Sys Rev Pharm 2021;12(3):338-346
A multifaceted review journal in the field of pharmacy

Spectrum of Diffuse Parenchymal Lung Diseases Other Than Idiopathic Pulmonary Fibrosis Based on Clinical, Radiological and Histopathological Correlation.

Yosri Mohamed Kamel Akl[a], Ahmed Hussein Elhabashy[b], Nahed Mohamed Mostafa[a], Mohammed Kamal Hasswa[a], Sabah Ahmed Mohamed Hussein[a]

[a] Pulmonology Department, Faculty of Medicine, Cairo University, Cairo, Egypt.
[b] Pathology Department, National Cancer institute, Cairo University, Cairo, Egypt

ABSTRACT

Background: Multiple modalities are available for diagnosis of diffuse parenchymal lung diseases. High-resolution roles computed tomography of lung was well established in formulating initial cases diagnosis with diffuse parenchymal lung diseases. Major utilities of transbronchial lung biopsy rests in making possibilities specific diagnosis diffuse parenchymal lung diseases cases and avoiding a surgical lung biopsy.

Objectives and Methods: The aim of this work was to study the spectrum of diffuse parenchymal lung diseases other than idiopathic pulmonary fibrosis based on clinical, radiological and histopathological correlation. This study included 120patients with chest high resolution computed tomography signs of diffuse parenchymal lung diseases not consistent with idiopathic pulmonary fibrosis. Flexible bronchoscopy was done with the bronchoalveolar lavage and transbronchial lung biopsy were obtained. The samples were processed for cyto-histopathology.

Results: Nodular pattern (73.33%) was the most high-resolution computed tomography (HRCT) predominant pattern followed by ground glass pattern (45%) and reticular pattern (26.67%). The most frequent diagnosis was sarcoidosis (40.83%) followed by hypersensitivity pneumonitis (20%). The overall diagnostic yield of transbronchial lung biopsy was 79.1% (95/120). All differential diagnoses showed extreme matching between HRCT and histopathology.

Conclusion: HRCT is a non-invasive method to evaluate and diagnose patients with diffuse parenchymal lung diseases. Transbronchial lung biopsy found to have reliable yields in with diffuse parenchymal lung diseases diagnosis.

Keywords: Diffuse parenchymal lung diseases, High resolution computed tomography, Histopathology

Correspondence: **Mohammed Kamal Hasswa**
Pulmonology Department, Faculty of Medicine, Cairo University, Cairo, Egypt
Corresponding Author: m.kamalhasswa@kasralainy.edu.eg

INTRODUCTON

Diffuse parenchymal lung diseases (DPLD), Referred as interstitial lung diseases, which were heterogeneous group of disorders and classified together related to its similar clinical, radiographic, physiologic, and pathologic manifestations. Descriptive term reflects pathologic appearance where abnormalities begin in interstitium, but that term is misleading, and associated with extensivlly alteration of alveolar and airway architecture [1,2]

HRCT of lung established in its roles in formulating diagnosis of DPLD; its abilities to monitor serial examinations might equally very important. DLD case in general undergo multiple HRCT examinations at different stages. This longitudinal imaging provided significantly an information comparing to single time point and using in variety of ways, as: 1) increase initial diagnosis accuracy; 2) assessment prognosis estimation of; 3) identify diseases progress of; 4) detected new processes acute or worsening symptoms; and 5) detected abnormalities or complications [3]

According to the joint consensus for American Thoracic Society and European Respiratory Society on idiopathic interstitial fibrosis (IPF), transbronchial lung biopsy (TBLB) is not helpful in making diagnosis of usual interstitial pneumonia (UIP), and presence of UIP pattern on HRCT is sufficient for diagnosis of IPF in cases who's not suitable for surgical lung biopsy. [1] Transbronchial lung biopsy is safety and very useful to DPLD diagnosis under experienced professionals. HRCT thorax is crucial prior to the procedure to know about the disease pattern and for selecting the lobe or the segment to be biopsied. The yield of TBLB is higher when centrilobular and peri-lymphatic involvement is found radiologically. [4] High predictive values and sensitivities on clinico-radiological and cytohistological correlations which is vedry important to evaluating DPLD. [5]

The purpose of this work was to study the spectrum of DPLD other than idiopathic pulmonary fibrosis based on clinical, radiological and his topathological correlation.

MATERIALS AND METHODS:

This study included 120 patients with DPLD other than

idiopathic pulmonary fibrosisas diagnosed by HRCT chest, who admitted in Chest department, Kasr Alainy Hospital, Cairo University (from May 2018 to December 2019) and our investigation was approved by institutional review board / Kasr Al-Aini Hospital/Cairo University (IRB #N-82-2018). All patients were informed with the full details of the study and the procedure of TBLB with informed consent was obtained. Patients with severe refractory hypoxemia, hypoventilation with hypercapnia, severe pulmonary hypertension, hemodynamic instability, coagulopathy, advanced systemic disease (e.g., Liver cell failure and renal failure) or recent myocardial infarction were excluded from the study.

Cases subjected for complete history taking, detailed clinical examination, routine laboratory investigation such (complete blood picture, liver & kidney functions, blood sugar, bleeding profile, arterial blood gases and autoimmune profile when indicated), six minute walk test, spirometric testing flow-volume loop by Master Screen PFT 2012, Care Fusion 234 GmbH, Germany (V-781267-057 version 03.00), high resolution computed tomography chest by Siemens 16-channel MDCT and transthoracic echocardiography with estimation of pulmonary artery systolic pressure (PASP). Bronchoalveolar lavage and transbronchial lung biopsy were performed using fiberoptic video bronchoscope Pentax EBK-I scan 5000, EB-1970 TK 3.2 mm working channelin a well-equipped room with advanced facilities.

Broncho alveolar lavage (BAL):

BAL is low risk techniques perform through flexible bronchoscopy, allowed to cellular and non-cellular components recovery from epithelial surface of alveoli and terminal bronchioles**.** BAL Analysis of cell counts, culture, and cytology provided valuable information which could led to make diagnosis or ruling out another. [6] BAL should planned to performed prior to other bronchoscopic procedures. Review radiographs to determine ideal site of alveolar lavage. Infuse 20mL of saline with a syringe, observing the flow of saline at the distal tip of the bronchoscope. Maintain wedge position, applied gentle suction (50-80mmHg), collecting lavage specimen in collection trap. Repeat up to 5 times as needed (total 100-120mL) to obtain an adequate specimen (40-60mL, usually 40-70% recovery of total instillate). [7]

Trans bronchial lung biopsy:

A thorough airway examination preceded the transbronchial lung biopsy because bleeding after lung biopsy would obscure adequate airway examination. The choice of biopsy site was depending onpre-procedure HRCT findings. We preferred to perform the biopsy from the dependent parts of the lungs; right or left lower lobes. In an event of bleeding, the blood is at least contained in this area before spilling into the other lobes. Once the biopsy site was chosen, the distal end of the bronchoscope was wedged into the specific segmental bronchus, then the forceps was introduced and advanced through the biopsy port into the working channel, and it was gently advanced through the distal end. The bronchoscope was advanced onto the wedged position. Chest radiographs were performed within 6 hours of transbronchialbiopsy in patients with chest pain or unexplained hypoxia to rule out pneumothorax [8]

Histopathological examination:

The specimens were fixed in 4% formaldehyde and sent to the histopathology laboratory. The specimens were evaluated by apathologist with experience in respiratory disease pathology. Biopsies were considered “non-diagnostic” when histopathologic criteria sufficient to define a characteristic histopathologic pattern were lacking (e.g., normallung or minimal nonspecific changes) or when samples were considered inadequate.

Alveoli were seen. Pathologic features evaluated in each adequate biopsy were: alveolar architecture, inflammatory infiltrate, granulomatous inflammation, atypical cells, interstitial fibrosis, fibroblast foci, vasculopathy, pigment deposition, and honey-comb change. The adequate biopsies were further categorized on the basis of the histopathological patterns into six patterns: adequate biopsy without a specific diagnostic abnormality (pattern 1); acute pneumonitis (pattern 2); neoplasia (pattern 3); chronic interstitial inflammation with orwithout fibrosis (pattern 4); granulomatous inflammation (pattern 5); andother specific causes (pattern 6). [9] The paraffin blocks were cut at 4micron thick and slides were stained by hematoxylin and Eosin. TheHematoxylin and Eosin (H &E) stained paraffin sections were studied.

Statistical methods

Analyzed our date by using Minitab 17.1.0.0 for (Minitab Inc., 2013, USA) as 1) Descriptive statistics: continues data was represented as mean and slandered deviation (SD), while categorical data as number and percentage (%). 2) Analytic statistics: Chi-Square Goodness of fit test used to determine whether the proportion in each category differ from the expectedproportion. Statistical tests were two-sided, $P < 0.05$.

RESULTS

The study included 120 patients with diffuse parenchymal lung disease as shown in their HRCT chest. Patients characteristics were presented in table (1). Mean age of the study patients was 44.52 years with age range from 18 up to 68 years, most of them were females (63.33%). Hazards of exposure was present in 35.83%ofpatients. Smokers were 23.3% ofpatients. RegardingHRCT chest predominant pattern, about7 patterns were considered predominant. The most frequent one was nodular infiltration (73.33%), which included 3 forms; the commonest one was perilymphatic nodules (43.33%) then centrilobular (19.17%), while random nodules were found in 10.83%of patients only. The second common CT pattern was ground glass opacities (45%) followed by the reticular pattern (26.67%), alveolar filling (20.83%) and air trapping (18.33%). The least frequent HRCT patterns that were reported in our studywere thecystic patternand crazy paving (5.83% and 1.67%) respectively. Table (1) also showed the additional HRCT findings including mediastinal lymphadenopathy (45.83%), pleural effusion (11.67%), traction bronchiectasis (10%), conglomerate masses and progressive massive fibrosis. The physiologic and functional parameters of the study patients were also presented in table (1).

Transbronchial lung biopsy (TBLB) achieved specific histopathological diagnoses in 95 patients (79.1%) out of 120 but non-specific histopathological features were present in the remaining 25 patients (20.9%). Bases on clinical and radiological data theses 25 patients were consistent with working diagnoses of sarcoidosis (10 patients), hypersensitivity Pneumonitis (6 patients), organizing pneumonia (4 patients), pulmonary Langerhans

cell histiocytosis x (2 patients), tuberculosis (1 patient), silicosis (1 patient) and pulmonary veno-occlusive disease (1 patient). TBLB results were helpful in 79.1% of the study patients and the spectrum of TBLB specific diagnoses included sarcoidosis (39 patients), hypersensitivity pneumonitis (18 patients), invasive mucinous adenocarcinoma of the lung (17 patients), organizing pneumonia (5 patients), tuberculosis (5 patients), silicosis and hemosiderosis (3 patients in each one), alveolar proteinosis (2 patients), pulmonary Langerhans histiocytosis, Kaposi sarcoma and lymphoma (each included 1 patient) (Figure 1).

Distribution of diagnoses based on HRCT and histopathology data were shown in table (2). Regarding the different diagnoses there was marked matching between HRCT features and histopathological diagnosis obtained using TBLB with statistically non-significant difference between HRCT diagnosis and TBLB results (P value > 0.05) except in patients with non-specific TBLB histopathology results (25 cases have not diagnosis by pathology, while HRCT achieved them a suggest diagnosis based on their clinical and radiological characteristic features; P <0.001). The final spectrum and distribution of our study cases (120 patients) based on Clinico-Radiologic-Pathologic Correlation was illustrated in figure (2). The majority were diagnosed as sarcoidosis (49 patients, 40.83%), hypersensitivity pneumonitis (24 patients, 20%) and invasive mucinous adenocarcinoma of the lung (17 patients, 14.17%) followed by organizing pneumonia (9 patients, 7.5%) tuberculosis (6 patients, 5%), and silicosis (4 patients, 3.33%). Pulmonary Hemosiderosis (2.5%), Pulmonary Langerhans cell histiocytosis (2.5%), pulmonary alveolar proteinosis (1.67%), PVOD (0.83%), Kaposi sarcoma (0.83%) and lymphoma (0.83) were less frequently encountered diagnoses.

DISCUSSION

DPLD cases were undergo multiple HRCT examinations at different stages. Longitudinal imaging data provides significantly information comparing to single time point and could using in variety of ways, including:1) increase accuracy of initial diagnosis; 2) prognosis assisment ; 3) disease progress; 4) detect new processes with acute or worsening symptoms; and 5) detect other abnormality or complications.[3]

TBLB is a established diagnostic technique useing by bronchoscopists. Major utilities of TBLB rests in the possibilities of making specific diagnosis for DPLD and avoided surgical lung biopsy. However, according to the joint consensus statement of the American Thoracic Society and the European Respiratory Society on idiopathic interstitial fibrosis (IPF), TBLB is not helpful in making a diagnosis of usual interstitial pneumonia (UIP), and the presence of a UIP pattern on HRCT is sufficient for the diagnosis of IPF in patients not subjected to surgical lung biopsy.[1]Bronchoscopy with TBLB is the most commonly used tool to obtain lung tissue for histopathological examination because the procedure is relatively safe with pneumothorax seen in 2-10% and bleeding in less than 2% of cases.[10]

This work aimed to study the spectrum of DPLD other than idiopathic pulmonary fibrosis based on clinical, radiological and histopathological correlation. This study included One hundred and twenty patients with DPLD other than IPF as shown by HRCT who were fit for transbronchial lung biopsy.

The mean age of the studied patients was44.52with SD±12.49 years with age range of 18 to 68 years, and this was higher than mean age of Akl et al[11] study patients (mean±SD;36.7 ±14.1), But was lower than the mean age of DPLD patients in other studies ofPandey et al[12](mean± SD; 55.15±10.06), Valappil et al[13](mean±SD; 55±15.45),Dhooria et al[14](mean±SD; 51.2± 13.9), Archana, et al[15] (mean age 52 years) and Griff et al[16] (mean±SD; 63±13). However, our results was very close to that obtained by some studies including that carried by Ahmed et al [17] (mean±SD; 39.96±13.31) and Sindhwani et al [18] (mean±SD; 49.6±15.7). Females were63.33%while males were 36.67% only. This indicates higher incidence of DPLD in females compared to males among the studypopulation which contradicts the studies carried by Pandey et al, [12] Archana, et al, [15] Sindhwani et al, [18] and Griff et al, [16]. The higher female prevalence in this study was consistent with the previous studies done by Valappil et al [13] and Dhooria et al [14] as female prevalence in these studies was 63.4% and 58.6% respectively. Also, some Egyptian studies carried by Akl et al [11] and Ahmed et al [17] showed a higher prevalence of females which may indicate that DPLD is more common in females among Egyptian population. History of exposure was present in 35.83% of ourstudy cases which wasin the form of bird exposure (27.5%), biomass exposure (4.17%) and glass exposure (3.33%). Smoking prevalence was23.3%. These results correlate with Ahmed et al [17] who found that25.5% of their patients were smokers and 21.8%were birdbreeders. Also Valappil etal[13] who studied 129 cases with DPLD, found that 32.5 % of them were smokers and 44.18% had history of exposure mostly to biomass and smoke.

Among the study patients, about 7 predominant patterns in the HRCT were described. The most frequent pattern was the nodular pattern (88 cases, 73.33%), which was subdivided into 3 subtypes; a) Peri-lymphatic nodules (52 cases, 43.33%), b) Centrilobular nodules (23 cases, 19.17%) and c) Random nodules (13 cases, 10.83%). The second common HRCT pattern in our study was the ground glass opacification (54 cases, 45%), followed by the reticular pattern (32 cases, 26.67%). while Alveolar filling was present in 25 patients (20.83%) and air trapping was found in 22 patients (18.33%). The least frequent reported HRCT patterns in our cases were the cystic pattern (7 cases, 5.83%) and crazy paving pattern (2 cases 1.67%).The commonest associated HRCT findings weremediastinal lymphadenopathy(55 cases, 45.83%), pleural effusion (14 cases, 11.67%) followed by traction bronchiectasis (12 cases, 10 %) while conglomerate mass in sarcoidosis cases and PMF in silicosis cases were less frequently detected (5 and 3cases respectively).The distribution of diagnoses based on HRCT among the studied population were sarcoidosis as the most common diagnosis (49 cases, 40.83%), followed by hypersensitivity pneumonitis (24 cases, 20%), lung adenocarcinoma (bronchoalveolar cell carcinoma) (17 cases, 14.17%), Organizing pneumonia (9 cases, 7.5%), tuberculosis (6 cases, 5%), silicosis (4 cases, 3.33 %), pulmonary langerhans cell histiocytosis (3 cases, 2.5%), pulmonary hemosiderosis (3 cases, 2.5%) and alveolar proteinosis (2 cases, 1.67%),Kaposi sarcoma, lymphoma and pulmonary veno-occlusive disease, each was present in 1 case (0.83%).

In agreement with our results, Valappil etal[13] stated that the most common chest radiography finding in their study was the reticulonodular pattern (97 patients, 75.19%) andthey found hilar prominencein 19 patients (14.7 %) and Consolidation in 8 patients (6.2%). Also, Sindhwani et al [18]

found radiological findings on HRCT in population were in form of bilateral nodules (28.6%), bilateral reticulo- nodular opacities (26.5%), bilateral ground glass opacities (20.4%), hilar and mediastinal lymphadenopathy (20.4%). Again, Ahmed et al [17] showed different patterns of parenchymal affection in their study population such as reticularshadows and fibrosis (25.5%), consolidation (21.8%), ground glass opacities (21.8%) and nodular lesion (14.5%), in addition to mediastinal lymphadenopathy (14.5%) and pleural effusion (20%). Pandey et al [12] classified the HRCT findings in their study into 3 categories of: Ground glass and consolidation (40%); Fibrosis (38.3%) and Nodules (21.7%).

The spectrum of our DPLD cases based on histopathology result of TBLB in our study included sarcoidosis (39 cases, 32.5%), hypersensitivity pneumonitis (18 cases, 15%), lung adenocarcinoma (17 cases, 14.17%), organizing pneumonia (5 cases, 4.17%), tuberculosis (5 cases, 4.17%), silicosis (3 cases, 2.5 %), pulmonary hemosiderosis (3 cases, 2.5%) and alveolar proteinosis (2 cases, 1.67%). Then Kaposi sarcoma, lymphoma and pulmonary langerhans cell histiocytosis each were present in1 case (0.83 %). 25 cases (20.83%) of our patients showed non-specific histopathological features and were diagnosed on clinic-radiological bases. So, the overall diagnostic yield of TBLB in our study was 79.17% and this was consistent with Archana et al [15] that prospectively studied 102 patients with DPLD who underwent TBLB over a 2-year period and TBLB confirmed diagnosis in 80 (78.4%) patients. Tuberculosis (21.2%) was the most common diagnosis in their study followed by non-specific interstitial pneumonia (18.7%), neoplasia (16.2%), sarcoidosis (11.2%), organizing pneumonia (5%) and hypersensitive pneumonitis (3.7%). Also, Sindhwani et al [18] conducted a prospective non- randomized study on 49 patients with DPLD without a characteristic IPF pattern who were subjected to TBLB. The overall diagnostic yield of TBLB in their study was 85.7% and NSIP, tuberculosis and sarcoidosis were the most common histology patterns found (22.4%, 18.4% and 16.3%, respectively) followed by alveolar proteinosis and bronchoalveolar carcinoma (each was present in 6.1%). Again, Pandey et al [12] conducted a study on 60 patients with clinical and radiological features of ILD who underwent TBLB and was able to confirm the diagnosis of ILD in 95% of the cases by pathology. Idiopathic Pulmonary Fibrosis was the most common diagnosis (38.3%) followed by hypersensitivity pneumonitis (13.3%), NSIP (11.6%), sarcoidosis (8.3%) and Organizing Pneumonia (6.6%). In another study by Valappil et al [13] on 129 cases of ILD, they found that the commonest spectrum of interstitial lung disease was connectivetissue disease-related ILD (34.9%) followed by IPF (23.3%), sarcoidosis (17.1%), cryptogenic organizing pneumonitis (6.2%) and hypersensitivity pneumonitis (5.42 %).

Bronchoalveolar lavage differential cell count analysis revealed that lymphocytes were the most predominate cell and this could be related to the high number of sarcoidosis and hypersensitivity patients among the study population. Regarding complications among the studied population, mild bleeding occurred in 4 (3.3 %) patients, moderate bleeding in 3 (2.5%) patients and pneumothorax occurred in 2 (1.6%) patients who required chest tube drainage [19]

In conclusion, Evaluation of DPLD is complex, where in many cases, lung biopsy might be very necessary to establishing the diagnosis. High resolution computed tomography is a valuable tool in detection, characterization, diagnosis, and evaluation of patients with DPLD especially when used in conjunction with clinical symptoms. Histopathological examination confirms the diagnosis of various DPLD and TBLB found to had reliable yield in DPLD diagnosis.TBLB can be performed safely (inexperienced hands) in patients with DPLD and offers promise for diseases diagnosis without risk and morbidity which could be in surgical lung biopsy.

AUTHORS CONTRIBUTION:

Y.M.K. Akl; Study conception or design - data analysis and interpretation – manuscript drafting, revision and final approval.

A.H. Elhabashy; study conception or design – doing the practical work - data analysis and interpretation – manuscript drafting, revision and final approval.

N.M. Mostafa; study conception or design - data analysis and interpretation – manuscript drafting, revision and final approval.

M.K. Hasswa; study conception or design –data collection, analysis and interpretation – manuscript drafting, revision and final approval.

S.A.M. Hussein study conception or design – doing the practical work - data analysis and interpretation – manuscript drafting, revision and final approval.

Ethical approval:

The Institutional Human Study Committee approved this study.

Conflict of interest:

None declared.

Funding:

None

REFERENCES:

1. Raghu G, Collard HR, Egan JJ, Martinez FJ, Behr J, Brown KK, et al. An official ATS/ERS/JRS/ALAT statement: idiopathic pulmonary fibrosis: evidence-based guidelines for diagnosis and management. Am J Respir Crit Care Med 2011; 183: 788.
2. King TE Jr, Pardo A, Selman M. Idiopathic pulmonary fibrosis. Lancet2011; 378:1949.
3. Elicker BM, Kallianos KG, Henry TS. The role of high-resolution computed tomography in the follow-up of diffuse lung disease. Eur Respir Rev 2017; 26: 170008.
4. Archana B, Vivek KU, Kusuma V, Huliraj N. Transbronchial Lung Biopsy in Diffuse Parenchymal Lung Disease: Diagnostic Yield and Complications. Indian J Chest Dis Allied Sci 2017; 59: 9-12.
5. Gupta A, Vasenwala SM, Akhtar K, Bhargava R, Ahmad I,Maheshwari V. Diffuse parenchymal lung disease diagnostic approach by radiology and histopathology. J Cytol Histol 2012; 3:1.
6. Reynolds HY. Bronchoalveolar Lavage. American Review ofRespiratory Disease. Am Thoracic Soc1987; 135:250-63.
7. Du Rand IA, Blaikley J, Booton R, Chaudhuri N, Gupta V, Khalid S, Mandal S. British Thoracic Society guideline for diagnostic flexible bronchoscopy in adults. Thorax 2013; 68: i1–i44.
8. Izbicki G, Shitrit D, Yarmolovsky A, et al. Is routine chest radiography after transbronchial biopsy necessary? A prospective study of 350 cases. Chest 2006;129(6): 1561–1564.

9. Kulshrestha R, Menon BK, Rajkumar, Vijayan VK. Pattern-based categorization on transbronchial lung biopsy. The Indian Journal of Chest Diseases & Allied Sciences 2012; 54: 9-16.
10. Raparia K, Aisner DL, Allen TC, Beasley MB, Borczuk A, Cagle PT, et al. Transbronchial lung cryobiopsy for interstitial lung disease diagnosis. A perspective from members of the Pulmonary Pathology Society. Arch Pathol Lab Med 2016; 140:1281-1284.
11. Akl Y, Elhendway A, Elnady MA, Moussa H, Abdelsalam E, Abuelhassan U. Medical thoracoscopic lung biopsy in undiagnosed non-UIP DPLD: diagnostic yield, complication rate, and cost-effectiveness, a single-experience study in Egypt. The Egyptian Journal of Chest Diseases and Tuberculosis 2020; 69:178–182.
12. Pandey A, Kumar R, Aditya V. To evaluate the role of radiological and histopathological examination in the diagnosis of interstitial lung Diseases. International Journal of Scientific Research 2019; 8: 67-68.
13. Valappil AT, Mehta AA, Kunoor A, Haridas A. Spectrum of DPLD: An experience from atertiary care referral centerfrom South India. The Egyptian Journal of Chest Diseases and Tuberculosis. 2018; 67:276 – 280.
14. Dhooria S,Mehta R,Srinivasan A,Madan K, Sehgal IS, Pattabhiraman V, et al. The safety and efficacy ofdifferent methods for obtaining transbronchial lungcryobiopsy in diffuse lung diseases. Clin Respir J.2018; 12:1711–1720.
15. Archana B, Vivek KU, Kusuma V,Huliraj N. Transbronchial lung biopsy in diffuse parenchymal lung disease: diagnostic yield and complications. Indian J Chest Dis Allied Sci. 2017; 59:9-12.
16. Griff S, Schönfeld N, Ammenwerth W, Blum T, Grah C, Bauer T, et al.Diagnostic yield of transbronchial cryobiopsy in nonneoplasticlung disease: a retrospective case series. BMCPulmonary Medicine. 2014; 14:171.
17. Ahmed S, El Hindawi A, Mashhour S. Spectrum of diffuseparenchymal lung diseases using medical thoracoscopic lungbiopsy: an experience with 55 patients during 2013-2015.Egyptian journal of chest diseases and tuberculosis. 2016;65: 717-722.
18. Sindhwani G, ShiraziN, Sodhi R, Raghuvansh S, Rawat J.Transbronchial lung biopsy in patients with diffuseparenchymal lung disease without 'idiopathic pulmonaryfibrosis pattern' on HRCT scan - Experience from a tertiarycare center of North India. Lung India.2015; 32 (5): 453–456.
19. Ravaglia C, Bonifazi M, Wells AU, Tomassetti S, Gurioli C,Piciucchi S, et al. Safety and diagnostic yield of transbronchial lung cryobiopsy in DPLD: a comparative study versus video-assisted thoracoscopic lung biopsy and a systematic review of the literature. Respiration. 2016; 91: 215-27.

Figures and Table

Table 1: Patients characteristics:

Character	Total number of patients (n=120)
• Age (mean ± SD)	44.52±12.49
• Sex	
- Male (n, %)	44 (36.67%)
- Female (n, %)	76 (63.33%)
• Smoking history (Yes) (n, %)	28 (23.33%)
• Exposure history (Yes) (n, %)	43 (35.83%)
- Bird exposure	33 (27.5%)
- Biomass exposure	5 (4.17%)
- Glass exposure	4 (3.33%)

-	Marble exposure	1 (0.83%)
•	Physiologic parameters (mean±SD)	
-	FEV1%	58.97±15.73
-	FVC%	61.20±13.95
-	FEV1/FVC%	77.55±10.76
-	FEF 25-75%	38.41±12.04
-	PaO2 (mmHg)	71.53±11.04
-	SO2%	93.00±4.18
-	6 MWD (m)	287.00±64.64
•	Echo heart	
-	Dilated right heart chamber (yes) (n, %)	11 (9.17%)
-	Pulmonary hypertension (yes) (n, %)	11 (9.17%)
-	EPASP (mean ± SD)	26.35 ±4.513
•	Predominant HRCT chest pattern (n, %)	
-	Nodular pattern	88 (73.33%)
○	Centrilobular nodules	23 (19.17%)
○	Peri-lymphatic nodules	52 (43.33%)
○	Random nodules	13 (10.83)
-	Reticular pattern	32 (26.67%)
-	Alveolar filling	25 (20.83%)
-	Ground glass opacities	54 (45%)
-	Air trapping	22 (18.33%)
-	Cystic pattern	7 (5.83%)
-	Crazy paving	2 (1.67)
•	Associated findings in HRCT (n, %)	
-	Lymphadenopathy	55 (45.83%)
-	Pleural effusion	14 (11.67%)
-	Traction bronchiectasis	12 (10%)
-	Conglomerate masses (in cases of sarcoidosis)	5 (4.17%)
-	PMF (in cases of silicosis)	3 (2.5%)
•	Bronchoalveolar lavage predominant cell count (n, %)	
-	Alveolar macrophages	12 (10%)
-	Hemosiderin laden macrophages	4 (3.33%)
-	Lymphocytes	79 (65.83%)
-	Malignant cells	6 (5%)
-	Neutrophils	19 (15.83%)

SD: Standard deviation, FEV1: Forced expiratory volume in first second, FVC: Forced vital capacity, FEF: Forced expiratory flow, PaO2: Partial pressure of oxygen in the blood, mmHg: Millimeter of mercury, SO2: Saturation of hemoglobin with oxygen, 6 MWD: six-minute walk distance, EPASP: Estimated pulmonary artery systolic pressure, HRCT: High resolution computed tomography, PMF: Progressive massive fibrosis.

Table 2: Distribution of diagnoses based on HRCT and histopathology data (*n*=120):

Diagnosis	HRCT (*n*, %)	Histopathology (*n*, %)	% of concordance between radiology & histopathology	P value #
Sarcoidosis	49, 40.83%	39, 32.5%	79.59	0.2
Hypersensitivity pneumonitis	24, 20%	18, 15%	75	0.3
Lung adenocarcinoma	17, 14.17%	17, 14.17%	100	1
Organizing Pneumonia	9, 7.5%	5, 4.17%	55.56	0.2
Tuberculosis	6, 5%	5, 4.17	83.33	0.7
Silicosis	4, 3.33%	3, 2.5%	75	0.8
Pulmonary Hemosiderosis	3, 2.5%	3, 2.5%	100	1
Pulmonary Langerhans cell histiocytosis	3, 2.5%	1, 0.83%	33.33	0.3
Alveolar proteinosis	2, 1.67%	2, 1.67%	100	1
Kaposi Sarcoma	1, 0.83%	1, 0.83%	100	1
Lymphoma	1, 0.83%	1, 0.83%	100	1
Pulmonary veno-occlusive disease	1, 0.83%	0, 0%	0	0.3
Non-specific	0, 0%	25, 20.83%	__	< 0.001

Categorical data represented as number and percentage.
#: Chi square goodness for fit test, P considered significant if < 0.05
HRCT: High resolution computed tomography

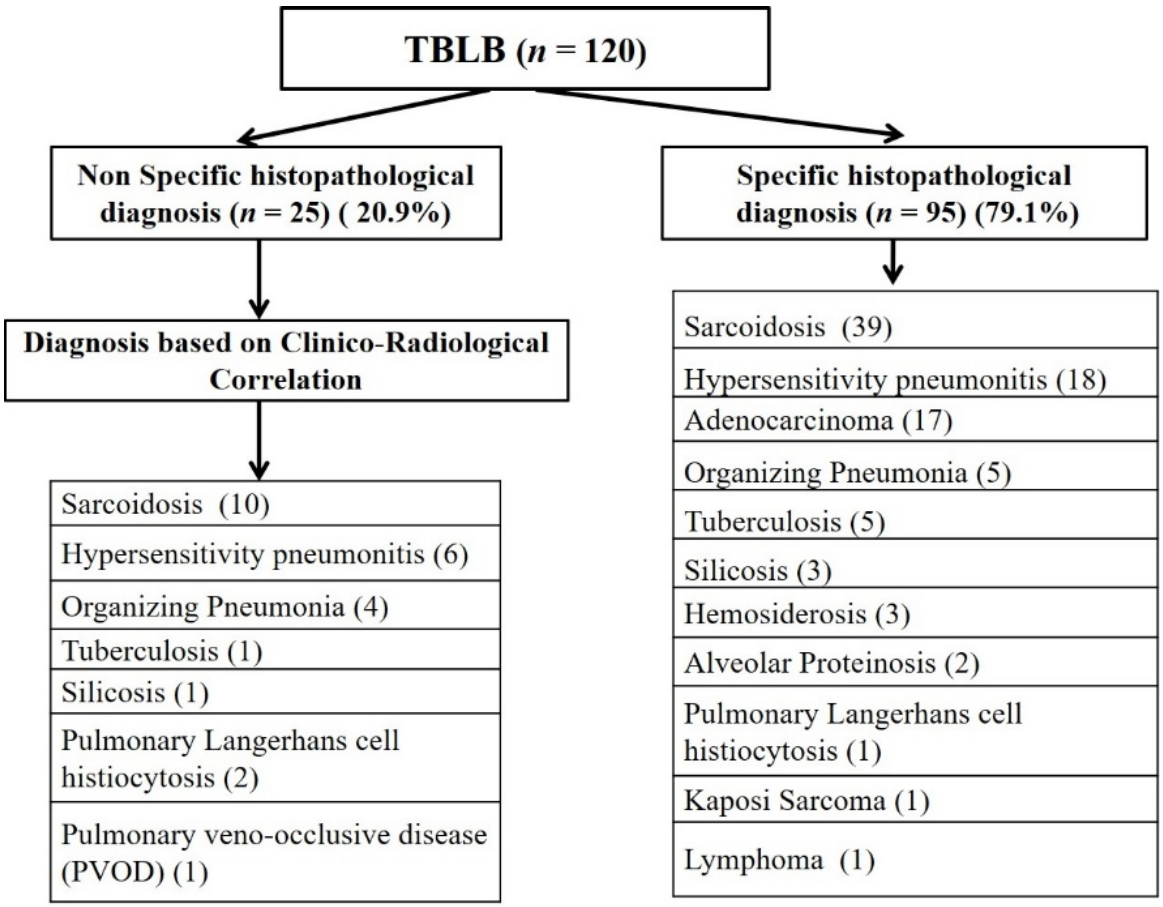

Figure (1): Utility and usefulness of transbronchial lung biopsy in diagnosis of DPLD other than idiopathic pulmonary fibrosis.

Diagnosis based on Clinico-Radiologic-Pathological Correlation ($n = 120$)

Sarcoidosis (49)
Hypersensitivity pneumonitis (24)
Adenocarcinoma (17)
Organizing Pneumonia (9)
Tuberculosis (6)
Silicosis (4)
Hemosiderosis (3)
Pulmonary Langerhans cell histiocytosis (3)
Alveolar Proteinosis (2)
Pulmonary veno-occlusive disease (PVOD) (1)
Kaposi Sarcoma (1)
Lymphoma (1)

Figure (2): Distribution of diagnoses based on Clinico-Radiologic-Pathologic Correlation

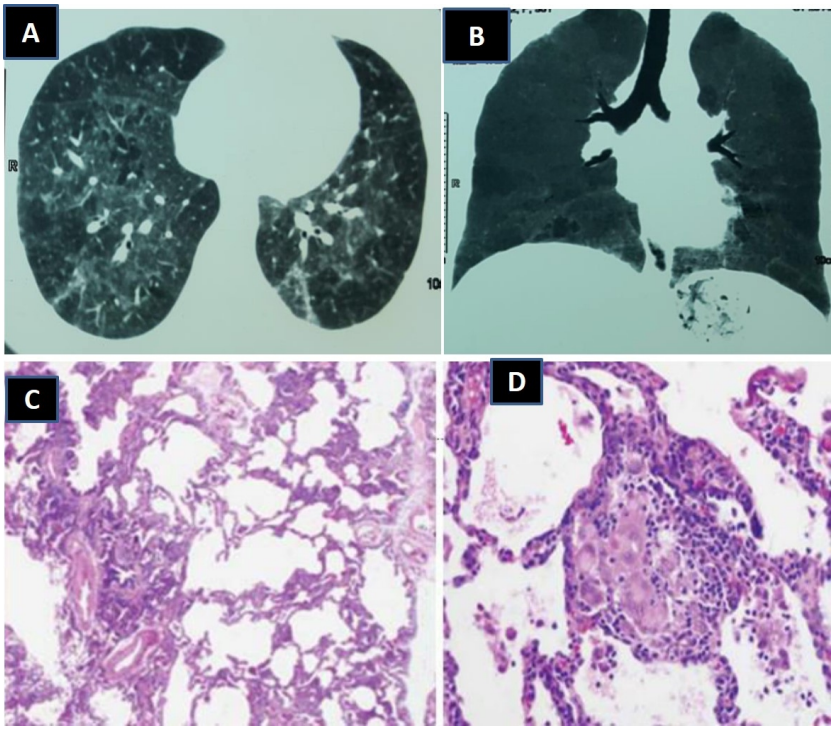

Figure (3): Female patient, 44 years old, non-smoker, pigeons' breeder. (A& B) HRCT chest axial and MinilPcuts showing ground glass opacification and air trapping. HRCT diagnosis was consistent with "Hypersensitivity pneumonitis". TBLB was done from right lower lobe basal segments (C & D) histopathology slides showing ill-defined interstitial granuloma with interstitial chronic inflammatory reaction and thick alveolar septae. Histopathology diagnosis was consistent with "Hypersensitivity pneumonitis"
Final Clinico-Radiologic-Pathological Diagnosis: "Hypersensitivity pneumonitis"

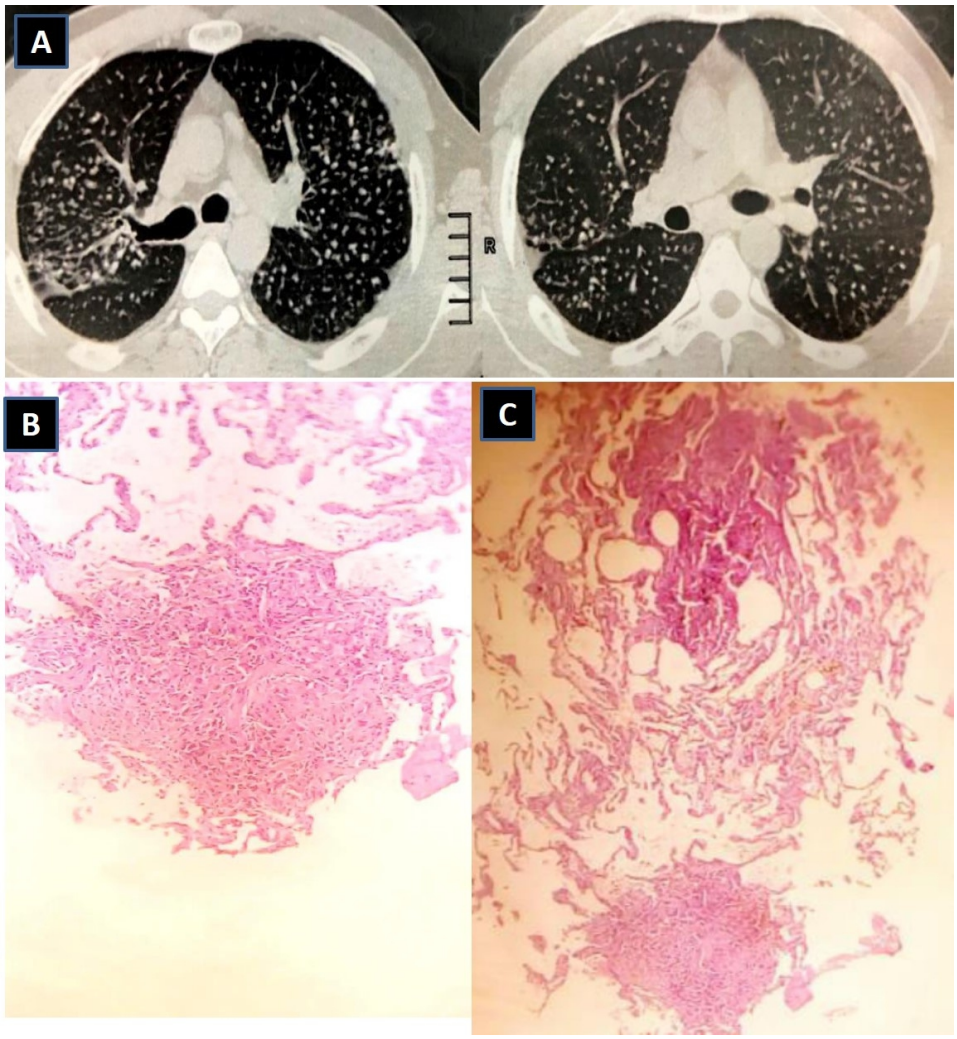

Figure (4): Male patient, 34 years old, smoker, complaining of dyspnea. (A) CT chest showing nodular distribution (Random nodules) as predominant pattern.
HRCT diagnosis: HRCT diagnosis was consistent with Miliary shadows mostly "Miliary tuberculosis". (B & C): histopathology slides showing multiple tiny minimal necrotic interstitial granulomatous looking reaction. Histopathology diagnosis was consistent with "Tuberculosis"
Final Clinico-Radiologic-Pathological Diagnosis: "Miliary tuberculosis"