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Studying the characteristics of interstitial pneumonia with auto immune features

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Abstract

Aim of the study: This was prospective observational study with the aim of studying patients having interstitial pneumonia with autoimmune system features (IPAF) and characterizing its prognosis in contrast with idiopathic interstitial pneumonias. Follow up those IPAF patients for diagnosing who will advance to a definitive CTD. **Material and methods:** This study included 55 patients who were diagnosed as diffuse parenchymal lung diseases by HRCT chest. All patients were subjected to clinical examination, HRCT, echocardiography, spirometry and collagen markers. **Results:** From 55 patients, 31 met the IPAF criteria, most of them were females, nonsmokers with mean age 47.56 ±10.9 years. The most common clinical finding was inflammatory arthritis. The most common serological finding was RF. The most common radiological pattern was NSIP. In outcome analysis, 2 of IPAF patients died during the follow-up period and 3 of 31 IPAF patients evolved to a definitive CTD. **Conclusion:** This study demonstrates that the recently defined criteria for IPAF are fulfilled by a significant proportion of patients. In this study we tried to shine a light on the basic characteristics of these patients and the nature of their disease with analysis of their clinical, morphological and serological criteria and prognosis of their disease.

Key Words: IPAF, RF, HRCT

1. Introduction

The idiopathic interstitial pneumonias (IIPs) are diffuse fiery or potentially fibrotic lung disorders that are assembled together dependent on comparable clinical, radiologic and histopathologic features. The determination of IIP requires the avoidance of known reasons for interstitial pneumonia, for example, environmental exposures, medication toxicity or connective tissue disease (CTD) **[1].** The CTDs are a spectrum of systemic autoimmune disorders and incorporate rheumatoid arthritis, systemic lupus erythematosus, inflammatory idiopathic myopathies, Sjögren's syndrome, systemic

sclerosis, and mixed connective tissue disease. In spite of the fact that these diseases have special and recognizing features, they share the common underlying mechanisms of systemic autoimmunity and immune-mediated organ damage. Interstitial lung diseases (ILDs) often occur as a complication of (CTD) **[2].** It has been perceived that patients with ILD may exhibit clinical or serologic highlights suggestive of an underlying autoimmune process but not fulfill diagnostic criteria for a defined CTD. European Respiratory Society/American Thoracic Society research statement 2015 defines interstitial pneumonia with autoimmune features (IPAF). The arrangement criteria are composed around three central domains: a clinical domain comprising of explicit extrathoracic highlights, a serologic domain comprising of explicit circulating autoantibodies, and a morphologic domain comprising of explicit chest imaging highlights, histopathologic highlights or pulmonary physiologic features. To be delegated having IPAF, the individual must meet all of the a priori requirements and have at least one feature from at least two of the domains **[3].**

TABLE 1 Classification criteria for "interstitial pneumonia with autoimmune features"

1. Presence of an interstitial pneumonia (by HRCT or surgical lung biopsy) *and*,
2. Exclusion of alternative aetiologies *and*,
3. Does not meet criteria of a defined connective tissue disease *and*,
4. At least one feature from at least two of these domains:
   A. Clinical domain
   B. Serologic domain
   C. Morphologic domain

A. Clinical domain
1. Distal digital fissuring (*i.e.* "mechanic hands")
2. Distal digital tip ulceration
3. Inflammatory arthritis *or* polyarticular morning joint stiffness ⩾60 min
4. Palmar telangiectasia
5. Raynaud's phenomenon
6. Unexplained digital oedema
7. Unexplained fixed rash on the digital extensor surfaces (Gottron's sign)

B. Serologic domain
1. ANA ⩾1:320 titre, diffuse, speckled, homogeneous patterns *or*
   a. ANA nucleolar pattern (any titre) *or*
   b. ANA centromere pattern (any titre)
2. Rheumatoid factor ⩾2× upper limit of normal
3. Anti-CCP
4. Anti-dsDNA
5. Anti-Ro (SS-A)
6. Anti-La (SS-B)
7. Anti-ribonucleoprotein
8. Anti-Smith
9. Anti-topoisomerase (Scl-70)
10. Anti-tRNA synthetase (*e.g.* Jo-1, PL-7, PL-12; others are: EJ, OJ, KS, Zo, tRS)
11. Anti-PM-Scl
12. Anti-MDA-5

C. Morphologic domain
1. Suggestive radiology patterns by HRCT (see text for descriptions):
   a. NSIP
   b. OP
   c. NSIP with OP overlap
   d. LIP
2. Histopathology patterns or features by surgical lung biopsy:
   a. NSIP
   b. OP
   c. NSIP with OP overlap
   d. LIP
   e. Interstitial lymphoid aggregates with germinal centres
   f. Diffuse lymphoplasmacytic infiltration (with or without lymphoid follicles)
3. Multi-compartment involvement (in addition to interstitial pneumonia):
   a. Unexplained pleural effusion or thickening
   b. Unexplained pericardial effusion or thickening
   c. Unexplained intrinsic airways disease# (by PFT, imaging or pathology)
   d. Unexplained pulmonary vasculopathy

Table (1): Classification criteria for interstitial pneumonia with autoimmune features **[4].**

2. Patients and Methods

The current study was a prospective observational study that was conducted on 55 patients who attended to outpatient clinic and inpatient of both chest and Internal medicine &immunology departments at Beni-Suef university hospital in the period from December 2017 till November 2018 complaining of dyspnea and diagnosed as diffuse parenchymal lung diseases by HRCT chest. The study was approved by the research ethical committee; Beni-Suef University and approval was obtained from each participant in the study.

2.1 Inclusion criteria:

- The study included Patients> 18 years of age with DPLD as diagnosed by HRCT who are clinically stable not in exacerbation.
- Both sexes were included.

2.2 Exclusion criteria:

- Patients with alternative explanations for ILD (e.g. hypersensitivity pneumonitis, radiation treatment, drug-induced, occupation associated, sarcoidosis, etc).
- Coexisting obstructive lung disease (FEV1/ FVC < 0.70), and emphysema greater than ILD on high-resolution CT chest images.
- Comorbid lung conditions (e.g. lung neoplasm, non-cystic fibrosis bronchiectasis).
- Patients who are diagnosed with definite collagen vascular disease according to American College of Rheumatology and EULAR 2018 and 2019.

2.3 All patients were subjected to:

- Complete history taking Clinical examination
- Routine labs
- Lab investigation specific for collagen vascular disorders and for vacuities (Rheumatoid factor by ELISA, Anti cyclic citrullinated peptide, Anti-nuclear antibody titer by IF, Anti double stranded DNA, anti-neutrophil cytoplasmic antibody p & c), myositis specific antibodies and other autoimmune antibodies as in depth investigations for selected cases.
- Arterial blood gases.
- High-resolution computed tomography (HRCT).
- Pulmonary function tests (Flow volume loop): Resting spirometry: performed by Master Screen Jaeger-Hochberg, Germany PFT No.781040.
- Transthoracic echocardiography using (GE vivid S5-USA) for assessment of cardiac condition with special concern to pericardial effusion presence and estimation of pulmonary hypertension by estimation of pulmonary artery systolic pressure (PASP) through tricuspid regurgitation.

Statistical analysis: Data were statistically described in terms of mean ± standard deviation (± SD), median and range, or frequencies (number of cases) and percentages when appropriate.

Comparison of numerical variables between the study groups was done using independent sample t test for two unrelated samples and paired sample t test for two related samples. For comparing categorical data, Chi-square (χ^2) test was performed. All statistical calculations were done using computer program IBM SPSS (Statistical Package for the Social Science; IBM corp, USA) release 22 for Microsoft Windows.

3. Results

The current study was conducted on 55 patients complaining of dyspnea and diagnosed as diffuse parenchymal lung diseases by HRCT chest. Concerning the demographics of the studied patients, the age ranged from 18 to 72 years with median age 66.5 years, mean age 47.14 ±12.4 SD. The majority were females (92.7%). 53 patients (96.4%) of them were non-smokers and only 2 patients were smokers **(Tab. 2)** complaining mainly of shortness of breath in 42 cases (76.4%) and cough in 13 cases (23.6%) **(Tab.3).** Pulmonary hypertension was diagnosed by echo ,there were 33 cases with pulmonary hypertension , 9 cases mild ,14 moderate and 10 cases severe pulmonary hypertension **(Tab.3).** Regarding the clinical manifestations of rheumatological diseases; 60% of the studied cases had no rheumatologic manifestation and 40% had rheumatologic manifestation (**Tab.3).** About the functional state of the studied populations, the base line PFTs values demonstrated a mild restrictive defect (mean forced vital capacity in percent predicted (FVC %) 63.4 ± 21.7). Concerning ABG of the studied patients PaCo2 ranged from 24 to 84 with Mean PaCo2 ±SD 39.48 ±12.3 while PaO2 ranged from 41 to 100 with Mean PaO2±SD 75.89 ±19.4 and SO2 ranged from 54 to 99 with Mean SO2 ±SD 91.72% ±0.9%. Regarding lab investigation for collagen vascular disorders and for vaculities as demonstrated in **Tab. (4)**; RF was positive in 20 cases (11 cases were positive at baseline and 9 cases were positive at follow up) so there was statistically significant increase in RF in follow up (p-value (0.046), while ANA, Anti CCP and ANCA-C all were increased at follow-up as compared with baseline but without a statistically significant difference between baseline assessment and follow-up as ANA positive cases increased from 1 to 4 cases while Anti CCP positive cases increased from 4 to 10 cases and ANCA-C positive cases increased from 1 to 2 cases. From all previous data the studied patients were divided according to meeting IPAF criteria into 2 groups**; Group I**, 31 patients met the criteria of IPAF and **Group II,** 24 patients didn't and considered as idiopathic interstitial pneumonia (IIP).

We had studied the Characteristics of those who met criteria of IPAF (Group I) and found that: The mean age was 47.56 ±10.9 years and 96.8% were females, (96.8%) never smokers and (67.7%) of them were taking systemic corticosteroids while (32.3%) were taking combined steroids and

immunosuppressive drugs at the time of evaluation **(Tab.6).** Regarding serological domain as demonstrated in **Tab. (4)**; RF rheumatoid factor > x2 upper limit of normal positive cases were significantly increased at follow-up as compared with baseline evaluation from 11 cases at baseline to 20 cases with a statistically significant p-value (0.046), while ANA, Anti CCP and ANCA-C all were increased at follow-up as compared with baseline but without a statistically significant difference between baseline assessment and follow-up as ANA positive cases increased from 1 to 4 cases while Anti CCP positive cases increased from 4 to 10 cases and ANCA-C positive cases increased from 1 to 2 cases .

Regarding mulicompartement subdomain within morphological domain , Pulmonary vasculopathy was the most common finding as pulmonary hypertension diagnosed by echo was found in 18 cases of the 31 IPAF cases (58.1%) and 10 of those 18 cases (32.3%) with pulmonary hypertension could not be explained and not comparable with extent of radiological affection ,followed by intrinsic airway disease (29%) presented by mosaic appearance and air trapping in HRCT and decreased FEV1 than FVC in those cases we consider this finding unexplained as majority of our cases were nonsmokers . Pleural disease was found in only one case (3.2%) as only 1 case showed pleural thickening in HRCT chest. Comparing both groups Group I (IPAF) and Group II we found that there was no big difference regarding demography as the most of IPAF patients 96.8% were females with mean age 47.56 ±10.9years and never smokers (96.8%), also the IIP patients group II were mostly females (87.5%) with mean age 46.58 ±14.3 years. 95.8% of them were never smokers. Also, as regard treatment at the time of evaluation the majority in both groups were taking systemic corticosteroids (67.7%) of group I and (87.5%) of group II while (32.3%) of group I and (12.5%) of group II were taking combined steroids and immunosuppressive drugs were. As regard echocardiographic pulmonary hypertension in both groups the percentages of cases with no pulmonary hypertension are 41.9% and 37.5% in group 1 and group 2 respectively while the percentages of cases with mild, moderate and severe pulmonary hypertension are comparable in both groups as shown in **tab.6**. In reference to HRCT pattern of patients in both groups, NSIP was the commonest HRCT pattern seen in both groups with a higher percentage in group 1 than group 2 as it constituted 48.4% of IPAF group and 29.2% of IIP group while other patterns were seen in both groups with comparable percentages as seen in **tab.7**. Difference was only found in presentation of patients with rheumatological symptoms as all of the IPAF patients had rheumatological symptoms while none of patients in the IIP group did. Statistical significant difference between IPAF and IIP group was only

found regarding presence of rheumatological symptoms (P-value = 0.001) while the other characteristics of both groups showed no statistical significant difference. Regarding prognosis by follow up of IPAF patients: In outcome analysis, 2 of 31 patients died during the follow-up period with respiratory failure and 3 IPAF patients evolved to a definite CTD in their follow up.

Table (2): Baseline Characteristics of the studied population; (N= 55)

		Descriptive Statistics
Age	Mean ±SD	47.14 ±12.4
	Minimum	18
	Maximum	72
Sex	Male	4 (7.3%)
	Female	51 (92.7%)
Smoking	Non smokers	53 (96.4%)
	Smokers	2 (3.6%)
Treatment	steroids	42 (76.4%)
	Combined steroids and immunotherapy	13 (23.6)

Table (3): Clinical and radiological findings of the studied population; (N= 55)

		Frequency	**Percent%**
Main Complaint	Shortness of breath	42	76.4%
	Cough	13	23.6%
HRCT changes	Nodular	6	10.9%
	Ground glass	27	49.1%
	Alveolar filling	1	1.8%
	Cystic	3	5.5%
	Reticular	18	32.7%
HRCT pattern	NSIP	22	40%
	NSIP/OP	2	3.6%
	UIP	7	12.7%
	Unclassifiable	23	41.8%
	0P	1	1.9%
HRCT associated	No association	41	74.5%
	LNs	13	23.6%
	Pl. thickening	1	1.8%
Multicompartment affection	No	12	21.8%
	Yes	43	78.2%
	• Pulmonary vasculopathy(P.HTN) • Airways disease • Pleural thickening	33 9 1	60% 16.4% 1.8%
Echo (pulmonary hypertension)	No	22	40.0%
	Mild (40-50)	9	16.4%
	Moderate (51-60)	14	25.5%
	Severe >60	10	18.2%
Distribution of studied population by rheumatological symptoms	No	33	60%
	Yes	22	40%

Table (4): Changes in Lab investigation for collagen vascular disorders and for vacuities at baseline and follow-up

		Baseline Evaluation	**Follow-up Evaluation**	***p-value***
ANA	Negative	54 (98.2%)	51 (92.7%)	0.182
	Positive	1 (1.8%)	4 (7.3%)	
RF	Negative	44 (80.0%)	35 (63.6%)	**0.046***
	Positive	11 (20.0%)	20 (36.4%)	
Anti CCP	Negative	51 (92.7%)	45 (81.80%)	0.075
	Positive	4 (7.3%)	10 (18.20%)	
Anti (ds)DNA	Negative	54 (98.2%)	55 (100.0%)	0.500
	Positive	1 (1.8%)	0 (0.00%)	
ANCA-C	Negative	54 (98.2%)	53 (96.4%)	0.500
	Positive	1 (1.8%)	2 (3.6%)	
ANCA-P	Negative	55 (100.0%)	55 (100.0%)	--[a]
	Positive	0 (0.00%)	0 (0.00%)	

Table (5): Classification criteria for interstitial pneumonia with autoimmune features (IPAF) in our cohort:

Classification criteria	**IPAF patients' n**
1. Presence of an interstitial pneumonia by HRCT	55
2. Exclusion of alternative etiologies and	55
3. Does not meet criteria of a defined CTD and	55
4.Meeting criteria of IPAF	31
5. At least one (1) feature from at least two (2) of these domains:	
A. **Clinical domain**	22
1. Inflammatory arthritis or polyarticular morning joint stiffness > 60 minutes	10
2.Distal digital fissuring (i.e. 'mechanic hands')	5
3. Raynaud's phenomenon	7
B. **Serologic domain**	31
1. RF > 2 X ULN	26
2. ANA, either diffuse, speckled, or homogeneous patterns at >1:320 titer or ANA nucleolar pattern at any titer or ANA centromere pattern at any titer	4
3. Anti-CCP	9
C. **Morphologic domain**	
1. Suggestive radiology patterns by HRCT:	31
a. NSIP	15
c. NSIP with OP overlap	1
b. OP	0
d. UIP	4
e. Unclassifiable	11
2. Unexplained multi-compartment involvement	28
a. Pleural effusion or thickening	1
b. Pericardial effusion or thickening	0
c. Intrinsic airways disease(by HRCT and PFTs)	9
d. Pulmonary vasculopathy(P.HTN)	18

Table (6) Comparison between both IPAF (Group 1) and IIP (Group 2):

		IIP (n& %) N= 24	**IPAF (n& %) N= 31**	**P-value**
Age	Mean ±SD	46.58 ±14.3	47.56 ±10.9	0.712
	Minimum	18	29	
	Maximum	72	67	
Sex	Male	3 (12.5%)	1 (3.2%)	0.215
	Female	21 (87.5%)	30 (96.8%)	
Smoking	No	23 (95.8%)	30 (96.8%)	0.687
	Yes	1 (4.2%)	1 (3.2%)	
Treatment	steroids	21 (87.5%)	21 (67.7%)	0.080
	steroids+ immunosupressives	3 (12.5%)	10 (32.3%)	
Echo **PAP**	Normal	9 (37.5%)	13 (41.9%)	0.971
	Mild	4 (16.7%)	5 (16.1%)	
	Moderate	6 (25.0%)	8 (25.8%)	
	Sever	5 (20.8%)	5 (16.1%)	

Table (7) HRCT pattern in both groups I and II:

HRCT pattern	**IIP N& (%)**	**IPAF N& (%)**	**Total N& (%)**
NSIP	7 (29.2%)	15 (48.4%)	22 (40%)
NSIP/ OP	1 (4.2%)	0 (0.0%)	1 (1.8%)
UIP	3 (12.5%)	4 (12.9%)	7 (12.7%)
Unclassifiable	12 (50.0%)	11 (35.5%)	23 (41.8%)
0P	1 (4.2%)	1 (3.2%)	2 (3.6%)
Total	24 (100.0%)	31 (100.0%)	55 (100.0%)

4. Discussion

"Interstitial pneumonia with autoimmune features" (IPAF),a new terminology proposed by the ERS/ATS research statement to characterize the heterogeneous group of patients with idiopathic interstitial pneumonia (IIP) who have a clinical flavour of underlying connective tissue disease (CTD) but do not meet the current American College of Rheumatology criteria for CTD. This group requires more studies to know more about the characteristics of these patients and how can these characteristics influence disease progression in them. Also we should know proper management of these patients and how to improve the quality of their life.

Comparing with other studies the demography and smoking state of that group differed , some found most of them females and lesser smoker as our cases**,** Chartrand et al **[5]** who worked on 56 patients with IPAF most of them were women, never smokers, who presented in their 6th decade.

Also Dai et al **[6]** study in which 56% of patients were females in their 6 th decade with 34% smokers. While others found Most of their cases male and smokers as Oldham et al **[7]** found that among 57 patients who met IPAF criteria 52% were females with mean age 63.2 years old and 54.9% of them were smokers. And Biffi et al **[8]** who worked on 102 patients (median age 67 years, 51% males). Forty-two (41%) patients were never smokers, 11 (11%) current smokers and 49 (48%) former smokers. Regarding age our cases were younger with mean age 47.56 ±10.9 while in other studies the mean age of cases is around 6th decade.

As regard the IPAF criteria (domains) defining the patients in the current study, 16 (51.6%) patients met IPAF criteria through a combination of clinical and serological domains, 22 (71%) by clinical and morphological domains, 31 (100%) by serological and morphological domains and 16 (51.6%) by all three domains. As the same in the current study Oldham et al **[7]** found that (14.6%) patients met IPAF criteria through a combination of clinical and serological domains, (8.3%) by clinical and morphological domains, (50.7%) by serological and morphological domains and (26.4%) by all three domains.

Similarly a study performed by Biffi et al **[8]** in which 21 patients met both morphological (radiological NSIP HRCT pattern) and serological domains, 4 met both morphological (radiological NSIP HRCT pattern) and clinical domains, and 16 patients met all the three domains.

In contrast, Chartrand et al **[5]** found that (52%) patients had at least one feature in each of the three IPAF domains; (37.5%) had at least one feature in both serologic and morphologic domains, (9%) had at least one feature in both clinical and morphologic domains, and (2%) had at least one feature in both clinical and serologic domains.

Regarding clinical domain, in the current study, the most common clinical findings were inflammatory arthritis/morning stiffness lasting >60 min (32.3%), Raynaud's phenomenon (22.6%), and mechanics hands (16.1%). When compared to other authors who found Raynaud's phenomena was the highest in presentation as with Oldham et al **[7]** Raynaud's phenomenon (27.8%), inflammatory arthritis/morning stiffness lasting >60 min (17.4%) and mechanics hands (10.4%). Also, Ahmad et al **[9]** Raynaud's phenomenon (74%), followed by arthritis and/or morning stiffness of more than 60 min (48%), and digital edema (n ¼ 9, 33%). Chartrand et al **[5]** also found that the most frequently identified clinical features were Raynaud's phenomenon (39%), distal digital fissuring (29%), Gottron's sign (18%) and inflammatory arthropathy (16%). But in the study of Biffi1 et al **[8]** found arthritis higher in incidence as the current study, he found that 47% of the studied population showed rheumatologic-

related signs and symptoms. The most common reported symptoms were gastro esophageal reflux (18%) and arthralgia/multiple joint swelling (13%). Distal digital fissuring ("mechanic hands") was present in 10% of patients, Raynaud's phenomenon in 7% of patients and unexplained digital edema in 1% of patients.

Among the serological domain Rheumatoid factor >x2 upper limit of normal was the most common serological finding (83.4%), followed by Anti CCP (29%) and ANA >1:320 (or nucleolar or centromere pattern of any titer (12.9%). Comparing to others authors most of them found ANA was the common serological positive finding as Oldham et al **[7]** who found that an ANA > 1:320 (or nucleolar or centromere pattern of any titer) (77.6%), followed by SSA (16.6%) and rheumatoid factor > x2 upper limit of normal (13%) and Chartrand et al **[5]** who found (ANA) (48%), anti-Ro (SSA) (43%) and anti-tRNA-synthetase antibodies (36%). Also, Ahmad et al **[9]** who found that among the 93% of patients with IPAF who fulfilled the serologic criteria for IPAF, most had positive antinuclear antibodies with a titer > 320 (or a nucleolar or centromere pattern, whatever the titer) (82%). The other autoantibodies frequently observed were anti-synthetase (17%), anti-CCP, and anti-SS-A antibodies (9%). Biffi1 et al **[8]** also found that ANA was the commonest serological finding among the studied population, Dai et al **[6]** who found that ANA was the commonest serological finding (49.2%) among IPAF patients followed by Anti RO ssA (36.1%). ANCA not measured by other authors in our study it was positive in 6.5% of IPAF patients.

Within the morphological domain, an NSIP pattern by HRCT was found in 48.4% of patients while unclassifiable pattern was found in 35.5% of patients and UIP was found in only 12.9% of patients so the least presentation was UIP, comparing to others most matched with our result Chartrand et al **[5],** Ahmad et al **[9]** and Oldham et al **[7]** studies within the morphological domain, found that an NSIP pattern by HRCT was the most frequently observed pattern while UIP and an overlap of NSIP and OP came after. This also matched the findings of a study done by ITO et al **[10],** who investigated 98 patients with IPAF. Among the 98 patients, 64.3% showed an NSIP pattern, 20.4% organizing pneumonia and the remaining 15.3% an NSIP+OP pattern. Also Dai et al **[6]** study in which NSIP was found to be the commonest HRCT pattern with a percentage 61.6% followed by OP (22%). But Collins et al **[11]** and Chung et al **[12]** their result not matched with the result of the current study, they found that UIP was the commonest pattern in both HRCT and histological examination of SLB.

Regarding multicompartement subdomain within morphological domain, Pulmonary vasculopathy was the most common finding as pulmonary hypertension diagnosed by echo was

found in 18 cases of the 31 IPAF cases (58.1%) and 10 of those 18 cases (32.3%) with pulmonary hypertension could not be explained and not comparable with extent of radiological affection ,followed by intrinsic airway disease (29%) presented by mosaic appearance and air trapping in HRCT and decreased FEV1 than FVC in those cases we consider this finding unexplained as majority of our cases were nonsmokers . Pleural disease was found in only one case (3.2%) as only 1 case showed pleural thickening in HRCT chest. This matched with Ahmad et al **[9]** who found that pulmonary vasculopathy was present in 22% of patients as a criterion of multi-compartment affection while intrinsic air way disease was found in 11 % of patients.

Similarly, in a study by Adegunsoye et al **[13],** pulmonary vasculopathy was also the most prevalent finding in 45 of 84 patients (53.6%) with IPAF. Against the present study Oldham et al **[7]** found that intrinsic airways disease was the most common multi-compartment finding (22.2%), followed by pleural disease (12.5%) and pulmonary vasculopathy (18.8%).

Comparing both groups, Group I (IPAF) and Group II, we found that there was no big difference regarding demography as the most of IPAF patients 96.8% were females with mean age 47.56 ±10.9years and never smokers (96.8%), also the IIP patients group II were mostly females (87.5%) with mean age 46.58 ±14.3 years. 95.8% of them were never smokers. Also, as regard treatment at the time of evaluation the majority in both groups were taking systemic corticosteroids (67.7%) of group I and (87.5%) of group II while (32.3%) of group I and (12.5%) of group II were taking combined steroids and immunosuppressive drugs were. As regard echocardiographic pulmonary hypertension in both groups the percentages of cases with no pulmonary hypertension are 41.9% and 37.5% in group 1 and group 2 respectively while the percentages of cases with mild, moderate and severe pulmonary hypertension are comparable in both groups as shown in **tab.6**. In reference to HRCT pattern of patients in both groups NSIP was the commonest HRCT pattern seen in both groups with a higher percentage in group 1 than group 2 as it constituted 48.4% of IPAF group and 29.2% of IIP group while other patterns were seen in both groups with comparable percentages as seen in **tab.6**.

Regarding prognosis by follow up of IPAF patients, in outcome analysis, 2 of 31 patients died during the follow-up period with respiratory failure and 3 IPAF patients evolved to a definite CTD in their follow up. The overall survival of patients with IPAF did not differ from that of IIP, as found in previous studies like Ahmad et al **[9]** and Oldham et al **[7].** Regarding PFTs of both IPAF and IIP groups before and after treatment there was no statistical significance between PFTs

of each group before and after treatment or between both groups**.**

Similarly, Chartrand et al **[5]** performed a prospective cohort study including 56 patients who met the IPAF criteria with baseline PFT values demonstrating a mild restrictive defect (mean forced vital capacity in percent predicted (FVC %) 68.4 ± 16.0). Modeled FVC %(slope ¼ 0.69/year) showed stability.

The stationary result regarding the function in follow up in the current study might need longer period of follow up to assess if it will remain stationary or decease or improve. However, by analysis of PFTs of patients' pre and post treatment on individual basis, 9 cases showed improvement, 6 cases showed decline while 40 cases showed no difference.

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