Crit Care Med 2000; 162:2213-2217.

14. King TE, Jr., Schwarz MI, Brown K, Tooze JA, Colby TV, Waldron JA, Jr., Flint A, Thurlbeck WM, Cherniack RM. Idiopathic pulmonary fibrosis. Relationship between histopathologic features and Mortality. Am J Respir Crit Care Med 2001; 164:1025-1032.

15. Haslam PL, Turton CW, Lukoszek A, Salisbury AJ, Dewar A, Collins JV, Turner-Warwick M. Bronchoalveolar lavage fluid cell counts in cryptogenic fibrosingalveolitis and their relation to therapy. Thorax. 1980 May; 35(5):328–339.

16. Rudd RM, Haslam PL, Turner-Warwick M. Cryptogenic fibrosingalveolitis. Relationships of pulmonary physiology and bronchoalveolar lavage to response to treatment and prognosis. Am Rev Respir Dis. 1981 Jul; 124(1):1-8.
**AUTHORS:**
1. Methuku Narender
2. Laxmi Kumari Somishetty
3. Matta Bhashini
4. Vavilala Satish Kumar Rao
5. Auzumeedi Sai Kumar
6. Subhakar Kandi

**PARTICULARS OF CONTRIBUTORS:**
1. Associate Professor, Department of Pulmonary Medicine, Guntur Medical College, Guntur, Andhra Pradesh.
2. Assistant Professor, Department of Pulmonary Medicine, Guntur Medical College, Guntur, Andhra Pradesh.
3. Senior Resident, Department of Pulmonary Medicine, Guntur Medical College, Guntur, Andhra Pradesh.
4. Assistant Professor, Department of Pulmonary Medicine, Osmania Medical College, Hyderabad.
5. Professor and HOD, Department of Pulmonary Medicine, Osmania Medical College, Hyderabad.
6. Professor, Department of Pulmonary Medicine, Osmania Medical College, Hyderabad.

**FINANCIAL OR OTHER COMPETING INTERESTS:** None

**NAME ADDRESS EMAIL ID OF THE CORRESPONDING AUTHOR:**
Dr. Methuku Narender,
Associate Professor,
Department of Pulmonary Medical College,
Guntur Medical College,
Guntur, Andhra Pradesh.
E-mail: naren.1967@hotmail.com

**Date of Submission:** 06/08/2015.
**Date of Peer Review:** 07/08/2015.
**Date of Acceptance:** 18/08/2015.
**Date of Publishing:** 21/08/2015.