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Clinical and Radiological Evaluation of Cases with Diffuse Parenchymal Lung Disease

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Abstract: DPLD is a category comprising a series of entities with similar clinical, radiologic, and lung function presentations, in which the principal pathological alterations affect the interstitial alveolar structures. Diagnosis can be made by the combination of clinical and roentgenographic features and pulmonary function tests. Aims and objectives of present study are to study the clinical and radiological presentations of all DPLD cases and correlate the history and clinical profile of the patients of DPLD with the radiological extent of the disease. It is hospital based observational study; data were taken from all the patients attending to the OPD and IPD of the GSL Medical College, Rajahmundry over a period of 2 years. We included all the patients with abnormal chest X – Ray findings showing diffuse parenchymal lesions. Detailed clinical history, physical examination, chest X – Ray, HRCT thorax, spirometry, 6 minute walk test and laboratory investigations were done. Total 30 patients were satisfied the inclusion criteria and gave the consent, of those peak age incidence was found between 51 – 60 yr, females predominant , more patients were presented between 1-3 years , most common symptom is cough and breathlessness , most patients have history of smoking, X – Ray lesions are mostly reticular type involved mostly lower and mid zones, spirometry shows predominantly moderately severe restriction. This study suggests that interstitial lung diseases are not uncommon in India. Interstitial lung disease must be suspect with specific symptoms, signs and further investigations like chest X-ray, HRCT chest and blood investigations should be done. Detailed occupational history, family history and drug history should be taken specific tests must be done to rule out autoimmune diseases which may be culprit for this disease. Increased awareness would serve to provide early diagnosis and this may impact on high mortality rate of this disease.
Keywords: DPLD, HRCT, 6 Minute walk test, IPF.

INTRODUCTION

Diffuse parenchymal lung disease (DPLD) is a category comprising a series of entities with similar clinical, radiologic, and lung function presentations, in which the principal pathological alterations affect the interstitial alveolar structures. Common clinical, radiological and pathophysiological features form the basis collectively referring to a complex group of disorders as the interstitial lung diseases. The prominent feature in interstitial lung diseases is fibrosis in the interstitium, which produces derangement of alveolar architecture and loss of functional alveolar capillary units. More than 150 known factors are associated with interstitial lung diseases. Diagnosis can be made by the combination of clinical and roentgenographic features and pulmonary function tests. Histopathological confirmation of the diagnosis is not required in most of the cases. There has been a resurgence of interest in the study of these disorders chiefly on account of the availability of less invasive methods. Development of high resolution computed tomography and availability of video-assisted thoracoscopic lung biopsy has added to our diagnostic strategies. Cigarette smoking, aspiration, certain drugs, radiation therapy, cancer, systemic diseases, environmental and occupational factors had been reported in association with the ILD in one third cases. However two-thirds cases of ILD have no reportable association. Our aim of the study was to find out common presentations, signs, radiographic findings, spirometry patterns and common aetiology of interstitial lung diseases.

Aims and Objectives of the study

- To study the clinical and radiological presentations of all DPLD cases
- To correlate the history and clinical profile of the patients of DPLD with the radiological extent of the disease

MATERIALS AND METHODS

Studydesign

It was a hospital based observational study.

Source of data

All patients attending the OPD, IPD of the department of pulmonary medicine GSL medical college and general hospital.

Study period

October 2014 to July 2016.

Inclusion criteria

- All patients attending the hospital with chest x ray showing diffuse parenchymal lesions.

Exclusion criteria

- Patients with lung lesions due to cardiovascular causes.
- Patients with chest x ray showing isolated localised opacity.
- People not giving consent for the study.

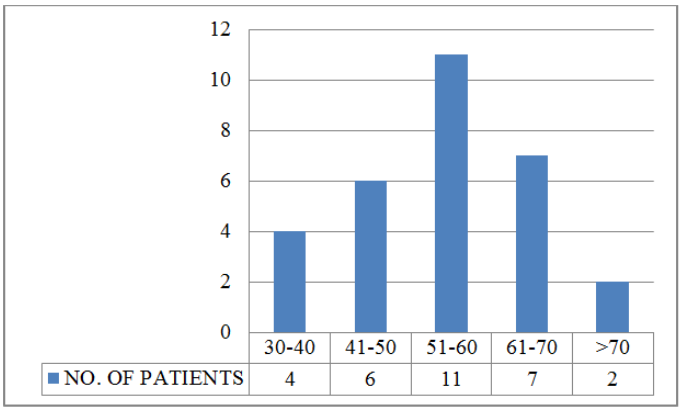
METHODS

Permission from the institutional ethical committee was taken before initiation of the study. Informed consent was taken from each patient before including them in the study. Detailed clinical history was taken from the patients and their relatives and was scripted in the proforma prepared for the purpose. Special importance was given to occupational history and smoking habits. Thorough physical examination of patients was done and findings were recorded in the proforma. All the patients were subjected for chest x-ray and high resolution CT scan after being diagnosed as diffused parenchymal lung disease. The pattern of chest x-ray was depicted under headings like reticular, nodular, reticulonodular, consolidation, fibrosis, etc. All lesions were recorded according to site and extent in chest x-ray. Similarly HRCT patterns were also recorded. Characteristics like honey combing, ground glass attenuation, centrilobular nodules, reticular opacities, mosaic attenuation, consolidation, bronchiectasis and traction bronchiectasis etc.were identified and recorded in respective patient's record. All the patients were subjected for pulmonary function test, six minute walk test, ECG and 2D echo cardiography.

Haematological investigations like complete blood count, eosinophil count, ESR, blood urea , serum creatinine, serum electrolytes, calcium, LFT and auto antibodies were performed. In some selected cases bronchoscopy with bronco-alveolar lavage and trans-bronchial biopsy was performed for reaching in diagnosis. The patterns of clinical presentations, and laboratory reports were analysed with reference to the radiological extent of the disease. All the data were entered in Microsoft excel sheet and statistically analysed. As it was a descriptive study there were no quantitative date. Few categorical data were anlysed by chi square test for statistically analysis.

RESULTS AND DISCUSSION

All the patients with diffused parenchymal lung disease attending to the department of pulmonary medicine during the study period were included in the study. Total number of study participants who gave consent for the study and satisfied the inclusion criteria was 30. In the present study peak incidence of the disease was found between 51-60 years of age group are 11 patients and followed by 61-70 years age group 07 patients (Graph 1). Mean age of presentation in the present study was 54.9%. In their retrospective study of 30 patients in Gagiya Ashok K *et al.* [1] peak incidence was found between 40-49 years age group and closely resemble the present study. In other studies like that of U Maheswari *et al.* [2]. IDA Johnston *et al.*[3], Dr.Abhishek.Tiwati *et al* [4]. and Sabah Ahmed *et al.*[5] the mean age of presentation was 50.6, 67.4, 48.8 and 39.96 respectively.



Graph-1: Age distribution of patients

IPF is commonly seen in the middle-aged patients, and the incidence advances with increasing age. As per western reports, nearly two-thirds of patients are over 60 years of age at the time of diagnosis. In the present study, only 9 (30%) patients were aged above 60 years. Although there is a clear trend towards higher incidence of IPF with advancing age, the age at presentation is almost a decade earlier than that reported in western studies. In ILD Indian registry[6], ILD occurs at young age compared to western countries & over all females are affected more than males. In IPF more males are affected in present study as evidenced by ILD Indian registry (M:F=2:1). Mean age of presentation in the present study was 54.9%. In other studies like that of U Maheswari *et al*., IDA Johnston *et al*. Dr.Abhishek.Tiwati *et al*. Sabah Ahmed *et al.* the mean age of presentation was 50.6,67.4,48.8 and 39.96 respectively. In our study the most common age group at presentation was 51-60 years with 11 patients including 6 females and 5 males. In ILD Indian registry ILD occurs at young age compared to western countries & over all females are affected more than males. In IPF more males are affected in present study as evidenced by ILD Indian registry (M:F=2:1).

Male and female incidence was 42.4% and 57.4% in Jindal *et al*.[7] study, while in present study 40% male and 60% female patients found. As there were more female patients in Jindal et al study, same as present study, collagen vascular disease group was more (50.8%) as observed in the present study(33.33%).Sex distribution comparison of various studies was showened in the table 1.

Table-1 : sex distribution comparision

Study	Male	Female
Present study	40%	60%
Jindal *et al*.	42.4%	57.4%
Mahashur *et al*.	53.4%	46.5%
M.Turner et al.	66.8%	32.2%
Sabah Ahmed *et al.*	58.2%	41.8%
Ashok.K.Gogia *et al*.	66.5%	33.5%
Gagiya Ashok K *et al*.	66.50%	33.50%
Ghulam shabbier *et al*.	36%	64%

Dyspnoea was present in 100% cases in present study which is similar to the observationn of Jindal *et al*. Mahasur *et al*. and J. Fulmer *et al*. and closely resemble (92%) in M. Turner *et al*. study & U Maheswari *et al*. (98.6%). Severe breathlessness (Grade 3) seen in 30% of patients which closely resembles (36%) the observation of IDA Johnston *et al*. Dysnoea distribution comparison of various studies was showened in the table 2.

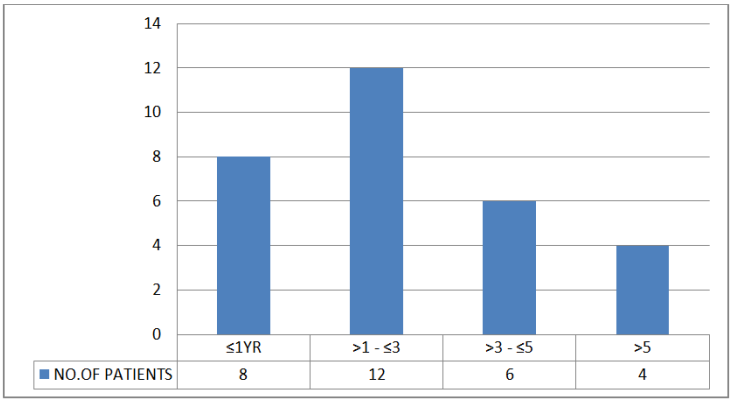
Table-2: dyspnea comparison

Study	SOB
Present study	100%
U Maheswari *et al.*	98.6%
M. Turner *et al.*	92%
Jindal *et al.*	100%
Mahasur *et al.*	100%
Gagiya Ashok K *et al.*	100%
J. Fulmer *et al.*	100%
PankajBadarkhe-Patil *et al.*	96%

Cough was found in 100% cases in present study, which correlate with Jindal *et al*. study (65.6%). Cough was usually dry (70% dry vs 30% productive). In other studies slight more incidence of cough (Mahasur *et al*.-82%[8], M. Turner *et al*.-73%[9], J. Fulmer *et al*.-86%).(chart 4). Clubbing was a common clinical sign and found in 56.66% cases in present study that closely resembles Mahasur *et al*., Jindal *et al.* study(50%), Gagiya Ashok K *et al*. (50%)& IDA Johnston *et al*. (54%). Joint pain was present in 26.66% cases that resembles the observation of M. Turner *et al.* (21%). In Jindal *et al*. study, more cases of joint pain was found which was due to more cases of collagen disease in Jindal *et al*. study(50.8%). Joint symptoms were more commonly found as compared to literature due to connective disorders.

In our study more patients with duration of illness presented between 1-3 years (12 Patients). Below 1 year - 8 patients, between 3-5 years - 6 patients and above 5 years - 4 patients present. In present study, patients presented with 1-3 years duration (40%) but

many patients also presented with less than 1 year (26.66%) which is closer to the observation of Gagiya Ashok K *et al*. study (23.31%). Percentage of patients presenting for more than 3 year duration was 33.33% among whom 13.33% were suffering for more than five years. In Gagiya Ashok K *et al*. study above 3 years 20% present. (Graph 2). Mahasur *et al*. had find that duration of illness was up to 1 year in 30%, 1-2 year in 18%, 3-5 year in 24% and beyond 5 year in 28%. In present study duration of illness was up to 1 year in 26.66% , 3-5 year in 20% which is similar to Mahasur *et al*. study.



Graph-2: Duration of illness

Out of 30 patients 13 does not have the anaemia (Hb >13gm/dl) remaining 17 patients had. Incidence of anemia of present study (56.66%) does not resemble to Jindal *et al*. (39.30%) study. Mild anemia(11.0-12.9 gr%) was present in 30% (9 patients) of cases, moderate anemia (8.0-10.9gr%) in 20% (6 patients) of cases and severe anemia (<8.0gr%) was found in only 2 cases in the present study.

Rheumatoid factor was positive in 20 % of cases in present study compared to Gagiya Ashok K *et al*. study in which it was in 16.65% cases. Even Turner *et al*. also found positive rheumatoid factor in 19 % of cases which is almost similar as the result of the present study. In the study of Jindal *et al*. it was observed in only 8.4% of cases.(table 4). Rheumatic factor positive in five patients, Anti CCP positive in four patients &anti-nuclear antibody positive in one patient (table 3).

Table-3: Collagen profile

TYPE OF ANTIBODIES	NO.OF PATIENTS
RHEUMATOID FACTOR (RA FACTOR)	5
ANTI NUCLEAR ANTIBODIES (ANA)	1
ANTI dsDNA	0
ANTI SM	0
SCL 70	2
ANTI CCP	4

In present study UIP is more common in older age than non UIP similarly seen in Aastha guptha *et al*.[10] in their study of 70 patients. The most common interstitial lung disease found in our study was usual interstitial pneumonia (UIP) / idiopathic pulmonary fibrosis (IPF) (n=16; 53.33%) followed by nonspecific interstitial pneumonia (NSIP) (n=6; 20%). In the present study the most common interstitial lung disease reported on HRCT was usual interstitial pneumonia / idiopathic pulmonary fibrosis (53.33%).Nonspecific interstitial pneumonia reported in 6 cases (20%) each. These findings like those reported by Muhammed SK *et al*. [11], Maheshwari U *et al.* and Sen T Udwadia ZF *et al*. [12]. In contrary to this less number of patientswith hypersensitivity pneumonitis (HSP), coal worker pneumoconiosis (CWP) and sarcoidosis were diagnosed in this study. The less incidence of such cases may be due small overall sample size.

Most common patterns seen on HRCT were reticular opacities(70%) (table 5). These findings correlated with findings of Muhammed SK *et al*. (table 4). HRCT was superior to chest radiograph in detection of all basic patterns and their distribution associated with ILD. Chest radiograph is a nonspecific investigation and can be utilized as initial investigation in work up of ILD. However, HRCT of lungs along with clinical data is essential for the diagnosis of ILD as reported by Potente G *et al*. [13], Grenier P *et al*.[14], Aziz ZA *et al*.[15], Raniga S *et al*.[16] and Ghulam Shabbier *et al*.[17].

Table 4: HRCT patterns comparison

	UIP	NSIP	COP
Present study	53.33%	20%	6.66%
PankajBadarkhe-Patil *et al.*	36%	14%	10%
Muhammed SK *et al.*	39%	24%	4%
Sen T Udwadia ZF *et al.*	43%	18%	2%

Septal thickening(50%), honeycombing(10%) and traction bronchiectasis (60%) were common findings observed in almost all cases of UIP seen predominantly in basal and subpleural region corresponding to the findings of the studies done by Maheshwari U *et al*. Akira M *et al*.[18], Nishiyama O *et al*.[19] and Misumi S *et al*.[20].

In NSIP, HRCT findings predominantly involved the lower lobes and subpleural regions like IPF but the distribution was patchy in contradictory to IPF which showed diffuse distribution of all findings. Honeycombing was also less common than IPF/UIP. These findings are like those reported by TS Kim *et al*.[21] and Elliot TL *et al*. [22].

High-resolution CT findings consist of ground glass opacities (36.66%) and/or consolidative areas (16.66%) distributed along the bronchovascular bundles and along the subpleural lungs. These findings suggestive of COP were as per study done by Ju Won Lee *et al*. [23]. Diffuse involvement was noted on HRCT in HSP which includes tiny centrilobular nodules with groundglass haziness and predominance in upper lobes. These findings were correlated with study done by DA Lynch *et al*. [24].

Ten (33.33%) cases which were CTD-ILD noted in present study in which 7 cases (23.33%) are RA-ILD (4 cases show UIP pattern & 3 cases show NSIP pattern), 2 cases are SS-ILD (NSIP pattern),1 case of SLE show UIP pattern.Out of 10 patients 5, serologically positive for rheumatoid arthritis were reported in our study. Out of ten,one was (9%) male and ten (91%) were females showing a clear female preponderance. Most common pattern found with rheumatoid arthritis was reticular opacity associated with UIP pattern in our study. One case of systemic lupus erythematous (SLE), showed features of UIP and another 2 cases of SS-ILD showed NSIP pattern. Similar association was observed in studies done by Chan TY *et al*. [25] and JmSeely *et al*. In the present study we found a strong correlation between scleroderma and NSIP pattern.

Most commonly found associated risk factor with interstitial lung disease in this study was connective tissue disorder (n=10; 33.33%). This important observation was similar to the results of study by Pankaj Badarkhe Patil *et al*. [26]. (38%). Smoking (n=17; 56.66%) was the second more common risk factor. In 2 isolated cases there was history of exposure to birds and grphite dust respectively. Any other exposure history was not elicited in this trial may be because of small sample size of the study population.

The most commonly found pattern associated with interstitial lung disease was reticular opacity (n=21; 70%) which is similar to to Pankaj Badarkhe-Patil *et al*. study (n=37; 64%). (table:5). Most common specific HRCT findings in our study population were traction bronchiectasis (n=18; 60%) followed by septal thickening (n=15; 50%) and ground glass opacity (n=11; 36.66%). Diffuse distribution of HRCT findings was seen in 14 cases (46.66%). Lower lobes were predominantly involved in 17 cases (56.66%). Incidence of Reticular & Reticulonodular patterns were 76.66% in present study which was similar to the observation of Gagiya Ashok K *et al.* study. Reticular & Reticulonodular patterns as compared to 51% in Johnston *et al*. study. Slight less percentage of cases in Johnston *et al*. may be because of that in present study selection of patient done mainly on typical X ray chest finding while Johnston *et al*. study patient with normal and ill defined opacities on chest X ray also included.

Table-5: HRCT features of the study population

TYPE OF LESIONS	No of patients
RETICULAR	21
NODULAR	04
RETICULO NODULAR	02
GROUND GLASS OPACITY	11
SEPTAL THICKENING	15
HONEY COMBING	10
MOSAIC ATTENUATION	01
CONSOLIDATION	05
TRACTION BRONCHIECTASIS	18

Mean FVC was 54.53 % which is very similar to Ashok K Gagiya *et al.* study(53.28) Pulmonary function tests were performed on computerized spirometer, through Kit Microsystems in 30 patients of

high resolution computed tomography (HRCT) proven interstitial lung diseases in Jindal *et al*. study (60.90). Majority of patients have FVC% of predicted between 30-59% in present study and in Mahashur *et al*. studies. In Mahashur *et al*. study, FVC% of predicted below 30% was found in 27% as compared to 6.66% in present study, which may be related to early refers or early diagnoses of interstitial lung diseases due to more advance in non-invasive investigation of interstitial lung diseases. FEV1/FVC ratio was more than 60% in most cases in present study (96.66%) and also in Mahashur *et al*. studies (94%). Mean FVC (% of predicted) was 54.53% in present study and closely resemble to Gagiya Ashok K *et al*. study (53.28%) & Jindal *et al*. (60.90%) study. FEV1/FVC % was normal or increased in both studies(table 6).

In all 30 patients hemogram, renal function tests, liver function tests were done. Renal function tests were normal in all patients.

Table-6: Spirometry – degree of restriction

DEGREE OF RESTRICTION FVC%	NO.OF PATIENTS
MILD (70-79% OF PREDICTED)	3
MODERATE (60-69% OF PREDICTED)	6
MODERATELY SEVERE (50-59%)	11
SEVERE (35-49%)	7
VERY SEVERE (Less than 35%)	3

Table-7: Summary of the all the parameters in the study group

Variable	Number of patients (Percentage)
Age distribution	
30 – 40 Years	04 (13.33)
41 – 50 Years	06 (20.00)
51 – 60 Years	11 (36.67)
61 – 70 Years	07 (23.33)
< 70 Years	02 (06.67)
Sex distribution	
Male	12 (40%)
Female	18 (60%)
Duration of illness	
< 1 Year	08 (26.67)
> 1 - ≤ 3 Years	12 (40.00)
> 3 - ≤ 5 Years	06 (20.00)
> 5 Years	04 (13.37)
Type of cough	
Productive	09 (30.00)
Dry	21 (70.00)
mMRC grading	
Grade 0	00 (00.00)
Grade 1	06 (20.00)
Grade 2	10 (33.33)
Grade 3	09 (30.00)
Grade 4	05 (16.67)
Suggestive Past History of	
Type2 DM	09 (30.00)
Hypertension	06 (20.00)
Pulmonary Tuberculosis	04 (13.33)
Smoking	17 (56.67)
Anaemia (Hb Percentage in gm/dl)	
No anaemia (> 13.0)	13 (43.33)
Mild anaemia (11 – 12.9)	09 (30.00)
Moderate anaemia (8.0 – 10.9)	06 (20.00)
Severe anaemia (<8.0)	02 (06.67)

In respiratory system examination 50% cases had bilateral velcro crepitation, which was dry and inspiratory. Creptations other than velcro creps were seen in 43.33% cases. It might be produced by fluid accumulation in the very small air passages, where drainage was hampered by peribronchial and interstitial fibrosis. Other findings were bronchial breathing in one case (3.33%) and rhonchi in 13.33% of cases.

Extrapulmonary complaints included weight loss in 13 cases (43.30%) ,fever 40 cases (40%), joint pains in 8 cases (13.2%),chest pain & skin lesions in 4 cases & haemoptysis in 1 case.

Various parameters in the study group are summarised in the table 7

CONCLUSION

Our study suggests that interstitial lung diseases are not uncommon in India. In patients with progressive dyspnoea ILD should be ruled out as this is the most common complaint in ILD patients. HRCT lung is a noninvasive investigation of choice in clinically suspected cases of interstitial lung disease as it is very effective in visualizing the distorted architecture of lung parenchyma. HRCT along with clinical data and relevant laboratory investigations helps in arriving at the closest differential diagnosis in interstitial lung disease.

LIMITATIONS OF THE STUDY

- As the present study is a hospital based clinical trial, sample size was only 30, which might not represent the exact sample of the community. So it was difficult to predict the prevalence of the disease.
- Though all the patients of DPLD attended to the hospital were taken into study, because of the presence of more number of cases having CTD-ILD, female preponderance was found in the study. That might have led to selection bias.
- Large multi-centric trial with large sample size is suggested to get a clear picture of clinical and radiological evaluation.

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