ORIGINAL RESEARCH PAPER

Volume-8 | Issue-2 | February-2019 | PRINT ISSN No 2277 - 8179

INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

# VARIED IMAGING MANIFESTATIONS OF INTERSTITIAL PNEUMONIA WITH AUTOIMMUNE FEATURES : AN OBSERVATIONAL STUDY

**Radiology**

**Dr Vidiyala Pujitha** Post Graduate Student In Md Radiology Nizam's Institute Of Medical Sciences Hyderabad.

**Dr Anu Kapoor*** MD,DNB(RD),CSST(UK),MNAMS Additional Professor, Department Of Radiology & Imageology Nizam's Institute Of Medical Sciences *Corresponding Author

**Dr N. Narendra Kumar** MD (RM), Associate Professsor Department Of Respiratory Medicine Nizam's Institute Of Medical Sciences

## ABSTRACT

**INTRODUCTION :**Interstitial lung diseases (ILDs) are a heterogeneous group of disorders characterized by inflammation and fibrosis of the lungs. Most of the patients with idiopathic interstitial pneumonia have clinical features that suggest an etiology of underlying autoimmune process but do not meet established criteria for a connective tissue disease . These patients occupy a gray zone between the Idiopathic interstitial pneumonia and connective tissue disease related ILD. European Respiratory Society/American Thoracic Society proposed the term "Interstitial pneumonia with autoimmune features" (IPAF) to describe these subset of patients who have underlying autoimmune basis for etiology but do not meet the diagnostic criteria of connective tissue diseases. . The present study describes the varied imaging manifestations of Interstitial pneumonia with autoimmune features with their clinical and serological correlation.

**MATERIALS AND METHODS** :The present study was a prospective observational study conducted in the Department of Radiology & Imageology at the Nizam's Institute of Medical Sciences, Hyderabad between May 2017 and October 2017. Patients referred to our department with clinical suspicion of ILD were evaluated using HRCT chest and the various patterns of ILD were analyzed in these patients. HRCT results were correlated with clinical and serological studies.

**RESULTS :**Our study group included a total of 14 patients with age range from 20-78 years (mean,49.5 years).The overall incidence of IPAF was noted to be higher in females with female : male ratio of 6:1.Most common clinical domain in our study was inflammatory polyarthritis. ANA positivity (1:320) was the most common serological finding observed in our study group. The most common radiological pattern of interstitial lung disease encountered in our study was NSIP (57.2%), followed by typical UIP (28.6%), Organizing pneumonia (7.1%) and Combined pulmonary fibrosis and emphysema (7.1%). Our associated findings included were pulmonary arterial hypertension in 35.8% cases, significant mediastinal lymphadenopathy in 14% of cases and dilated esophagus in 50% cases.

**CONCLUSION :** This study demonstrates that the recently defined criteria for IPAF are fulfilled by a significant proportion of patients referred for imaging evaluation of ILD. Radiologist may be the first person to identify this subset of patients as all of them present with ILD at the time of diagnosis and based on the HRCT patterns an autoimmune basis for underlying etiology can be suggested. HRCT plays an important role in establishing the diagnosis in these patients as it is one of the major domain in the classification criteria of IPAF as proposed by European Respiratory Society/American Thoracic Society.

## KEYWORDS

Combined pulmonary fibrosis and emphysema, IPAF, Interstitial pneumonia with autoimmune features, Non specific interstitial pneumonia,organizing pneumonia, Usual interstitial pneumonia.

## INTRODUCTION :

Interstitial lung diseases forms a group of heterogenous lung disorders which affect the pulmonary interstitium (1) and are characterized by inflammation and fibrosis of the lung parenchyma (2). Interstitial lung diseases include a wide spectrum of disorders from Idiopathic interstitial pneumonia to the secondary variants commonly associated with connective tissue diseases. For diagnosing ILD as Idiopathic interstitial pneumonia all the underlying etiological factors needs to be ruled out such as environmental exposure to organic and inorganic dust, connective tissue diseases, medication intake etc. Identifying an underlying etiology is important from the clinical perspective as it has impact on the treatment. Some of the Interstitial lung diseases occupy the gray zone between idiopathic interstitial lung disease and interstitial lung disease associated with connective tissue diseases. The European Respiratory Society/American Thoracic Society proposed the term "Interstitial pneumonia with autoimmune features" (IPAF) to describe these subset of patients who have underlying autoimmune basis for etiology but do not meet the diagnostic criteria of connective tissue diseases (3). HRCT plays an important role in diagnosing these subset of patients as it has been included in the major domain in the classification criteria proposed by ERS for IPAF.

According to the existing literature (3) the radiological patterns of IPAF include Usual interstitial pneumonia, Non specific interstitial pneumonia, Lymphoid interstitial pneumonia,Organizing pneumonia like features. These patterns are commonly found in CTD-ILD, and their presence should raise the suspicion for an underlying autoimmune process. Multicompartment involvement with pulmonary arterial hypertension, pleural and pericardial effusions are described in the classification criteria. Features of intrinsic airway disease such as airway obstruction, bronchiolitis and bronchiectasis are also included in the list of imaging findings.

The purpose of the present study was to describe the varied imaging manifestations of IPAF as seen on HRCT and to correlate them with clinical and serological findings.

## MATERIALS AND METHODS :

The present study was a prospective observational study conducted in the Department of Radiology & Imageology at the Nizam's Institute of Medical Sciences, Hyderabad between May 2017 and October 2017. Patients referred to our department with clinical suspicion of ILD were evaluated using HRCT chest and the various patterns of ILD were analyzed in these patients. HRCT results were correlated with clinical and serological studies.

## DATA COLLECTION METHODS AND ASSESSMENT :

A standard proforma was used to systematically collect data from the medical files (printed and electronic). Data collected included demographic information (age, race/ ethnicity, sex), information regarding drug usage such as Amiadarone, Methotrexate, Nitrofurantoin and anti cancer drugs and environmental, occupational exposure to organic and inorganic dust. Patients clinical records are carefully evaluated for the presence of autoimmune features such as rash, joint pains, raynaud's phenomenon, telangectesias, gottron's patches, mechanic hands etc which were included in the clinical domain of IPAF classification. Serologic autoantibody testing which was performed as part of a standardized clinical evaluation was analyzed . Laboratory studies included antinuclear antibody (ANA) with immunofluorescence pattern and titers, rheumatoid factors (RF) (considered significant if titer ≥2 x upper limit of normal),cyclic

citrullinated protein antibody, myositis-specific antibodies, anti-Ro/Anti-Sjögren's-syndrome-related antigen A (SSA) antibody, anti-La/SSB antibody, anti-ribonucleoprotein (RNP) antibody, anti-Smith antibody and anti-Scl-70 antibody.

**IMAGING WORKUP:**

HRCT of the chest was performed in all cases using 16 slice MDCT (Brilliance 16,Philips medical systems, Cleveland, USA).Imaging was performed in supine position with breath holding at maximum inspiration. Contiguous axial sections of 1mm slice thickness from apices of lung to costo phrenic angles were taken. Parameters of 120Kv, tube current of 200mAs, FOV of 300.00mm, rotation of 0.5seconds were used. Additional evaluation by CECT/prone/expirato ry CT of thorax were performed wherever indicated. Each scan was interpreted by two expert thoracic radiologists at our centre , and HRCT patterns were classified for each patient as one or more of the following:

a. Usual interstitial pneumonia (UIP)
b. Non-specific interstitial pneumonia (NSIP)
c. Organizing pneumonia (OP)
d. Combined pulmonary fibrosis and emphysema ( CPFE)

Based on a combination of clinical, serologic, radiologic or pathologic features, each patient was found to have an autoimmune basis for their ILD.

**RESULTS :**

The mean age of our study population was 49.5 years with age range from 20 to 78 years. Our study group comprised 14 patients out of which 12 were females and 2 were males with female : male ratio of 6:1. All the patients in our study had presenting complaints of cough and shortness of breath for which they were subjected to HRCT Chest for further evaluation. Cough in all the patients was dry type not associated with sputum production or occasionally associated with scanty sputum. Dyspnea was of exertional type, aggravated with work. A detailed clinical history and physical examination was performed in all the cases by the physician and patients medical records were analysed for the presence of symptoms or signs which constituted the clinical domain. Most common clinical domain in our study was inflammatory polyarthritis with early morning stiffness which was present in 50% patients (n=7) followed by Raynaud's phenomenon which was seen in one case (n=1). In six patients ( 42.8%) no symptoms or signs pertaining to clinical domain were observed. In the present study ANA positivity (1:320) was the most common serological finding observed followed by Rheumatoid factor positivity(>2times normal value).

The radiological patterns of interstitial lung disease encountered in our present study were Non specific interstitial pneumonia (NSIP), Usual interstitial pneumonia (UIP), organizing pneumonia (OP) and Syndrome of Combined Pulmonary fibrosis and emphysema (CPFE). Out of the above mentioned radiological patterns, the most common HRCT pattern encountered was NSIP which accounted for 8 cases (57.2% ) including 7 females and 1male. Second most common HRCT pattern was Typical UIP , which is seen in 4 cases (28.6%). Organizing pneumonia pattern was seen in 1 case(7.1%) .Syndrome of Combined Pulmonary fibrosis and emphysema (CPFE) was seen in 1 male (7.1%).

In majority of cases of NSIP, the distribution was bilaterally symmetric with lower lobe predominance. Spectrum of imaging findings in NSIP in our study included diffuse ground glass opacities with interstitial thickening, traction bronchiectasis and bronchiolectasis. All the cases of Typical UIP pattern showed reticulation with honey combing (100%) with subpleural predominance of interstitial thickening and apicobasal gradient with lower lobe predominance. Honey combing was seen in 100% of cases. In our study we encountered one case of organizing pneumonia with patchy areas of bilateral air space consolidation predominantly in the subpleural and peribronchial distribution. One patient was diagnosed as a case of CPFE with a UIP pattern of ILD showing apicobasal gradient and lower lobe predominant subpleural interstitial thickening and honey combing associated with paraseptal emphysema with subpleural bullae . Pulmonary arterial hypertension was seen in 35.8% cases. Significant mediastinal lymphadenopathy is seen in 14% of cases. Associated finding of dilated esophagus was seen in 7 out of 14 cases (50% cases).

**DISCUSSION :**

Our study group comprised of 14 cases of IPAF . The mean age of our study population was 49.5 years with age range from 20 to 78 years. A study done by Sandra et al (4 ) had a mean age of 54.6 + 10.3 years which is similar to our study. Our study comprised of 12 females ( 85.7% ) and 2 males (14.3 %). Majority of the patients in our study are females. Studies done by Sandra et al ( 4 ) , Oldham et al (5 ) and Rahul Sharma et al (6) also show female preponderance in IPAF similar to our study. Existing knowledge of IPAF indicates a female dominance as is seen in most autoimmune disorders.

Most common clinical domain in our study was inflammatory polyarthritis with early morning stiffness followed by Raynaud's phenomenon. We hypothesize that these signs are generally recognized by clinicians as strongly suggestive of CTD, and therefore when present in patients with ILD should prompt the diagnosis of IPAF.

The most common HRCT pattern of ILD in our study encountered was NSIP which accounted for 8 cases (57.2%) including 7 females and 1male. Second most common HRCT pattern was that of Typical UIP, which was seen in 4 cases (28.6%). Organizing pneumonia pattern was seen in 1 case(7.1%). Syndrome of Combined Pulmonary fibrosis and emphysema (CPFE) was seen in 1 male(7.1%). In a retrospective study conducted by Kais Ahmad et al (7 ) in 2016, out of 57 patients who met the IPAF criteria in their study, the most common HRCT pattern was NSIP (53%) followed by UIP pattern ( definite or possible ) in 28% of patients of which 4 cases had syndrome of Combined pulmonary fibrosis and emphysema and an overlap of NSIP and OP in 20% of cases.

**Radiological findings suggesting the diagnosis of NSIP in our study :**

In majority of cases of NSIP, lower lobe predominance of ILD was observed. The disease was bilaterally symmetrically in 7 cases of NSIP, however in one case asymmetric involvement of right lung was noticed. Ground glass opacity a salient feature of NSIP and it was seen in all the cases of NSIP. Traction bronchiectasis or bronchiolectasis is almost universal in patients with fibrotic NSIP and is related to underlying fibrotic changes. In our study it was seen in 4 cases of NSIP. Subpleural sparing which is classical for NSIP was seen in 10 cases in our study.

**Radiological features suggesting the diagnosis of UIP in our study :**

All the cases of Typical UIP in our study showed reticulation with honey combing (100%) with subpleural predominance of interstitial thickening, apicobasal gradient with lower lobe predominance.

**Radiological features suggesting the diagnosis of Organizing pneumonia :**

Only one case with organizing pneumonia was noted in our study and present with patchy bilateral air space consolidation with peribronchial and subpleural distribution. Significant mediastinal lymphadenopathy was also noted in this case in the absence of any associated features.

**Radiological findings suggesting the diagnosis of Combined Pulmonary Fibrosis And Emphysema :**

We encountered 1 case of CPFE with UIP pattern of ILD showed apicobasal gradient and lower lobe predominant subpleural interstitial thickening and honey combing along with paraseptal emphysema in both upper lobes. This patient had a history of smoking and ANA positivity. CPFE pattern in IPAF was described in only one study in literature which was conducted by Kais Ahmad et al. They encountered 4 cases of combined pulmonary fibrosis and emphysema in their study.

In our study 35.7% of cases showed evidence of pulmonary arterial hypertension with a mean main pulmonary arterial diameter of 31.7 mm.

Significant mediastinal lymphadenopathy is considered when the short axis diameter is more than 10mm. In 14.3% of our cases there was significant lymphadenopathy. 57 % cases showed subcentimetric lymphadenopathy and in 28.7% cases there was no lymphadenopathy. In our study significant lymphadenopathy was seen in organizing pneumonia and NSIP patterns of ILD. The presence of lymphadenopathy in ILD is well described in the literature and

attributed to evoked inflammatory response. In a study by Warrik et al ( 8 ) ,the cause of lymphadenopathy in ILD patients was due to lymphoid hyperplasia evoked by chronic inflammatory process.

## LIMITATIONS :

- Small sample size and short duration of the study
- No surgical lung biopsy , histopathology conformation.
- Limited follow-up data available in our patients at the time of the analysis precludes conclusions on long-term prognosis of IPAF.

## CONCLUSION :

Interstitial pneumonia with autoimmune features (IPAF) is a term which describes a subset of ILD patients with clinical features and auto antibodies suggestive of a connective tissue disease but do not meet the criteria of CTD. European Respiratory Society/American Thoracic Society research proposed that individuals with interstitial pneumonia, and a combination of certain clinical, serologic, and/or morphologic features that raise suspicion for the presence of an underlying systemic autoimmune disease, be labelled as having "interstitial pneumonia with autoimmune features" (IPAF). HRCT plays an important role in these subset of patients as it is one of the major domain in the classification criteria of IPAF. HRCT helps in diagnosis of patients with IPAF based on the specific imaging patterns. Diagnosing autoimmune features in a patient with ILD has implications with regard to treatment and the long-term outcome. A multidisciplinary team approach involving departments of Pulmonology, Rheumatology, Radiology and Pathology contributes to better diagnosis and management of these patients.

**TABLE1 :RADIOLOGICAL PATTERNS OF IPAF WITH GENDER DISTRIBUTION**

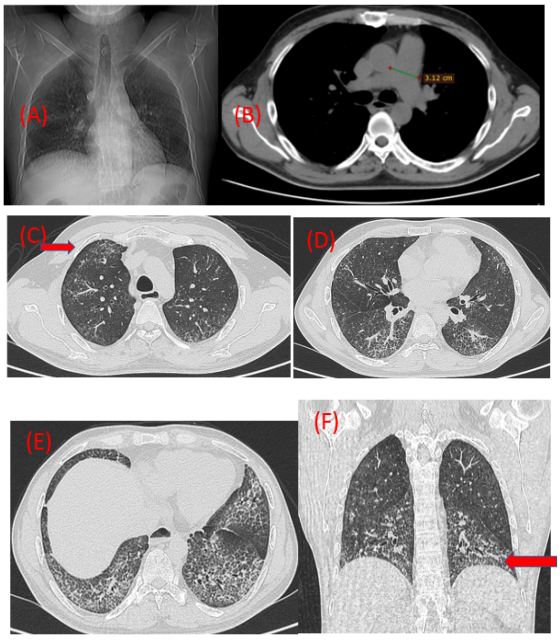
| SERIAL NO | HRCT PATTERN | MALES | FEMALES | PERCENTAGE |
|---|---|---|---|---|
| 1 | **NSIP** | **1** | **7** | **57.2%** |
| 2 | **TYPICAL UIP** | **0** | **4** | **28.6%** |
| 3 | **OP** | **0** | **1** | **7.1%** |
| 4 | **CPFE** | **1** | **0** | **7.1%** |

**TABLE2 :DEMOGRPAHIC, CLINICAL, SEROLOGICAL, RADIOLOGICAL DATA IN OUR CASE SERIES (n=14)**

| S no | Age (yrs) | Sex | Clinical domain | Serological positivity | HRCT pattern | Pulmonary HTN | Lympha -denopathy | Dilated esophagus |
|---|---|---|---|---|---|---|---|---|
| 1 | 65 | F | Inflammatory arthritis | ANA | NSIP | NIL | Subcentimetric | Present |
| 2 | 60 | F | Inflammatory arthritis | ANA | UIP | NIL | Present | Nil |
| 3 | 53 | F | Nil | ANA | NSIP | NIL | Subcentimetric | Present |
| 4 | 67 | F | Nil | ANA | UIP | PRESENT | Subcentimetric | Nil |
| 5 | 35 | F | Inflammatory arthritis | ANA | NSIP | NIL | Subcentimetric | Present |
| 6 | 30 | F | Raynaud's | ANA | NSIP | NIL | NIL | Present |
| 7 | 47 | F | Inflammatory arthritis | Anti- RF | NSIP | PRESENT | Subcentimetric | Nil |
| 8 | 48 | F | Nil | ANA | NSIP | PRESENT | Subcentimetric | Present |
| 9 | 76 | F | Inflammatory arthritis | ANA | NSIP | NIL | Subcentimetric | Present |
| 10 | 60 | M | Nil | ANA | CPFE | NIL | Nil | Nil |
| 11 | 49 | F | Nil | ANA | NSIP | PRESENT | Nil | Nil |
| 12 | 40 | M | Nil | ANA | NSIP | NIL | Subcentimetric | Present |
| 13 | 20 | F | Inflammatory arthritis | ANA | NSIP | NIL | Subcentimetric | Nil |
| 14 | 42 | F | Inflammatory arthritis | ANA | OP | PRESENT | PRESENT | Nil |

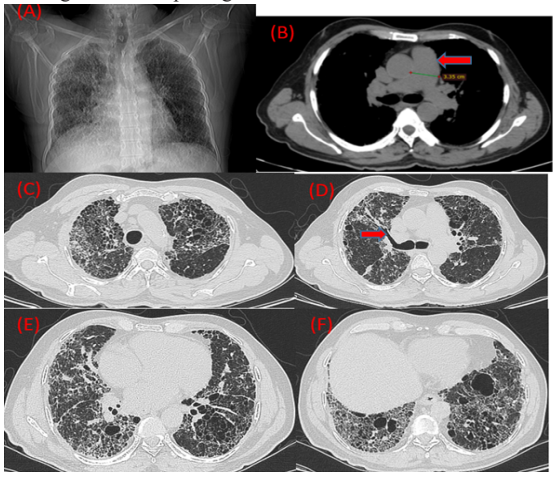
## ILLUSTRATIONS :

**CASE 1 :IPAF -CLASSICAL NSIP PATTERN** : A 33 year old male presented with cough and dyspnea**. Morphological criteria** : NSIP pattern of ILD**. Serological criteria** : ANA was positive with homogenous pattern (4+) . Based on the morphological and serological criteria patient is diagnosed as a case of IPAF.




scanogram of chest (a) showing reticular opacities predominantly involving bilateral lower zones. axial hrct images (b,c,d,e) showing ground glass opacity with reticulation with apico basal gradient and immediate subpleural sparing (arrow). coronal image (f) shows traction bronchiectasis with bronchiolectasis (arrow).

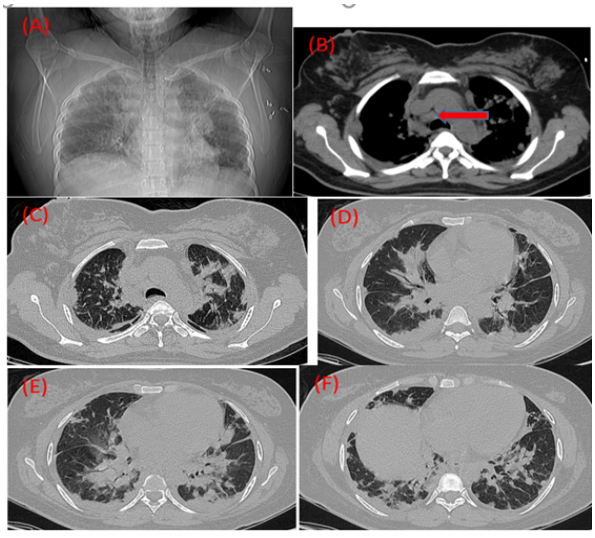
**CASE 2: IPAF -TYPICAL UIP PATTERN**. A 50 year old male patient presented with cough and SOB. **Morphological criteria** :HRCT showed ILD with Typical UIP pattern. **Serological criteria**: Anti RF positivity of 382IU/ml. He was diagnosed as IPAF depending on serological and morphological criteria.




scanogram (a) of chest showing reticuloalv eo lar opacities diffusely scattered in b/l lungs.a xial ncct chest in mediastinal window (b)

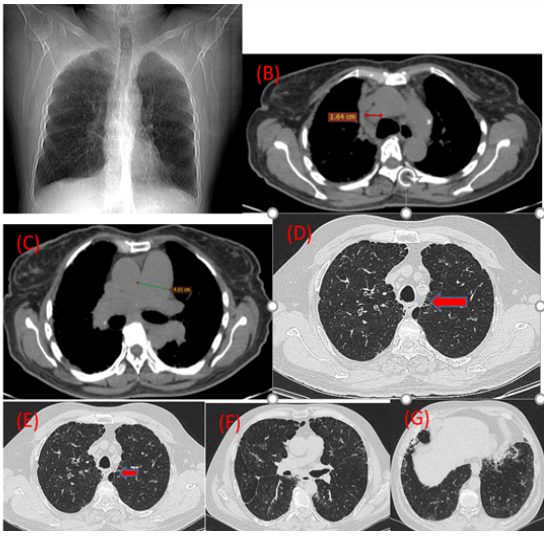
showing dilated mpa measuring 33.5mm. axial hrct images showing diffuse interlobular and intralobular interstitial thickening with diffuse macrocystic honeycombing along with areas of traction bronchiectasis (arrows)and bronchiolectasis- features consistent with typical uip pattern with pulmonary hypertension.

**CASE 3 : IPAF -ORGANIZING PNEUMONIA PATTERN** : A 42 year old female with no comorbities presented with cough and shortness of breath. **Serological criteria** :peroxisomal 3+ ANA positivity. she was diagnosed as IPAF and was started on immunosuppressants.




Scanogram of the chest showing multiple patchy areas of consolidation in b/l lungs. Axial ncct in mediastinal window showing enlarged pretrac heal lymphnode. Hrct images (c,d,e,f) showing muliple areas of patchy air space consolidation in bilatral lungs both in subpleural and peribronchial distribution- features consistent with organizing pneumonia pattern.

**CASE 4 :IPAF - COMBINED PULMONARY FIBROSIS AND EMPHYSEMA**.A 60 year old male known smoker since 20 years presented with dry cough and dyspnea. Morphological criteria :HRCT showed emphysema along with UIP pattern of ILD. Serological study demonstrated ANA positivity (4+) .




Scanogram of chest (a) showing bilateral emphysematous lungs.axial ncct chest in mediastinal window (b,c) showing pretracheal lymphadenopathy and pulmonary hypertension.hrct images(d,e,f,g) showing paraseptal and centrilobular emphysematous changes (arrows) in b/l upper lobes along with interstitial thickening and honeycombing in b/l lower lobes

**REFERENCES** :

1. King TE (August 2005). "Clinical advances in the diagnosis and therapy of the interstitial lung diseases". American Journal of Respiratory and Critical Care Medicine. 172 (3): 268–79. doi:10.1164/rccm.200503-483OE. PMID 15879420.
2. Cushley MJ, Davison AG, du Bois RM, Egan J, Flower CD, Gibson GJ, Greening AP, Ibrahim NB, Johnston ID, Mitchell DM, et al. The diagnosis, assessment and treatment of diffuse parenchymal lung disease in adults. Thorax 1999;54:S1–S30
3. Fischer A, Antoniou KM, Brown KK, et al. An official European Respiratory Society/American Thoracic Society research statement: interstitial pneumonia with autoimmune features. Eur Respir J 2015; 46: 976–87.
4. Sandra Chartrand, Jeffrey J. Swigris, Lina Peykova, Joyce S. Lee, Kevin K. Brown,Aryeh Fischer, Clinical features and natural history of interstitial pneumonia with autoimmune features: A single center experience, DOI: 10.1016/j.rmed.2016.09.002
5. Oldham et al , Characterisation of patients with interstitial pneumonia with autoimmune features
6. Sharma R, Talwar D, Tuteja M et al; Clinico-Radiological and Autoimmune Profile Correlation in Patients With Autoimmune Featured Interstitial Lung Disease (AIFILD): An Observational Study in Indian Scenario,Chest 2016;149(4_S):A456
7. K. Ahmad1, T. Barba1, J. Traclet1, C. Khouatra1, V. Cottin1, Idiopathic Interstitial Pneumonia With Autoimmune Features: Clinical Characteristics And Prognosis In A French Cohort, Am J Respir Crit Care Med 193;2016:A4944.
8. Warrick JH, Bhalla M, Schabel SI, Silver RM. High resolution computed tomography in early scleroderma lung disease. Rheumatol 1991; 18:1520-1528.