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Clinical, Radiological and Pathological Characteristics of Hypersensitivity Pneumonitis and its Association with the Duration of Exposure in a Tertiary Centre

Sourabh Pahuja¹, Arjun Khanna^{1*}, Pallavi Periwal², Ankit Kumar Sinha³, Dhruv Talwar⁴, Satyam Agarwal¹, Pradeep Bajad¹ and Deepak Talwar⁵

¹Department of Pulmonary Medicine, School of Medicine, Amrita Vishwa Vidyapeetham, Faridabad, Haryana, India

²Department of Pulmonary Medicine, Shalby Hospital, Jaipur, Rajasthan, India

³Department of Pulmonary Medicine, Yashoda Super speciality Hospital, Kaushambi, Uttar Pradesh, India

⁴Department of Pulmonary Medicine, All India Institute of Medical sciences, Patna, India

⁵Department of Pulmonary medicine, Metro hospital, Sector 11, Noida, Uttar Pradesh, India

ABSTRACT

Background: Hypersensitivity pneumonitis (HP) has varied presentation, and it is unknown as to which individuals exposed to a potential antigen will develop HP. HP can often progress to permanent lung fibrosis, with significant social and economic consequences, besides reduced survival. To the best of our knowledge, this is the first such paper from India comparing characteristics of HP with duration of exposure.

Methods and Materials: A retrospective observational study was conducted on 60 adult patients who meet the criteria of Hypersensitivity pneumonitis according to Schuyler's criteria, at a tertiary care centre between February 2022 to June 2023. Clinical data including patient's history, clinical manifestation, laboratory findings and HRCT findings was obtained from patient's medical record files.

Results: 73.3% patients were female. Most common offending antigen was avian droppings. In 11.7% the antigen could not be identified. 56.7% were homemakers. The most common HRCT finding was ground glass haziness (90%) and most common radiological pattern was Fibrotic Non-specific Interstitial pneumonitis (NSIP). 71.67% patients had a restrictive ventilatory defect. 90% had chronic HP. Longer the duration of exposure, more severe is the restriction and less distance was covered on 6 minute walk test (6MWT). With increasing duration of exposure, more patients developed Unique interstitial pneumonitis (UIP) pattern rather than fibrotic or cellular NSIP.

Conclusion: Continued long-term exposure causes most patients to develop parenchymal fibrosis. Longer duration of exposure is associated with worse ventilatory parameters and outcomes.

*Corresponding author

Arjun Khanna, Department of Pulmonary Medicine, School of Medicine, Amrita Vishwa Vidyapeetham, Faridabad, Haryana, India.

Received: July 21, 2024; **Accepted:** July 27, 2024, **Published:** August 05, 2024

Keywords: Hypersensitivity Pneumonitis, Clinical Spectrum of HP, HP Characteristics

Introduction

Hypersensitivity pneumonitis (HP), is a complex immunologically induced inflammatory disease of lung parenchyma which develops in response to inhalation of a variety of antigens in susceptible but non atopic individuals to which the patient has been sensitized after repeated exposures and develops on a background of patient's genetic susceptibility and environmental risk factors [1,2].

In 3 European countries, HP accounts for 4-15% of all Interstitial lung diseases (ILD) [3]. In India different studies showed that it accounts for 2.4-10% of all ILD patients [4-6]. The Indian registry for ILD showed HP as the most common ILD in India with 47%

of total ILD cases [7]. Studies on high-risk populations suggest that HP accounts for 19% in farmers exposed to mouldy hay and 6-20% in people exposed to bird droppings [8,9].

Over 200 to 300 antigens derived from protozoa, molds, animals, insects, bacteria, low molecular weight chemicals and other organic sources have been identified [10,11]. Farming, birds and water contamination account for 75% of cases.

The clinical presentation may be acute, subacute or chronic. The symptoms of acute attack are like flu and appear some 4 – 6 hr after the patient inhales the antigen. After repeated episodes the pattern of disease may change to a sub-acute or chronic form with a considerable overlap, with persistent cough and phlegm, shortness of breath, loss of appetite and weight loss.

A practical approach to diagnose HP is to suspect every case of interstitial lung disease, detailed history taking including a detailed environmental exposure history and examination. is mandatory. Lacasse et al. emphasized the following variables as significant predictors of HP: i) exposure to known offending antigen; ii) positive precipitating antibodies; iii) recurrent episodes of symptoms; iv) inspiratory crackles; v) symptoms 4 – 8 hr after exposure; and vi) weight loss [12].

The aim of this study is to know the clinical, radiological and pathological characteristics of HP and its association with the duration of exposure to the inciting antigen. Patients were diagnosed with hypersensitivity pneumonitis, according to Schuyler's criteria [13].

Methods and Material

A retrospective observational study was conducted on 60 adult patients who meet the criteria of Hypersensitivity pneumonitis according to Schuyler's criteria, at Department of respiratory, sleep, allergy & critical care Medicine at the Metro Centre for Respiratory Diseases, Metro Hospital, Noida. Clinical data including patient's history, clinical manifestation, laboratory findings and HRCT findings was obtained from patient's medical record files between February 2022 to June 2023, retrospectively.

Inclusion Criteria

- Patients included who were diagnosed according to Schuyler's criteria.
- Patients whose clinical and other investigational data was complete and available in hospital files for analysis.
- Adult > 18 years of age of either sex.

Exclusion Criteria

History of acute pulmonary tuberculosis or acute myocardial infarction.

Patients with known CTD/ILD and other known cause of ILD.

Clinical data including patient's history, exposure history, clinical manifestation, laboratory findings and HRCT findings was obtained from patient's medical record files available at the Metro Centre for Respiratory Diseases.

All HRCT Chest scan was reviewed by radiologist. Signs including ground glass opacities, mosaic attenuation, nodules, fibrosis, emphysema, honeycombing were evaluated. Spirometry Test: FVC, FEV1 and FEV1/FVC%, DLCO, 6MWT was assessed. Sputum for AFB and Autoimmune profile were noted. After collecting all relevant data as mentioned six significant predictors of HP as per HP study was applied and statistically analysed.

Statistical Analysis of Data

All the statistical analysis was performed using SPSS version 20. The clinical profile of patients was analyzed by chi-square test for qualitative variables and student t test and one way ANOVA for quantitative variables. 5% probability level was considered as statistically significant i.e., $p < 0.05$.

Results

Out of 60 patients, 16(26.7%) were male and 44(73.3%) were female. 10% (6) patients were smokers while 90.0% (54) were non-smokers. The age of the subjects in this study ranged from 24 to 73 years with a mean of 55.15 ± 11.11 years.

34(56.7%) were homemakers, 5(8.3%) were office goers, 4(6.7%)

were farmer's, 2(3.3%) were factory workers, and 1(1.7%) each were a cement shop owner, chemical industry worker, clerk, doctor, engineer, grain storekeeper, milkman, nurse, shopkeeper, store manager, student, teacher, textile industry worker and wildlife photographer.

History of exposure to pigeon or avian droppings was 19(31.7%), to grain dust 5(8.3%), to molds 4(6.7%), to drugs 2(3.3%), and one each to incense stick/ hawan smoke, chemicals, acetaldehyde fumes, cotton dust, bangle manufacturer, sugarcane, jute, air conditioning fumes. There is a history of more than one type of exposure in 25% (15/60) patients which includes pigeons or avian droppings in 60% (9/15). There was no history of significant exposure in 11.7% (7) patients. Mean duration of exposure was 14.46 ± 12.48 years.

The total duration of symptoms ranged from 0.02 to 240 months with a mean duration of 21.95 ± 38.59 months. The most common general symptom was myalgia complained by 60% (36) patients, fever reported in 56.7% (34), weight loss by 22(36.7%) and loss of appetite in 1/3rd patients (20). Respiratory symptom of dyspnea was reported by all 100%. Cough in 96.7% (58) patients while it was productive in only in 15% (9). Chest pain was noticed by 12(20%) and wheeze in 11.7% (7) patients.

Almost 60% (36) of patients had received some form of treatment prior to being seen at our center. Nearly half were on steroids 28(46.7%) and 8.3(5) were on domiciliary oxygen, while 40% (24) were on inhaled corticosteroids and equal number on inhaled bronchodilators too. Eleven (18.3%) patients were on even oral bronchodilators. Nine (15%) patients were on pirfenidone and 35% (21) on NAC. 15% patients received immunosuppressive agents, mostly on azathioprine (8/9; 89%) while 1(1.7%) was on hydroxychloroquine. Five (8.3%) patients were on ATT empirically.

General physical examination revealed clubbing in 26.7% (16) followed by pedal edema in 9(15%), pallor in 3(5%), elevated jugular venous pressure in 2(3.3%).

Respiratory system examination revealed most commonly crackles in 78.3% (47), wheeze in 5% (3) patients and inspiratory squeaks in 8(13.3%). Examination was normal in 2(3.3%) patients.

The most common HRCT finding was ground glass haziness seen in 90% (54) patients followed by mosaic attenuation in 65% (39), centrilobular nodules were seen in more than half (55%), reticular abnormalities and traction bronchiectasis seen in 45% each (27). Peribronchovascular involvement was seen in 41.7% (25), bronchial dilatation in 61.7% (37/60) and honeycombing in 28.3% (17) patients. Rare findings were mediastinal lymphadenopathy in 10% (6), consolidation in 6.7% (4) while emphysema and cysts were seen in 5% (3) each. Subpleural fibrosis was seen in 45% (27) patients but pleural thickening in only one case. Most common radiological pattern was Fibrotic NSIP in nearly half (29) patients, cellular NSIP in 35% (21) while UIP was seen in 16.7% (10) patients.

Spirometry and 6MWT findings are shown in Table 1 and 2 respectively. Overall, 71.67% patients had a restrictive ventilatory defect, 25% (15) had mixed abnormality and pure obstructive ventilatory defect in 1(1.7%) patient. Only 1(1.7%) patient had normal PFT.

Table 1: Pulmonary Function Test - Spirometric Findings

N	PFT parameters	MEAN±SD (RANGE)
60	FEV1/FVC	79.04±9.12 (49.32-100)
60	Pre FVC %	61.83±22.34 (22-123)
60	Pre FVC (Litre)	1.68±0.63 (0.77-3.65)
60	Post FVC %	64.05±21.80 (22-128)
60	Post FVC (Litre)	1.74±0.63 (0.90-3.81)
60	Pre FEV1 %	58.75±22.18 (21-115)
60	Pre FEV1 (Litre)	1.32±0.54 (0.65-3.10)
60	Post FEV1 %	61.90±22.25 (24-121)
60	Post FEV1 (Litre)	1.39±0.54 (0.75-3.14)
52	DLCO(ml/mmHg/ML)	12.65±4.03 (6.47-23.31)
52	DLCO %	54.60±16.87 (27-99)

Table 2: Findings on 6MWT

N	6MWT parameters	MEAN±SD (RANGE)
60	Distance covered(meters)	267.97±10.78 (108-460)
60	% of predicted distance	50.47±13.52 (23.35-82.37)
60	Spo2 (start)	94.22±2.53 (88-99)
60	Spo2 (min)	83.18±6.32 (67-95)
60	% desaturation	11±5.05 (3-25)

Eighteen patients (30%) underwent fibroptic bronchoscopy.

Table 3: Duration of Exposure and its Association

Parameters	Duration of Exposure				P value
	6- 28 Days	1Month-1 Year	1 Year-10 Years	>10 Years	
Fever	2	2	14	12	0.321
Myalgia	2	2	15	13	0.390
Loss of appetite	2	1	8	6	0.169
Loss of weight	2	1	11	6	0.138
SOB	2	2	25	24	
Cough	2	2	24	23	0.982
Chest Pain	1	0	6	2	0.251
Clubbing	0	0	7	8	0.049
X-ray- Normal	0	1	1	2	0.006
UL/BL	0/1	0/1	1/23	0/23	0.786
Upper zone	0	0	10	3	
Lower zone	0	1	6	10	0.001
All	0	0	0	2	

The mean of BAL lymphocytosis was 29.17±6.91 with a range between 20-40%. Transbronchial lung biopsy (TBLB) was done in 18(30%) patients; endobronchial biopsy (EBB) was done in 17(28.3%) patients. Video assisted thoracoscopic biopsy was done in 4(6.7%) patients.

Out of 60 patients, 22(36.7%) patients underwent lung biopsy. The most common histopathological finding was bronchiolocentric cellular interstitial pneumonia and it was present in 22(36.7%) patients. Small, non-necrotizing poorly formed loose granulomas were present in 21(35%) patients, while chronic bronchiolitis were seen in 13(21.7%) patients.

Ten percent (6) patients were diagnosed as acute HP while 90% (54) were Chronic HP.

83.3% (50) were able to practice exposure avoidance to some extent. Oral steroids were given to nearly all (56) patients while azathioprine was given to 22(36.7%) patients. Pirfenidone was given to 3(5%) patients only. One third patients were given home oxygen and 11(18.3%) were given domiciliary NIMV.

Further follow up of these patients was collected. Mean follow up was for 53.88±41.03 days with a range of 14-240 days. Overall 65% (60) patients were stable, 10(16.7%) patients showed partial improvement, ten patients (16.7%) worsened despite being on treatment. Only one patient with Acute HP (1.7%) got cured completely with no residual changes.

Duration of Exposure and its Association with Clinical, Respiratory Physiology, Radiological and Histopathological Findings: (Table 3, 4)

More duration of exposure in HP showed more involvement of lower zones and more extensive involvement (≥2 zones) in X-rays (p= 0.001). Also, longer the duration of exposure, more severe is the restriction with FVC being significantly lower as well as FEV1/FVC ratio being higher (p< 0.05) and they also covered less distance on 6MWT (p=0.04). Lower the duration of exposure better were the outcomes of patients (p<0.05), compare to the patients with longer duration of exposure.

Upper+Mid	0	0	7	8	
Mid+Lower	1	0	1	0	
Radiological pattern (C.NSIP/F. NSIP/ UIP)	2/0/0	2/0/0	11/10/4	4/14/6	0.068
HPE-Interstitial pneumonitis	2	1	11	6	
HPE-chronic bronchiolitis	1	1	7	3	0.787
HPE-granuloma	2	1	10	6	0.835
Improved	1	2	5	1	.003
Cured	1	0	0	0	.000
Worsened	0	0	4	5	0.780
Stable	0	0	16	19	0.022

Key- SOB- shortness of breath, UL/BL- unilateral/bilateral, HPE- histopathological examination

Table 4: Duration of Exposure and its Association

Parameters	Duration of Exposure				P value
	6- 28 Days	1Month-1 Year	1 Year-10 Years	>10 Years	
Spo2%	89.5±3.53	92.5±7.78	93.52±4.15	90.42±6.22	0.214
RR(min)	28±8.49	26±0.0	24.08±5.30	25.45±4.50	0.607
Temperature	99.2±1.41	99.5±0.70	98.55±0.98	98.35±0.72	0.215
Pao2(mmHg)	60.50±6.36	50.0	69.16±10.74	64.38±8.52	0.174
Paco2(mmHg)	35.3±4.66	33.0	37.06±8.05	36.6±5.72	0.909
Spo2(ABG)	90.0±4.24	86.0	93.78±3.11	90.14±6.11	0.153
FEV1/FVC	70.23±0.77	77.36±10.79	77.81±6.33	83.02±9.30	0.045
Pre FVC(L)	1.44±0.50	2.63±1.44	1.85±0.66	1.53±0.53	0.050
Pre FVC%	56.5±13.43	69.5±14.84	67.08±24.68	58.0±22.25	0.540
Post FVC(L)	1.48±0.42	2.80±1.42	1.90±0.65	1.60±0.54	0.045
Post FVC %	58.5±17.67	74.5±12.02	68.36±22.98	61.0±23.09	0.619
Pre FEV1(L)	0.93±0.17	2.11±1.39	1.43±0.53	1.26±0.48	0.102
Pre FEV1%	47.5±12.02	64.5±23.33	62.24±23.84	58.87±23.37	0.820
Post FEV1(L)	1.06±0.06	2.22±1.30	1.52±0.53	1.30±0.48	0.076
Post FEV1%	50.0±18.38	69.0±18.38	65.48±23.39	61.79±24.05	0.785
DLCO(ml/mmHg/ ML)	9.88±1.16	13.6±3.63	13.01±3.92	12.45±4.61	0.760
DLCO%	46.0±14.14	50.0±1.41	57.11±15.46	52.09±19.3	0.679
Distance covered(meters)	237±97.58	360±50.91	297.7±90.11	240.8±69.23	0.041
Spo2- start(6MWT)	92±0.0	93.0±4.24	95.04±2.49	94.04±2.54	0.230
Spo2- min(6MWT)	83±5.65	81.5±9.19	84.3±6.49	81.95±6.39	0.630
% Desaturation	9.0±5.65	11.5±4.94	10.64±4.96	12.08±5.41	0.720

Radiology and its Correlation with Clinical, Respiratory Physiology and Histopathology: (Table 5 and Figure 1)

In our study we had found with increasing duration of exposure, more patients developed UIP pattern rather than fibrotic or cellular NSIP (p value<0.05). Different radiological patterns in HP had different outcome and UIP pattern was associated with worse outcomes.

Table 5: Radiological Pattern and its Association

Parameters	Radiological Pattern			P value
	Cellular NSIP	Fibrotic NSIP	UIP	
Duration of exposure	8.93±10.25	17.54±11.05	17.60±11.33	0.027
Spo2 (%)	93.33±4.79	91.41±5.17	90.50±6.40	0.292
Respiratory rate	23.90±4.79	24.90±4.91	26.50±5.28	0.395
Temperature	98.67±0.96	98.55±0.96	98.17±0.38	0.348
Pao2(mmHg)	69.36±11.43	64.71±8.76	61.25±6.65	0.275
Paco2(mmHg)	37.96±6.95	36.17±5.07	35.5±2.51	0.696
Spo2 @ ABG	93.0±4.19	91.32±4.84	88.25±7.32	0.266
FEV1/FVC	76.50±11.49	81.78±7.47	76.45±5.64	0.079
Pre FVC(L)	1.95±0.75	1.56±0.53	1.48±0.43	0.045
Pre FVC %	70.52±21.31	54.86±17.43	63.80±31.34	0.045
Post FVC	1.99±0.76	1.63±0.53	1.57±0.44	0.083
Post FVC%	71.66±19.50	57.37±17.01	67.4±32.84	0.061
Pre FEV1(L)	1.51±0.72	1.25±0.38	1.14±0.39	0.123
Pre FEV1%	64.71±22.96	54.10±18.06	59.70±29.73	0.249
Post FEV1(L)	1.59±0.70	1.32±0.40	1.20±0.38	0.091
Post FEV1%	67.71±22.28	57.49±18.35	62.5±30.85	0.279
DLCO(ml/mmHg/ML)	12.96±2.97	12.90±4.57	11.09±4.40	0.503
DLCO (%)	59.06±16.80	51.91±15.83	53.38±20.33	0.383
Distance Cover (6MWT)	283.33±85.94	257.59±84.02	265.80±80.11	0.566
Spo2- start	94.42±2.42	94.17±2.45	93.9±3.14	0.859
Spo2 min@ 6MWT	85.57±5.48	82.58±6.63	79.90±5.64	0.048
% Desaturation	8.85±3.90	11.52±5.60	14.0±3.74	0.019

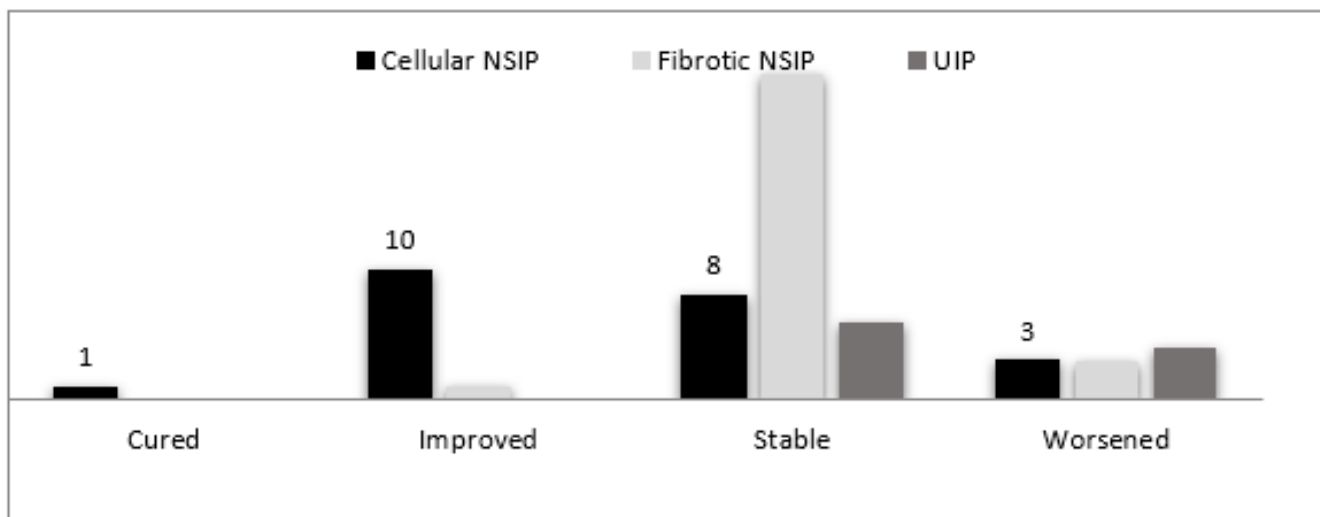


Figure 1: Association between Radiological Pattern in HP and Outcomes

Discussion

In our study, 26.7% were male and 73.3% were female. 10.0% patients were smokers while 90.0% were non-smokers. The mean age of the patients was 55.15±11.11 years. These findings are consistent with previous studies, which have shown the prevalence of HP to be more in females, between the ages of 45-65 years, and in non-smokers [2,14].

Traditionally, HP has been associated with occupational and recreational activities. However, newer causative agents continue to be identified each day and domestic environment is also being implicated. Majority were homemakers (56.7%) in our study. Recent studies also suggest that exposure in the home environment may play an increasing role in causing HP [15].

Exposure to the offending agent could be identified in 88.3% of HP cases in our study while inciting agent was not clear in 11.7% cases. The most common antigen identified was pigeon or avian droppings in 31.7% cases. Both the prominent international reports published earlier have demonstrated similar findings [2,14]. However, this is in contrast to the Indian ILD registry data, where the most common exposure was air-coolers [16]. Other antigens identified in our study were grain dust in 8.3%, moulds in 6.7%, drugs in 3.3%, while single case each (1.7%) reported exposure to incense stick/ hawan smoke, chemicals, acetaldehyde fumes, cotton dust, bangle manufacturing dust, sugarcane, jute and AC fumes. There was more than one exposure in 25% patients and pigeon or avian droppings were again the most common identified in over 60% of these cases.

The most common respiratory symptom was dyspnea which was present in all the patients. Cough was present in 96.7% patients. Non-specific general symptoms such as myalgia were present in 60.0% patients, fever in 56.7%, weight loss in 36.7% and loss of appetite in 33.3% patients. These findings have been in consistent with the three large cohorts of HP patients [2,14,16]. In all studies dyspnea was the most common symptom present. In our patients 'flu like symptoms' were more common being seen in more than half of the cases.

The most common finding on systemic physical examination was clubbing, present in 26.7% patients, while on respiratory system examination crackles were the most common finding present in 78.3% and inspiratory squeaks in 13.3% patients and wheeze were seen in 5% patients. These findings were more in consistent with HP study by Lacasse Y et al, where clubbing was present in 21% patients and crackles in 87% patients, while in Mayo clinic study clubbing was present in 5% patients and crackles in 56% patients [2,14]. This difference could be due to longer duration of exposure in our study with a mean of 14.46±12.48 years, while it was only 14 months in Mayo study.

60% patients had received some form of treatment prior to evaluation at our center. Most commonly they had received either oral steroids (46.7%) or inhaled corticosteroids (40%) and 35% had received NAC, 15% were on pirfenidone while 15% of the patients had received immunosuppressive agents such as azathioprine and hydroxychloroquine. Before presenting to us 8.3% of the patients had been diagnosed with Pulmonary Tuberculosis on radiological grounds and were given empiric anti-tubercular treatment. This throws light on practice of giving ATT by physicians in this part of the world. However, 32% patients in Mayo study also received corticosteroids before their evaluation [14]. Indian patients also received other therapies more frequently as mostly patients were considered IPF and triple therapy was still being practiced during the timelines of our study.

In our study, most of the patients (71.67%) had a restrictive ventilatory abnormality, 25% patients had a mixed ventilatory abnormality while only 1.7% patient each had an obstructive ventilatory defect and normal spirometry respectively. Previous studies done on HP also show more or less similar findings on PFT. Restrictive ventilatory abnormality is the most commonly reported findings, present in 64%,53% and 91% patients respectively but mixed ventilatory abnormality was present in 1% in HP study and no case was reported in Mayo study while obstructive ventilatory abnormality was seen in 1% & 16% patients respectively in these two studies [2,14,17]. The difference in prevalence of mixed ventilatory defect which not only showed reduce FVC but also

reduce FEV1, could be because of difference in home environment as most of our patients were homemakers and also had exposure to various biomass fuels used for cooking in India.

Normal Spirometry was present in 34% and 10% patients in other studies and was significantly more than 1.7% of our study and signifies ongoing exposure, late presentation and late diagnosis of patients in our country which is clearly seen by practice of being treated as obstructive airway disease by inhaled bronchodilators and steroids as well as oral bronchodilators in 42% of cases prior to the correct diagnosis [2,14]. 49(94.23%) had reduced diffusion capacity. This is in consistence with previous international data, which have also demonstrated a similar reduction in the DLCO, commensurate with restrictive ventilator defect [2]. Exercise induced hypoxemia was demonstrated in 98.3% patients while hypoxia at rest was present in 25% patients [14,18].

High-resolution computed tomography (HRCT) is an indispensable tool in diagnosing HP as biopsy is not performed in all the cases. In our study, the most common HRCT finding in our study was ground glass haziness, present in 90% patients, centrilobular nodules in 55% and mosaic attenuation in 65% patients. These were consistent with previous study as shown below in Table 6 [14]. Mediastinal lymphadenopathy and consolidations were not reported by others but in our patients are likely to be related to acute exacerbation of HP.

Table 6: HRCT Findings Comparison

HRCT Findings (In %)	Our Study (N = 60)	Mayo study28 (N = 85)
Ground glass haziness	90%	65%
Centrilobular nodules	55%	33%
Mosaic attenuation	65%	43%
Honeycombing	28.3%	11%
Traction Bronchiectasis	45%	15%

The most common radiological pattern was the Fibrotic NSIP in 48.3% patients; cellular NSIP in 35% while UIP in 16.7% patients. None of the previous studies had divided the radiological pattern to a particular category as criteria to divide them.

Lung biopsy although not always feasible to perform, helps in establishing diagnosis of HP, especially when the diagnosis is suspected in view of clinic-radiological findings. In our study, 36.7% underwent some form of lung biopsy. 30% underwent fibreoptic bronchoscopy and TBLB while VAT's biopsy was done in 6.7% patients. Endobronchial biopsy (EBB) was done in 28.3% patients when sarcoidosis was in the differential diagnosis. Lung biopsy was done in 87% patients in Mayo study and lower biopsy rates in our patients is due to reluctance on part of both patients as well as treating physicians in getting it done. However, lung biopsy is not always indicated for the diagnosis HP especially when clinic radiological findings are almost confirmatory [10]. The mean of BAL lymphocytosis was 29.17±6.91% with a range of 20-40%. G Raghu et al, had shown that BAL lymphocytosis >50% is diagnostic of HP, while >25% is suggestive of granulomatous disease and diagnosis of HP requires other supporting evidence [19]. 83.3% of patients who underwent fibreoptic bronchoscopy showed lymphocytosis >25%.

The most commonly reported histopathological finding was bronchiolocentric cellular interstitial pneumonia; present in all patients who underwent biopsy. Small, non-necrotizing poorly formed loose granulomas were seen in 95.45% patients, while chronic bronchiolitis in 59.09% patients. In previous studies also the most common histopathological finding was bronchiolocentric cellular interstitial pneumonitis with poorly formed septal granulomas [14].

The best management of HP is avoidance of the inciting agent and the only current accepted medical treatment is oral or systemic corticosteroids [20,21]. Corticosteroids were given to 93.3% patients while other immunosuppressive mainly azathioprine was given to 36.7% patients who had side effects related to corticosteroids.

The mean duration of exposure was highly variable ranging from 6 days to 35 years. Increasing duration of exposure had not only shown significant association with respiratory physiology and radiology but also with the outcome of the patients. Patients with longer duration of exposure had more involvement in lower zones and more than one zone in chest X-rays ($p=0.001$). Our study also showed longer duration of exposure to the inciting antigen led to more severe restrictive ventilatory defects on the lung function testing as their FEV1/FVC ratio was higher and FVC was significantly lower ($p < 0.05$). Also, these patients covered less distance on the 6MWT ($p=0.04$). With longer duration of exposure, most patients worsened clinically or remained stable rather than improving and it was statistically significant ($p<0.05$). In our study we also found that with increasing duration of exposure more patients developed 'UIP' pattern rather than fibrotic or cellular NSIP pattern ($p<0.05$). Different radiological patterns had different outcomes and the UIP pattern was associated with the worse outcomes. Hanak et al, also shows that patients with fibrosis, honeycombing and traction bronchiectasis (UIP pattern) had longer duration of exposure, poor pulmonary function (reduced FVC, increase FEV1/FVC, decrease DLCO with p value <0.05) and poorer outcomes in terms of increase death (42% in fibrotic group and 2% in non-fibrotic group) [22]. To the best of our knowledge there are no large-scale Indian studies that correlate the duration of exposure to clinical, radiological and pathological characteristic of HP.

The limitations of this study are that it is a retrospective single centre-based study. Cases of HP referred to our tertiary centre are probably skewed toward those that are chronic and difficult to diagnose and so referral bias is likely. Limited follow-up in this study did not allow detailed analysis and ultimate long-term prognosis. Further studies are needed in this respect.

Conclusion

We conclude that most patients seen at our centre had chronic HP. Majority of our patient were female and homemakers, emphasizing the growing role of home environment in causing HP. The most common inciting cause was pigeon or avian droppings while, in 11.7% of the patients the responsible antigen could not be identified.

With continued long-term exposure, most patients developed parenchymal fibrosis. Longer duration of exposure was associated with worse ventilatory parameters and outcomes. Additional research is needed to develop methods for identifying the offending antigens suitable in our patients, and to understand the natural history and prognostic factors for this disease.

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