How to Cite:
Akl, Y. M. K. ., Soliman, Y. M. A., Assal, H. H. . ., Abdullah, M. A., Ibrahim, I. M. H., Ghaffar, H. A. A., Soliman, R., Gad, M. A., & El-Hinnawy, Y. H. (2022). Factors affecting bronchoalveolar lavage cellularity in patients with hypersensitivity pneumonitis. *International Journal of Health Sciences*, *6*(S7), 1030–1044. https://doi.org/10.53730/ijhs.v6nS7.11514

Factors affecting bronchoalveolar lavage cellularity in patients with hypersensitivity pneumonitis

Yosri Mohamed Kamel Akl
Professor of Chest Diseases Faculty of Medicine, Cairo University, Egypt

Youssef Mohamed Amin Soliman
Professor of Chest Diseases Faculty of Medicine, Cairo University, Egypt

Hebatallah Hany Assal
Professor of Chest Diseases Faculty of Medicine, Cairo University, Egypt

Mohamed Abdelwaly Abdullah
Chest specialist, Giza chest hospital, Ministry of health and population, Egypt
Corresponding Author

Iman Mohamed Hamdy Ibrahim
Assistant Professor of diagnostic radiology Faculty of Medicine, Cairo University, Egypt

Heba A. AbdEl Ghaffar
Lecturer of Immunology, Clinical and Chemical Pathology department Faculty of Medicine, Cairo University, Egypt

Rania Soliman
Lecturer of Immunology, Clinical and Chemical Pathology department Faculty of Medicine, Cairo University, Egypt

Maha A. Gad
Lecturer of Immunology, Clinical and Chemical Pathology department Faculty of Medicine, Cairo University, Egypt

Yasmine Hamdy El-Hinnawy
Ass. Professor of Chest Diseases Faculty of Medicine, Cairo University, Egypt

***Abstract*---**Background: Hypersensitivity pneumonitis (HP) refers to the inflammatory lung condition that results from inhalation of various (mostly organic) antigens leading to development of lymphocytic alveolitis and granulomatous pneumonitis. Pathogenesis

of the disease is not fully understood and identification and removal of the causative agents remains the cornerstone of treatment and a major determinant of prognosis. Bronchoscopy and BAL can be used to characterize alveolitis and inflammatory cells infiltrate assuming to have a main role inthe pathogenesis of the disease process. Aim : to improve the characterization of alveolitis in HP on a number of patients with well-defined stages of disease activity and to assess the frequency of cellularity, CD4 and CD8 alveolitis. Subjects and methods: 88 HP cases diagnosed by thorough history, clinical examination, HRCT (with scoring system for each radiological pattern), spi rometry, and FOB with BAL for cellularity and flowcytometry (FCM) to determine CD4/CD8 ratio.Results: The mean total cell count (TCC)/cmm was (397±241) in subacute cases and (247±291) in chronic cases with statistically significant difference P-value 0.002. Mean lymphocytes percent was (45±19%) in subacute cases and 39±20% in chronic cases with no statistically significant value. There was no difference between subacute and chronic cases regarding CD4/CD8 ratio but there was a positive correlation between time elapsed since last exposure and CD4/CD8 ratio with P-value 0.006 and r = 0.505. Conclusion: BAL can aid in the diagnosis of HP if done with experienced technique. Greater than 40% BAL lymphocytosis supports HP diagnosis while less than 20% suggests another diagnosis.

***Keywords*---**(HP, FCM, BAL, lymphocytosis).

Introduction

HP is one of the main conditions identified in differential diagnoses of diffuse parenchymal lung diseases (DPLDs) **(1).**

It is important to diagnose HP accurately because its prognosis and treatment are distinct from other forms of ILD, including idiopathic pulmonary fibrosis (IPF). However, making the diagnosis of HP remains challenging due to variability of clinical findings and lack of consensus criteria **(2).**

The BAL cell profile in HP is characterized by a significant increase in the total cell count, especially a remarkable elevation in the percentage of lymphocytes, which often exceeds 50%. This marked BAL lymphocytosis is the most consistent finding in this disease, and it has been reported in all the clinical presentations **(3).**

Evaluation of CD4+/CD8+ T lymphocyte subpopulations has given contradictory results. It is the general belief that HP is characterized by an exaggerated accumulation of CD8+ T cells with a decrease in the CD4+/CD8+ ratio, and a number of studies have supported this notion. Nevertheless, some authors have found that both subsets are increased without changes in the CD4+/CD8+ ratio, while others have reported an opposite finding with a predominance of CD4+ on the surface phenotypes of BAL T cells and an increased CD4+/CD8+ ratio **(3).**

Method

Material and methods

An Observational- analytical study on Adult population presenting to the chest department of Kasr Alainy hospital diagnosed of having hypersensitivity pneumonitis (88 cases).

Inclusion criteria:

Adults with diffuse parenchymal lung disease diagnosed by history, clinical, and radiological criteria as HP**.**

Exclusion criteria:

· Patients with solitary nodule or other focal process
· Patients who had an established diagnosis other than HP
· Patients with a known history of connective tissue disease or other known diagnoses of interstitial lung disease such as histiocytosis, pneumoconiosis, lymphangioleiomyomatosis, drug-induced pneumonitis or eosinophilic pneumonia

Methodology

All patients were subjected for the following:

Full medical history with particular attention to personal history (including: demographics such as age, sex, body mass index), complaint, duration, current history, history of smoking, date of exposure to antigens that can cause HP like raising birds and work in fields containing rotten straw or grains, living at home with water damage or using a hot tub, sauna, swimming pool and other potential sources at home or work, and the history of any chronic diseases or common conditions.

Full clinical examination

HRCT chest scan by Siemens 16-channel MDCT: the protocol included Scans were obtained at end of inspiration and in supine position from the lung apices to the bases. Contrast medium was not injected in any patient. Data were reconstructed with 1.0mm section thickness and at 10-mm intervals for transverse images.

HRCT score:

Mooney et al, **(2013)** suggested a scoring system for visual assessment and quantification of the extent of affection in HRCT of patients had hypersensitivity pneumonitis. Their proposed scoring system was adopted by our working group so; the presence of HRCT findings (ground-glass opacity, consolidation, mosaic perfusion, and traction bronchiectasis, reticulation and honeycombing) was assessed independently in three (upper, middle and lower) zones of each lung. The upper lung zone was defined as the area of the lung above the level of the tracheal carina, the lower lung zone was defined as the area of the lung below the

level of the inferior pulmonary vein and the middle lung zone was defined as the area of the lung between the upper and lower zones. Each lung zone was scored on a four-point scale 0 = no involvement, 1 = 1%-25% involvement, 2 = 26%-50% involvement, 3 = 51%-75% involvement, or 4 = 76%-100% involvement).The average total score for each variable was calculated as the mean score of the six lung zones **(4).**

FOB and BAL

FOB and lavage: The patient can be placed in a semi recumbent position or in supine position. After local anesthesia and performing bronchoscopy Bronchoalveolar lavage (BAL) is performed instilling of 100–150 cc of normal saline through the bronchoscope. The bronchoscope should be placed occluding the selected segmental or subsegmental bronchus. Normal saline is flushed in 20–50 cc aliquots and then aspirated at low pressure, separating the first syringe that represents bronchial content, and using the rest of the aspirate (alveolar content) to analyze chemical, cytological and microbiological components **(5).**

FOB and BAL will be conducted by the members of the group of investigators in the chest department of Kasr Alainy hospital Fiberoptic-bronchoscopy unit.

Cellularity

The cellular analysis should be performed within 1 hour if the BAL fluid is in nutrient-poor media (e.g., saline) or within 2 to 3 hours for optimal results if the BAL fluid is in a nutrient-supplemented medium. The total cell count (nucleated immune cells) is usually obtained via a hemocytometer, and cell viability is determined by Trypan blue exclusion. Differential cell counts are performed via cytocentrifugation with staining (Wright-Giemsa or May- Grunwald-Giemsa). The presence of squamous epithelial cells suggests that BAL fluid is contaminated with

upper airway secretions, and the presence of large numbers of bronchial epithelial cells suggests that the BAL may not have adequately sampled distal airspaces **(3).** The analysis is done in microbiology unit of the clinical pathology department main lab Kasr Alainy hospital.

Flowcytometry (FCM)

· Measurement of CD4/CD8 lymphocytes ratio in BAL samples.
· Equipments used: flowcytometer (10 color BDFACSCanto), automatic pipettes, centrifuge, vortex stirrer.

Spirometry by Master screen PFT 2012, CareFusion 234 GmbH, Germany (V-781267-057 version 03.00) Pulmonary function tests (PFTs) included forced expiratory volume in one second (FEV1), vital capacity (VC), forced vital capacity (FCV), FEV1/VC, functional residual capacity (FRC), and expiratory reserve volume (ERV) **(6).**

Six minute walk distance: The 6MWD was performed using the methodology specified by the American Thoracic Society **(7).** Patients were directed to the goal of walking as far as possible within 6 minutes. 6MWT was carried out in a long, 30-meter-long, meter per- meter corridor. The heart rate and oxygen saturation were collected at the beginning and end of 6MWT. When the test was completed, the covered distance was calculated. Desaturation percent change was calculated by recording oxygen saturation before and after the 6MWD using pulsoximeter and percent desaturation from baseline was calculated.

Diagnosis of HP

A diagnostic model was proposed by Vasakova and colleagues, 2017, where patient with clinical and radiologic (HRCT) evidence of an ILD of an unknown etiology without other specific patterns (e.g., LAM, PLCH), features typical of sarcoid and no specific features and/or serology positive for CTD will then undergo a detailed history of exposures to environmental factors known to induce HP ("HP Inducers"), assure images of HRCT are also in expiration; BAL fluid cellular and microbiologic investigation to rule out mycobacterial infection.

Confident clinical diagnosis of HP when combination of:

(1) Exposure history to specific antigens, and/or SsIgGs,
(2) Compatible clinical features,
(3) Typical HRCT features (predominant ground-glass opacities, poorly defined centrilobular nodules; mosaic attenuation, air trapping rarely, consolidation in acute cases and predominant fibrosis, peribronchovascular fibrosis, honeycombing, mosaic attenuation, air trapping, centrilobular nodules in chronic cases),
(4) Inflammatory BAL (typically lymphocytosis) predicted a high confidence diagnosis of HP without need for biopsy.

Probable HP and possible HP were involved in our study without resorting to histopathology. Probable HP involved two entities: the first entity included
(a) Typical HRCT pattern of HP,
(b) Negative history of exposure and/or SsIgGs,
(c) BAL fluid cellular analyses: inflammatory pattern, predominantly lymphocytosis.

The second entity involved :
(i) HRCT patterns of UIP, NSIP, CPFE and OP,
(ii) Positive history of exposure and/or SsIgGs,
(iii) BAL fluid cellular analyses: inflammatory pattern, predominantly lymphocytosis.

Possible HP involved:
(I) Typical HRCT patterns of HP or HRCT patterns of UIP, NSIP, CPFE and OP,
(II) Positive history of exposure and/or SsIgGs,
(III) BAL fluid: normal cellular or mixed inflammatory cellular pattern (without predominant lymphocytosis) or without BAL (i.e., NOT performed) **(8)**.

Classification of HP to acute, subacute and chronic:

Acute HP is presented by a flu-like symptoms occurring a few hours or days after a (usually) substantial exposure. Symptoms gradually decrease over hours/days and may recur with re-exposure. Subacute HP may result from repeated low-level exposure to inhaled antigens. It is characterized by an insidious onset over weeks to a few months. Chronic HP is slowly progressive (insidious) chronic respiratory disease more than six months. **(8).**

Statistical methods

Data was coded and entered using the statistical package SPSS version 21. Data was summarized using number and percent for qualitative variables, mean and standard deviation for quantitative variables which are normally distributed while median and interquartile range were used

for quantitative variables which are not normally distributed. Comparisons between groups were done using: Chi-square tests for qualitative variables, analysis of variant (ANOVA) for quantitative variables which are normally distributed, while non-parametrical tests: Kruskal Wallis test and Mann-Whitney test were used for quantitative variables which are not normally distributed. Correlations were done to test for linear relation between variables and P value less than or equal to 0.05 was considered as statistically significant.

Results

Table (1)
Demographics and patient characteristics

Number of subjects n:	88
Mean age, years (SD)	46 (16)
Mean BMI (SD)	30 (8)
Gender	
Male N (%)	15 (17)
Female N (%)	73 (83)
Smoking habits	
Active smoker N (%)	0
Passive smoker N (%)	4 (5)
Non-smoker N (%)	84 (95)
Type of HP causative antigen	
Bird breeder N (%)	47 (53)
Unknown N (%)	16 (18)
Miscellaneous N (%)	25 (29)
Clinical presentation	
Acute N (%)	3 (4)
Subacute N (%)	20 (23)
Chronic N (%)	65 (73)
Symptoms and examination	
Dyspnea N (%)	80 (91)
Dry cough N (%)	57 (65)

Wheezes N (%)	6 (7)
Expectoration N (%)	32 (36)
Inspiratory crepitations N (%)	41 (46)
Squawks N (%)	28 (32)
Expiratory rhonchi N (%)	12 (14)
Clubbing N (%)	3 (3)
Comorbid conditions,complications	28 (32)
Duration of illness (m) Mean (SD)	33 (44)
Treatment duration (m) Mean (SD)	18 (26)
Time elapsed since last exposure (m) Mean (SD)	13 (14)

SD: standard deviation, miscellaneous includes: plastic factory (isocyanate), car care (metal-working glues and spray paints), clothes industry (feathers and textiles), teacher (vocational education: metal working fluid) and plasterer (espartosis, isocyanates surface coating) . Comorbid conditions, complications: DM, hypertension, IHD and pulmonary hypertension. (m) months.

Among occupations, 62 cases (73%) were housewives. There were 16 cases with unknown antigenic exposure and 31 cases still in contact with antigen, so only 41 cases had time elapsed since last exposure.

Regarding previous treatment (steroids and other immune suppressive agents), 58% (51 cases) were previously treated while 42% (37 cases) were not.

Table (2)
BAL cellularity and CD4/CD8 in studied population

	BAL cellularity TCC /cmm or microliter	**lymphocytes %**	**neutrophils %**	**macrophages %**	**CD4/CD8**
Mean **SD**	312 310	42% 20%	27% 23%	31% 17%	1.8 2.5
Range	20-1200	12-73%	4-70%	10-80%	0.1-12
Median (IQR)	215 (60-355)	40% (22-60)	18%(10-58)	29%(19-40)	0.8(0.4-2)

TCC: total cell count, IQR: interquartile range

Table (3)
Comparison between subacute and chronic cases regarding cellularity and CD4/CD8 using Mann-whitney test

	Subacute cases (20)	**Chronic cases (65)**	**P-value**
BAL cellularity TCC /cmm or microliter Mean SD Range	397 241 60-715 340(270-600)	247 291 20-1200 165(50-	0.002

Median (IQR)		325)	
Lymphocytes % mean SD Range Median (IQR)	 45% 19% 20-67% 50%(27-60)	 39% 20% 12-73% 38%(21-59)	 0.273
neutrophils % mean SD Range Median (IQR)	 30% 22% 10-70% 23%(15-30)	 27% 24% 4-60% 14%(6-60)	 0.091
macrophages % mean SD Range Median (IQR)	 26% 14% 10-43% 30%(10-35)	 34% 18% 12-80% 29%(20-48)	 0.129
CD4/CD8 Mean SD Range Median (IQR)	 1.5 1.7 0.4-4.3 0.7(.5-3.4)	 1.9 2.8 0.1-12 0.9(.4-2)	 0.816

There was statistically significant difference between both groups regarding total cell count with p-value 0.002.

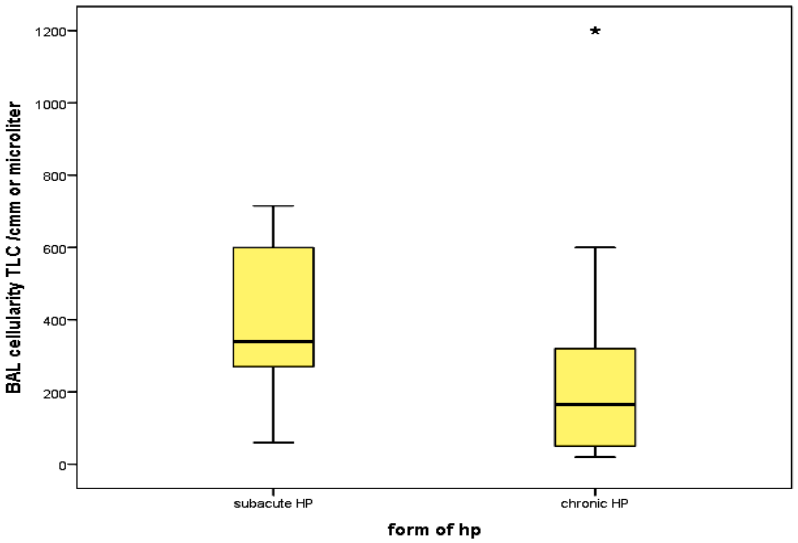

Figure (1) Box plot comparing the median of subacute and chronic cases regarding BAL cellularity showing statistically significant difference

Table (4)
Influence of delay between last exposure on BAL cell recovery, CD4/CD8 and 6MWD using Mann-Whitney test

Time elapsed since last exposure			
	< 1 week (31 cases)	**>1 week (41 cases)**	**P-value**
BAL cellularity TCC /cmm or microliter			
Mean	312	372	
SD	304	350	0.414
Range	20-935	50-1200	
Median (IQR)	255(34-539)	235(130-600)	
lymphocytes %			0.363
mean	41%	35%	
SD	24%	14%	
Range	12-71%	15-57%	
Median (IQR)	44%(16-65)	35%(22-50)	
Neutrophils %			
mean	34%	30%	
SD	22%	24%	0.314
Range	5-60%	5-70%	
Median (IQR)	27%(12-60)	18%(10-58)	
macrophages %			
Mean	25%	35%	
SD	11%	20%	0.02
Range	9-43%	10-80%	
Median (IQR)	27%(13-34)	33%(20-50)	
CD4/CD8			
Mean	2.7	1.2	
SD	3.6	1.2	.04
Range	0.1-12	0.3-3.8	
Median (IQR)	0.9(.4-4)	0.6(.3-2)	
6MWD			
Mean	231	298	
SD	36	32	0.00
Range	180-280	240-350	
Median (IQR)	223(210-270)	300(280-320)	

There was statistically significant difference regarding time elapsed since last exposure more or less than one week with CD4/CD8, 6MWD and P value was 0.04 and 0.00 respectively

Table (5)
Comparison between HP cases exposed to avian antigens or not regarding CD4/CD8 using Chi-square test

			Exposure birds		Total
			Absent	Present	
CD4/CD8 ratio	<1	Count	17	25	42
		% within exposure birds	53.1%	67.6%	60.9%
	1-4	Count	12	8	20
		% within exposure birds	37.5%	21.6%	28.9%
	>4	Count	3	4	7
		% within exposure birds	9.4%	10.8%	10.1%
Total		Count	32	37	69
		% within exposure birds	100.0%	100.0%	100.0%

There was no statistically significant difference between both groups with p value 0.385

Table (6)
Comparison between HP cases males and females regarding CD4/CD8 using Chi-square test

			sex		Total
			F	M	
CD4CD 8 ratio	<1	Count	34	8	42
		% within sex	63%	53%	61%
	1--4	Count	16	4	20
		% within sex	30%	27%	29%
	>4	Count	4	3	7
		% within sex	7%	20%	10%
Total		Count	54	15	69
		% within sex	100.0%	100.0%	100.0%

There was no statistically significant difference between both groups with p-value 0.439

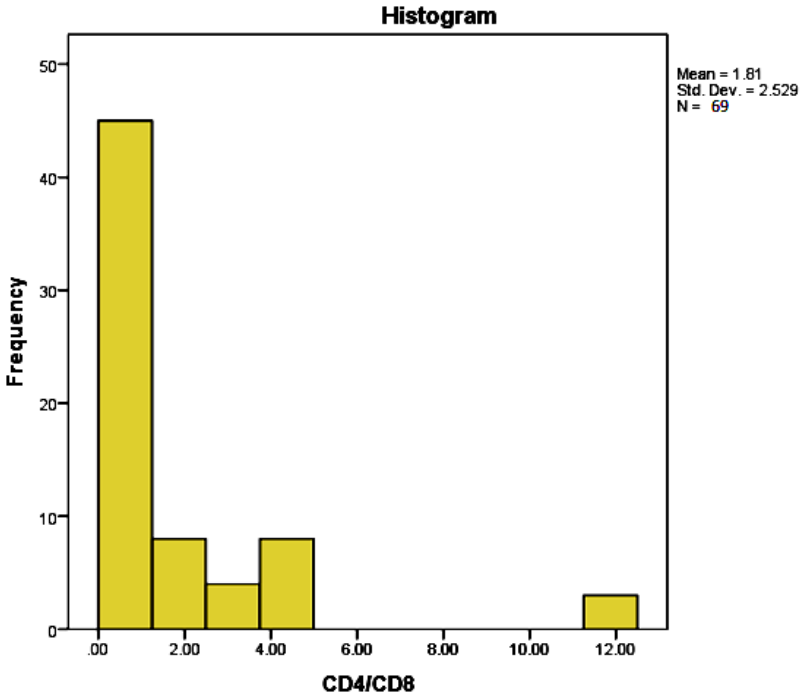

Fig. (2): Bronchoalveolar lavage CD4/CD8 ratio on 69 patients with hypersensitivity pneumonitis (X axis is BAL CD4/CD8 ratio, with one column by unit, Y is the number of subjects)

Correlations

Table (7)
For correlationsThere was no correlation between CD4/CD8 and (treatment duration, 6MWD).

		duration TTT(m)	FVC%	6MWD
CD4/CD8	Correlation Coefficient	.260	-0.291	.118
	p value	.105	.02	.387

A negative correlation exists between CD4/CD8 and FVC%: P value 0.02 and r equals -0.291

Radiological findings

Main radiological patterns found in HP were: ground glass opacities (GGO), mosaic, reticulations, traction bronchiectasis, honeycombing and patchy consolidations.

The average total score for each variable was calculated as the mean score of the six lung zones.

The main pattern found was GGO with a mean 1.96 followed by reticulations with a mean 1.72 and then mosaic pattern with a mean 0.93.
GGO was found in 76 cases (86.4%), mosaic in 68 cases (77.3%) and reticulations was found in 85cases (96.6%).

By comparing upper, middle and lower lung zones regarding the three main patterns found: GGO, mosaic and reticulations,: GGO was present in 63.6%, 63.6%, and 86.4% in upper, middle and lower lung zones respectively. Mosaic pattern was found in 36.4%, 40.9% and 77.3% in upper, middle and lower lung zones respectively. Reticulations were found in 77.3%, 50% and 90.9% in upper, middle and lower lung zones respectively. So there was lower zone predominance regarding the main three patterns found in HP.

4% of cases had no fibrosis, 42% had mild fibrosis, 45% moderate and 9% had severe fibrosis.

There was a negative correlation between 6MWD and lymphocytic count $p=0.05$, $r = - 0.228$

There was no correlation between extent of fibrosis and total cell count (TCC) or lymphocytic count.

Discussion

Hypersensitivity pneumonitis (HP) is characterized by a diffuse lymphocytic inflammation affecting the small airways and pulmonary parenchyma. HP has been classified into acute, subacute and chronic on the basis of its clinical presentation. Long-term outcome of the subacute/chronic forms is variable, but the disease may evolve to fibrosis or emphysematous changes and lead to irreversible lung damage **(8)**.

The mean age in our study was (46 ±16) in comparison to Morell and colleagues with mean age 47, Caillaud and colleagues with mean age (51 ±13) and Adams and colleagues with mean age (62 ±11). This study included 83% females, Morell study included 76% females out of 86 cases, Caillaud study had 35% females and Adams study included 49% females. The causative antigen was mainly avian in our study and also previously mentioned studies except Caillaud where 80% were famer's lung disease. Present study showed that 73% of cases were housewives with 16 cases with unknown antigenic exposure assuming that domestic environment had possible causative agents of HP **(2).**

This study demonstrated that mean TCC/microliter was 312 ±310 (SD) and median was 215 in comparison to Caillaud et al. which was 594 ± 401. Mean lymphocytes (%) was (42± 20%) in comparison to Caillaud et al. who showed lymphocytic count (53 ± 24%) which may be caused by the fact that our study had 73% chronic cases and 4 % acute cases while Caillaud studied 30% chronic and 35% acute that agrees with Adams results who showed that the median BAL lymphocyte count was higher in inflammatory compared to fibrotic HP **(9).**

There was statistically significant difference between subacute and chronic cases regarding TCC/microliter with mean (397 ± 241), (247 ± 291) respectively, in accordance with Caillaud et al., but there was no statistically significant difference between both groups as regard macrophages or lymphocytes which were significant in **Caillaud et al.,** study which also can be explained by other factors like different types of antigens, persistence of antigenic exposure, geographic factors and host response factors **(9).**

Ohtani and colleagues studied chronic bird fancier lung BFL and found that lymphocytosis reached more than 20% in 68% of the cases and more than 15% in 80% of BFL patients showing a histologic pattern of usual interstitial pneumonia, nonspecific interstitial pneumonia, or cryptogenic organizing pneumonia **(10).**

There was no statistically significant difference regarding time since last exposure (more or less than one week) as regard cellularity in comparison to Caillaud et al. who found statistically significant difference between acute (<24 hours exposure) and chronic forms regarding neutrophils with P value < 0.05 which can also be explained by the small percent of acute cases in our study which was 4% **(9)**

The mean CD4/CD8 ratio in this study was 1.8 ± 2.5 (SD) and median was 0.8. Also 61% of cases (42 cases) had CD8 alveolitis with ratio <1 while 10% (7 cases) cases had CD4 alveolitis with ratio >4 and 29% (20 cases) with ratio ranged between 1 and 4. In comparison to Caillaud et al., the mean ratio was 3.8 ± 6.1 and median was 2.1, furthermore, 33% of their cases showed CD8 alveolitis, 24% showed CD4 alveolitis and in 41% ranged between 1 and 4. Morell and colleagues found that 62% of their 13 bird fancier lung BFL cases had CD4/CD8 < 1 and 38% had CD4/CD8 > 1.2 with no difference between acute, subacute and chronic cases may be due to small number of cases in their study **(11).**

This study showed that there was statistically significant difference regarding time since last exposure more or less than one week for CD4/CD8 ratio with P value 0.04. Also there was a negative correlation between ratio and age: P value 0.003 and r equals -0.352, a negative correlation between ratio and duration of illness P value 0.05 and r equals -0.238 and a positive correlation between ratio and time since last exposure P value 0.006 and r equals 0.505. No relation between ratio and stage of the disease, type of antigen, sex and treatment duration. In comparison Caillaud et al. ratio was neither related to stages or etiologies of HP, nor to time elapsed since last antigen exposure. The only significant difference (p=0.02) was found between sexes (63 men, ratio= 2.7 ± 3.8 and 35 women, ratio= 5.7 ± 8.5) **(9).**

One limit of present study is that all patients were from single academic center so there was a potential for bias. Also we did not have a control group of patients who underwent bronchoscopy in the diagnostic workup of ILD who were subsequently given diagnoses other than HP so we were unable to assess sensitivity and specificity of bronchoscopy.

Another factor that may affect our result was that 53% were bird fancier's, miscellaneous 29% and 18% had unknown antigenic exposure. In comparison to Caillaud et al. who found 80% farmer's lung, 19% bird fanciers disease and 1% miscellaneous which may affect cellularity and CD ratio. Antigen identification in prior cohorts is variable, ranging from 42.9 to 75%, likely reflecting the difference in inclusion criteria between studies **(2).**

In our study the main HRCT patterns found were: GGO found in 76 cases (86.4%), mosaic in 68 cases (77.3%) and reticulations was found in 85 cases (96.6%). In comparison to Rival et al. who found 82% GGO followed by air trapping 48% and then nodular pattern in 42% while reticular pattern was found only in 16% of cases **(1).** Morell and colleagues studied BFL patients and found that GGOs were found in 68% of cases, mosaic pattern in 61%, bronchiectasis in 46%, nodular pattern in 41% and septal thickening in 29% **(11).** Lima and colleagues studied subacute and chronic HP cases and found that GGOs were present in 80% of cases and findings indicative of fibrosis (reticulations, traction bronchiectasis and honeycombing) in 74% of cases with mosaic pattern in 43% **(12).** Salisbury and colleagues found GGOs in 92% of cases, mosaic attenuation or air trapping in 77% of cases, traction bronchiectasis in 65% of cases and reticulations in 52% **(13).**

Another finding in our study was that there was lower zone predominance regarding the main three patterns found in HP: GGOs, mosaic and reticulations represented as 86.4%, 77.3% and 90.9% respectively. In comparison to Rival et al. where sparing of lung bases occurred in 80.6% of cases. Rival et al. study included 38 HP cases (only acute and subacute) while this study had 73% chronic cases that obviously affected the results **(1).** Salisbury and colleagues found mainly lower zone predominance as regard craniocaudal distribution **(13).**

Present study shows a negative correlation between 6MWD and lymphocytic count. Abdel Khalik M., study had 40 IPF cases and found a negative correlation between neutrophils and 6MWT with no statistical significance but with significance to FEF25–75% **(14).** So present study postulated that severity of alveolitis may diminish 6MWD but this requires further investigations.

References

Abdel-Khalik M, Zakaria M, Khorshed M, Ahmed S. & Elhenawy, Y. (2012): Role of BAL cellularity in assessment of severity of idiopathic pulmonary fibrosis. *Egyptian Journal of Chest Diseases and Tuberculosis*, 61(3), 129-134.

Adams T.N, Newton C.A, Batra K, Abu-Hijleh M, Barbera T, Torrealba J. & Glazer C.S. (2018). Utility of broncho-alveolar lavage and transbronchial biopsy in patients with hypersensitivity pneumonitis. *Lung*, *196*(5), 617-622.

ATS Committee on Proficiency Standards for Clinical Pulmonary Function Laboratories. (2002): Statement AT: Guidelines for the Six-Minute Walking-Test. Am J Respir Crit Care Med, 166, 111-117.

Caillaud M. D, Vergnon J, Madroszyk A.M, Melloni B, Murris M. & Dalphin J. (2012). Bronchoalveolar lavage in hypersensitivity pneumonitis: a series of 139 patients. Inflammation & Allergy-Drug Targets (Formerly Current Drug Targets-Inflammation & Allergy), 11(1), 15-19.

Díaz-Jimenez J.P. and Rodriguez A.N. (2013): Interventions in Pulmonary Medicine, DOI 10.1007/978-1-4614-6009-1_2, © Springer Science+Business Media New York.

Graham B.L, Steenbruggen I, Miller M.R, Barjaktarevic I.Z, Cooper B.G, Hall G.L. & Oropez C.E. (2019). Standardization of Spirometry 2019 Update. An Official American Thoracic Society and European Respiratory Society Technical Statement. American journal of respiratory and critical care medicine, 200(8), e70-e88.

Lima M.S, Coletta E.N, Ferreira R.G, Jasinowodolinski D, Arakaki J.S, Rodrigues S.C. & Pereira C.A. (2009). Subacute and chronic hypersensitivity pneumonitis: histopathological patterns and survival. Respiratory medicine, 103(4), 508-515.

Meyer K.C, Raghu G, Baughman R.P, Brown K.K, Costabel U, Du Bois R.M. & Rottoli P. (2012). An official American Thoracic Society clinical practice guideline: the clinical utility of bronchoalveolar lavage cellular analysis in interstitial lung disease. American journal of respiratory and critical care medicine, 185(9), 1004-1014.

Mooney J.J, Elicker B.M, Urbania T.H , Agarwal M.R, Ryerson C.J, T. Nguyen L.M, Woodruff P.G, Jones K.D, Collard H.R, King Jr T.E and Koth L.L. (2013): Radiographic Fibrosis Score Predicts Survival in Hypersensitivity Pneumonitis. chest; 144(2):586–592.

Morell F, Roger A, Reyes L, Cruz MJ, Murio C, Munoz X (2008): Bird fancier's lung: a series of 86 patients. Medicine (Baltimore);87:110–130.

Ohtani Y, Inase N, Miyake S, Yoshizawa Y. & Saiki S. (2002): Fatal outcome in chronic bird fancier's lung. The American journal of medicine, 112(7), 588-590.

Rival G, Manzoni P, Lacasse Y, Polio J.C, Westeel V, Dubiez, A. & Dalphin J.C. (2016). High-resolution CT predictors of hypersensitivity pneumonitis. Sarcoidosis vasculitis and diffuse lung disease, 33(2), 117-123.

Salisbury M.L, Gross, B.H, Chughtai A, Sayyouh M, Kazerooni E.A, Bartholmai B.J. & Konopka K.E. (2018): Development and validation of a radiological diagnosis model for hypersensitivity pneumonitis. European Respiratory Journal, 52(2), 1800443.

Suryasa, I. W., Rodríguez-Gámez, M., & Koldoris, T. (2021). The COVID-19 pandemic. *International Journal of Health Sciences*, *5*(2), vi-ix. https://doi.org/10.53730/ijhs.v5n2.2937

Vasakova M, Morell F, Walsh S, Leslie K. & Raghu G. (2017): Hypersensitivity pneumonitis: perspectives in diagnosis and management. American journal of respiratory and critical care medicine, 196(6), 680-689.