The Diagnostic Yield of Open Lung Biopsy in relation to clinical and radiological features in Patients with Suspected Interstitial Lung Disease

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Abstract:

Background: The diagnosis of interstitial lung disease (ILD) is frequently delayed, because clinical clues are neglected and respiratory symptoms are ascribed to more common pulmonary diagnosis such as asthma and chronic obstructive pulmonary disease in the primary care setting.

Objective: To evaluate the diagnostic yield of open lung biopsy in patients with suspected ILD in relation to clinical and radiological features.

Patients and methods: Thirty-five patients were admitted with suspected interstitial lung disease (ILD), and scheduled for open lung biopsy (OLB) in Ghazi AL-Hariri hospital for surgical specialty, were included in this study. Data collected from the patient's files (who were subjected to open lung biopsies which had been histopathologically studied in the period from 1st of January 2013 to 31st of May 2015) and were studied retrospectively.

Results: There were 11 (31.4%) males and 24(68.6%) females, the mean age was 46±14 years , dyspnea was the common presenting symptoms in patients 24(68.6%) , dry cough was the presenting symptoms in10 (28.6%)patients , bilateral diffuse crepitations were heard in 20 (57.2%) patients, bilateral fine basal crepitation were heard in 11 (31.4%) , clubbing with bilateral fine basal crepitations heard in 4 (11.4%) ,chest-x- rays findings were: lower zone infiltration in 11 (31.4%), reticulonodular infiltration in 10 (28.6), nodular infiltration in8 (22.9%) and opacities in6 (17.1%). CT findings were: basal infiltration in11 (31.4%), reticulonodular infiltration in 10 (28.6%), nodular infiltration in 8 (22.9%) and ground glass appearance s in 6 (17.1%). Histopathological examination (obtained from Open lung biopsy) results were: had usual interstitial pneumonia (idiopathic pulmonary fibrosis) 21(60%), 7 (20%) metastasis, 5 (14.3%) pulmonary TB and 2(5.7%) broncho-alveolar cell carcinoma.

Conclusion: Open lung biopsy can give a high diagnostic yield and confirm or alters the diagnosis in a significant number of patients with suspected interstitial lung diseases. The usual interstitial pneumonia pattern is the commonest histopathologic pattern seen in ILD patients.

Keywords: interstitial lung disease, Open lung biopsy.

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Introduction:

Interstitial lung diseases are a challenging group of over150 disorders characterized by varying degrees of fibrosis and inflammation of the lung parenchyma or interstitium (1). There are few epidemiological studies on ILD and they differ both in the methods used to establish the diagnosis and the frequencies of the various clinical studies (2). The term interstitial lung disease is confusing because these processes affect-airways, vasculature, and pleura in addition to affecting the lung parenchyma (3). ILD most commonly presents with dyspnea or dry cough, Systemic features, such as weight loss or fatigue, are also common at presentation (4). Although interstitial lung disease (ILD) patients account for approximately 15% of the respiratory disease in general practice, ILD diagnosis can be delayed since clinicians often neglect early clinical clues or ascribe respiratory symptoms to a more common pulmonary condition such as chronic obstructive pulmonary disease (5). An initial work-up begins with a comprehensive history and physical examination with a meticulous occupational, environmental and drug history as well as an evaluation of any symptoms of connective tissue disease (5). Two major histopathological patterns are: (a granulomatous pattern) and (a pattern in which inflammation and Fibrosis). Granulation pattern has a good prognosis but inflammation and fibrosis pattern has a poor prognosis (6). Diagnosis and diagnostic procedures: *Chest x-ray:* is an essential test, may be normal in early or limited disease (7). Plain chest radiographs can be misleadingly negative in up to 10 percent of all patients with clinically significant interstitial lung disease (1).*High resolution CT chest*: high-resolution computed tomography (HRCT) of the chest is usually a key component of the diagnostic evaluation. Approximately 20% of patients with ILD have subtle interstitial abnormalities not detectable on a chest radiograph. For this reason, HRCT should even be considered in symptomatic patients with a normal chest radiograph (3), which

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gives greater precision than the chest radiograph in diagnosing ILD and in characterizing the pattern and extent of the disease (8,9). Pulmonary function tests: typically show reduced lung volumes, impaired gas transfer, and hypoxemia. A reduction in the transfer factor for carbon monoxide and transfer coefficient are characteristic of diseases of the lung parenchyma and its blood supply (7). Surgical or Open lung biopsy (SLB/OLB): Basic diagnostic tool for investigating a patient with suspected ILD (10,11). Procedure used for obtaining large samples of lung tissue necessary for diagnosis and staging of disease activity in patients with ILD (12,13). Lung biopsy is a key element in the diagnosis of some ILDs and in the classification of the idiopathic interstitial pneumonias, whereas in other diseases such as extrinsic allergic alveolitis is rarely needed (14, 15, 16, 17, and 18). OLB remains an important method for the accurate diagnosis of patients with ILD. Ultimately, nearly one-third of patients with ILD will undergo surgical biopsy to establish a diagnosis (19). Surgery may still be needed to establish an accurate diagnosis, to identify potential treatable causes and to rule out other processes (i.e. infection and malignancy) (19). The decision to perform lung biopsy in patients with ILD is based on the likelihood that pathological examination of the tissue obtained will yield specific information about the cause of the disease process and whether this information can be used to alter the treatment being received by the patients (20).

Patients and methods:

Study design & settings

A retrospective of patients with suspected interstitial lung diseases (ILD) admitted to Ghazi AL-Hariri hospital for surgical specialty for period from 1st of January, 2013 through 31st of May, 2015. Inclusion criteria All patients with suspected ILD (depending on clinical features, pulmonary function test (spirometry), chest X-ray, and chest computed tomography. Exclusion criteria incomplete patient data. Data collection The data were collected through reviewing the files of suspected ILD patients and filling a prepared questionnaire. All the patients were included in the study had imaging studies in form of CXR and HRCT, restrictive pattern by spirometry, and open lung biopsy with histopathological examination. The questionnaire included the followings:

Sociodemographic characteristics: Age, and gender, Smoking history, Presenting symptoms, Physical findings, Chest x-ray findings, CT scan findings and Histopathology examination findings of open lung biopsy.

Statistical analysis

Descriptive statistics presented as (mean ± standard deviation) and frequencies as percentages. Multiple contingency tables conducted and appropriate statistical tests performed, Chi-square used for categorical variables and Fishers exact test was used when expected variables were less than 20%. In all statistical analysis, level of significance (p value) set at ≤ 0.05 and the result presented as tables and/or graphs.

Results:

A total of 35 suspected interstitial lung diseases patients (ILD) were included in present study with mean age 46±14 years, 68.6% of them were aging more than 40 years. Females were more than males with male to female ratio as 0.45:1 (figures 1,2). Twenty suspected patients with ILD were nonsmokers, 6 patients were current smokers and 9 patients were ex-smokers. The common presenting symptom among suspected ILD patients was shortness of breath in about (68.6%), dry cough was presenting symptom in (28.6%), fever was presenting symptom in (2.9%). The main physical findings of suspected ILD patients were bilateral diffused crepitations heard in (57.2%), bilateral fine basal crepitations heard in (31.4%) and clubbing with bilateral fine basal crepitations heard in (11.4%).

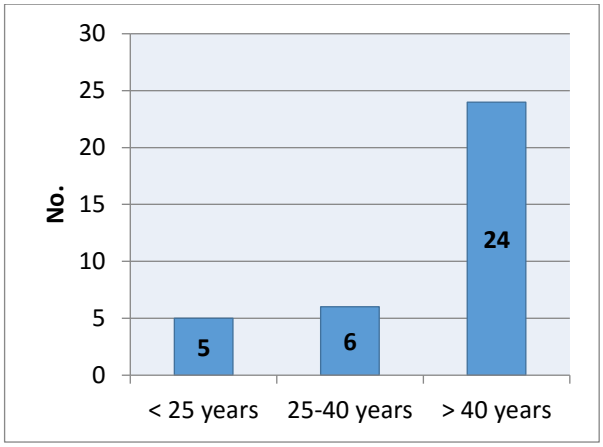

Figure 1: Age distribution.

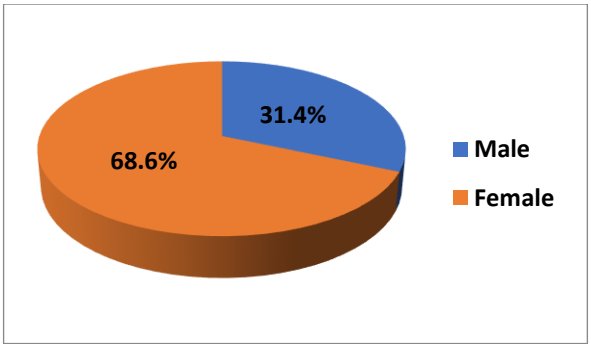

Figure 2: Gender distribution.

Abnormal findings of chest x-ray were distributed as followings; lower zone infiltration in (31.4%), reticulonodular infiltration in (28.6%), nodular infiltration in (22.9%) and opacities in (17.1%). The CT scan of the chest findings of suspected ILD patients were basal infiltration in (31.4%), reticulonodular infiltration in (28.6%), nodular infiltration in (22.9%) and Ground glass appearance in (17.1%). Histopathological examination of open lung biopsy revealed that 60% of studied patients had interstitial lung disease (usual interstitial

pneumonia), 20% metastasis, 14.3% tuberculosis and 5.7% broncho-alveolar cell carcinoma. No significant association were observed between ILD and age, gender, or smoking (p>0.05), table 1. There was no significant association between ILD and presenting symptoms. There was a significant association between physical findings and ILD (p<0.001), table 2. There was a significant association between chest X-ray findings and ILD (p<0.001). Also, a significant association was observed between findings of CT scan of the chest and ILD (p<0.001). Table 3. There was a significant association between histopathology findings by open lung biopsy and ILD (p<0.001), table 4.

Table 1: Distribution of socio demographic characteristics according interstitial lung diseases.

Variable	No ILD		ILD		χ^2	P
	No.	%	No.	%		
Age					1.007*	0.6
< 25 years	3	60.0	2	40.0		
25-40 years	2	33.3	4	66.7		
> 40 years	9	37.5	15	62.5		
Gender						
Male	3	27.3	8	72.7	1.08*	0.2
Female	11	45.8	13	54.2		
Smoking					0.4*	0.7
Current smoker	2	33.3	4	66.7		
Ex-smoker	3	33.3	6	66.7		
Non-smoker	9	45.0	11	55.0		

**Fishers exact test*.

Table2: Distribution of presenting features and physical findings according interstitial lung diseases.

Variable	No ILD		ILD		χ^2	P
	no.	%	no.	%		
Presenting symptoms					1.4*	0.4
Shortness of breath (SOB)	11	45.8	13	54.2		
dry cough	2	20.0	8	80.0		
Fever	1	0	0	100.0		
Physical findings						
Bilateral diffuse crepitations	14	70.0	6	30.0	17.5*	<0.001
Bilateral fine basal crepitations	0	0	11	100.0		
Clubbing+bilateral finebasal crepitation	0	0	4	100.0		

Table 3: Distribution of CXR and CT scan findings according interstitial lung diseases.

Variable	No ILD		ILD		χ^2	P
	no.	%	no.	%		
Chest x-ray					35.0*	<0.001
Reticulnodular infiltration	0	0	10	100.0		
Opacities	6	100.0	0	0		
Nodular infiltration	8	100.0	0	0		
lower zone infiltration	0	0	11	100.0		
CT scan of the chest					35.0*	<0.001
Basal infiltration	0	-	11	100.0		
Reticulonodular infiltration	0	-	10	100.0		
Nodular infiltration	8	100.0	0	-		
Ground glass appearance	6	100.0	0	-		

Table 4: Distribution of lung biopsy findings according interstitial lung diseases.

Histopath-ology finding	No ILD		ILD		χ^2	P
	no.	%	no.	%		
Broncho-alveolar cell carcinoma	2	100.0	0	0	35.0*	<0.001
Usual interstitial pneumonia	0	0	21	100.0		
TB	5	100.0	0	0		
Metastasis	7	100.0	0	0		

Discussion:

Diffuse interstitial (or parenchymal) lung diseases (ILDs) represent a very large group of more than 200 different entities, many of which are rare or "orphan" diseases (4). Prevalence of ILD was 60% in this study, which is in concordance with the reports in other comparable studies as *Deping Zhang and Yin Liu* (21), reported a prevalence of 69.2%and *Hidir Esme et. al.* (22), have reported a prevalence of 62.5 % in their 24 case report of suspected ILD. Regarding age of the cohort of this study, the mean age was (46 ±14 sd years) which is comparable to *Sultan*,s study (2012). (23). Male to female ratio was 0.45:1, with 68.6 % of the study group being female. This goes well with the reported data by *Ferran Morell* et. al. (2), and *Dominic Morris* et. al. (4). This report is contradicting with what *Hidir Esme et. al.* (23) have reported 70% of his 24

patients were males. In our study, there were no significant association observed between ILD and age, or gender. Regarding smoking there is no significant association with ILD, as 57.1% of our cohort were non-smoker. This might be related to the gender of study sample as plenty of our group are females, while *Keith C Meyer* (3) in his report showed a concordance between smoking and Respiratory Bronchiolitis ILD, and Desquamative Interstitial Pneumonia (DIP), and Pulmonary Langerhans Cell Histiocytosis (PLCH). The most common presenting symptom in this study was dyspnea (Shortness of breath) in 68.6%, followed by Dry cough, while fever was the least presenting symptom. Our reported data were similar to *Sultan,s* study (2012) (23), and *Dominic Morris* and *Vipin Zamvar* (2014) (4). Dyspnea usually reflects restriction of expansible capacity of lung interstitium with progressive loss of lung function, and patients may suffer acute exacerbations with acceleration of lung function loss that may often lead to grave complication (23, 24). In this study, there were no significant association between ILD and either of the presenting symptom. This may be due to small study sample. Bilateral diffuse crepitations is the main physical finding in this study, which represents 57.2%, the next was bilateral fine basal crepitations, while clubbing with fine crepitations was the least finding. This is similar to what have been reported by *Sultan*,s study (2012) (23). The current study reveals a significant association between physical findings and ILD ($p<0.001$). Regarding plain chest X ray, lower zone infiltration was the most common finding in this study, while reticulonodular infiltration is the commonest infiltration pattern. This is similar to what have been reported by *Sultan*,s study (2012) (23). CT scan is more specific than plain chest radiograph in diagnosing the subtype of ILD (25) .In general, a complete lack of pulmonary parenchymal changes in CT imaging virtually exclude diagnosis of ILD, although ILD may rarely still be present with lungs having microscopic involvement that does not reach the threshold of the detection of an abnormality that is detectable by CT (25).In this study, basal infiltration and reticulonodular infiltration were the main findings in ILD patients group. There was a significant association between chest X-ray findings and ILD ($p<0.001$). Also, a significant association was observed between findings of CT scan of the chest and ILD ($p<0.001$). These findings are relatively similar to what have been reported by *Sultan*,s study (2012) (23). Histopathological study of open lung biopsy revealed usual interstitial pneumonia pattern as a common and major finding in patients with suspected interstitial lung disease, this is in agreement with the results of *Sultan*,s study (2012) (23). There was a significant association between histopathology findings by open lung biopsy and presence or absence of ILD.

Conclusion:

Dyspnea (Shortness of breath) is the most common presenting symptom in ILD patients.

Chest CT scan findings are useful in evaluation and diagnosis of patients with suspected ILD.

Open lung biopsy can give a high diagnostic yield and confirm or alters the diagnosis in a significant number of patients with suspected interstitial lung diseases. The usual interstitial pneumonia pattern is the commonest histopathologic pattern seen in ILD patients.

Authors' Contributions:

Saja A.Hussein, Data collector

Qasim Mohammed Sultan , Supervisor.

Abdulrasool Noori Nassr, Data collector

Basil Fawzi Jameel, Statically analyzer

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