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Observational findings of transbronchial lung biopsy in patients with interstitial lung disease: a retrospective study in Aleppo University Hospital

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Background: Clinicians face a significant obstacle when attempting to diagnose interstitial lung disease (ILD) patients. However, a thorough clinical examination together with the proper imaging and diagnostic techniques may provide a reliable diagnosis of a particular kind of ILD, and invasive tests such as rigid bronchoscopy or surgical lung biopsy may not be necessary. The aim of this study is to determine the histologic outcomes of an ILD transbronchial lung biopsy (TBLB) carried out at the university hospital in Aleppo.

Methods: This retrospective cohort research was done between 1 January 2020 and 18 April 2022 at the pulmonary department of Aleppo University Hospital, Syria, using patient records. In our study, 174 patients were examined. We included patients over the age of 18 who were referred or admitted to our department at Aleppo University Hospital after being diagnosed with diffuse parenchymal lung disease based on high-resolution computed tomography and clinical symptoms, while excluding other respiratory diseases such as tuberculosis and coronavirus disease 2019.

Results: Patients in the research were 53 ± 7.1 years old on average. Cough and dyspnea were the most common clinical complaints among the patients, which accounted for 79.12 and 78.16%, respectively. A significant fraction of ground-glass opacity was detected on the high-resolution computed tomography, amounting to 102 (58.62%) and 74 (42.53%) for the reticular lesions, respectively. As a complication there were 40 patients with bleeding, of whom 24 had moderate bleeding, and 11 had major bleeding. We also had three patients with pneumothorax. The diagnostic yield of the TBLB in our ILD patients was 66.66%.

Conclusion: An adequate diagnostic accuracy (66.66%) was detected in the TBLB in confirming the diagnosis of ILD; in addition, the bleeding was the most prevalent complication of this procedure. More interventional studies are needed to compare the diagnostic accuracy of this procedure with other invasive and noninvasive diagnostic methodologies of ILD.

Keywords: ground-glass, interstitial lung disease, reticular opacities, transbronchial lung biopsy

Background

Interstitial lung diseases (ILDs) include a broad spectrum of more than 300 diseases, affecting the pulmonary parenchyma with varying degrees of inflammation and/or fibrosis[1]. Their prevalence is estimated at (14–50)/100,000 of the population[2]; the approach and diagnosis of ILDs is still a concern for the pulmonologist, as the proportion of cases that remain undiagnosed is estimated at 15–24% of cases[3]. The association between clinical, radiological, and histologic findings is fundamental for standard

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HIGHLIGHTS

- Interstitial lung disease (ILD) diagnosis is a considerable challenge for clinicians.
- The purpose of this research is to ascertain the histologic results of a transbronchial lung biopsy performed on ILD.
- The transbronchial lung biopsy confirmed the diagnosis of ILD with a satisfactory level of diagnostic accuracy.
- To compare the diagnostic effectiveness of this method to that of other invasive procedures, further interventional studies are necessary.

diagnosing ILDs[4]. The ILD is classified into idiopathic and non-idiopathic diseases. The nonidiopathic ILDs is associated with known causes, occupational, environmental, drug, and/or radiation exposure, as well as systemic illnesses such as autoimmune, infectious, or tumor diseases[5]. The idiopathic ILDs, idiopathic pulmonary fibrosis (IPF), a well-known example of this condition, has the same histology as usual interstitial pneumonitis (UIP). Other types of idiopathic interstitial pneumonia with histopathological manifestations include desquamative interstitial pneumonia, respiratory bronchiolitis-associated interstitial lung disease (RB-ILD), acute interstitial pneumonitis, also known as Hamman–Rich syndrome, nonspecific interstitial pneumonia (NSIP), and cryptogenic organizing pneumonia. Rare idiopathic ILDs contain pulmonary Langerhans cell histiocytosis, eosinophilic granulomas,

tuberous sclerosis, lymphangioleiomyomatosis, Hermansky–Pudlak syndrome, and lymphoid interstitial pneumonia. Granulomatous variants of diffuse parenchymal lung diseases, such as sarcoidosis and hypersensitivity pneumonia, are included in a different group Hypersensitivity sensitivity pneumonia[1]. Some of these types of ILD, including RB-ILD, desquamative interstitial pneumonia, and pulmonary Langerhans cell histiocytosis are associated with smoking. For the diagnosis of ILD, high-resolution computed tomography (HRCT) has a sensitivity of 95% and a specificity approaching 100%, which assess the activity and potential reversibility of diffuse lung disease, although some cases still need lung biopsy[6]. A primarily reticular pattern on computed tomography (CT) shows fibrosis; the septa take on the appearance of being jagged or angulated due to the fibrosis-related architectural deformation. Whereas ground-glass pattern is associated with an increased inflammatory, which may reflect the presence of alveolar disease, interstitial disease, and it may be a manifestation of cellular lung infiltration or active inflammation[7,8]. Furthermore, a unique procedure called trans-bronchial lung biopsy (TBLB) is performed using biopsy forceps during flexible bronchoscopy. Obtaining lung tissue samples is often done with the intention of diagnosing ILD or locating lung lesions[9]. Fiberoptic bronchoscopy is furthermore thought to be less stressful for the patients and requires less anesthetic. This study aims to determine the histologic findings of TBLB in ILD in Aleppo University Hospital.

Methods

Study setting

This retrospective cohort study was conducted on the patient's recordings from 1 January 2020 to 18 April 2022 at the respiratory department of Aleppo University Hospital, Syria. A total of 174 patients were included in our study; they were referred or hospitalized to our department after diagnosis of ILD. At first, depending on the patient's recordings, we determined the medical history, clinical findings, and radiographic findings of HRCT scans of the patients accepted in our department as ILD patients. After that, we performed flexible bronchoscopy (Olympus BF type PE2) under local anesthesia using xylocaine (4% spray – 2% instillation through the working channel), then taking an endoscopic TBLB by using disposable biopsy forceps (Olympus, model no. FB-231D, working length: 1150 mm, minimum channel size: 2.0 mm). We followed the guidelines[10,11] for flexible fiberoptic bronchoscopy and TBLB, and the biopsy site was selected according to the radiologic lesion location on HRCT. The results of biopsies were studied in the Histopathology Department of Aleppo University Hospital. The process included entering the bronchoscope into the third bronchial branch and then fixing it in position, inserting the forceps until the specialist felt resistance or the patient felt pain; we asked the patient to take a deep inhalation, open the forceps, and then asked the patient to exhale deeply accompanied by closing the forceps. We determined many inclusion and exclusion criteria to select the included patients in our study as the following: *Inclusion criteria* – referred or hospitalized patients to our department in Aleppo University Hospital and above 18 years, after defining the diagnosis of diffuse parenchymal lung disease depending on HRCT and clinical findings with excluding another respiratory disease such as tuberculosis (TB) and coronavirus

disease 2019, etc. *Exclusion criteria* – patients with a contra-indication to conduct bronchoscopy or TBLB such as hypoxia, cardiac arrhythmias, hemorrhage abnormalities, etc. Patients with CT pathognomonic patterns follow the diagnosis criteria of ILD[12]. Patients with typical manifestations and clinical history of connective tissue disease-associated ILDs, such as rheumatoid arthritis, systemic sclerosis, systemic lupus erythematosus, etc. Patients diagnosed with occupational lung disease depend on clinical, radiological, and laboratory examinations. The patients diagnosed with coronavirus disease 2019 depend on nasal smear PCR or TB, depending on the sputum gene Xpert MTP/RIF.

We confirm that the work has been reported in line with the Strengthening The Reporting Of Cohort Studies in Surgery (STROCSS) criteria[13].

Measures

The required information of the included patients was recorded using a uniform form. The form was divided into multiple sections: First section: demographic variables, including age, gender, address, occupation, hobbies, and habits. Second section: medical history, including medication history, previous laboratory test results (autoantibody for connective tissue diseases), and biomarkers. Third section: patients' clinical findings, including presented signs and symptoms associated with ILD (like cough, hemoptysis, dyspnea, etc.). Fourth section: radiologic features, including HRCT lung findings [ground-glass opacity (GGO), nodular opacities, consolidation, cavitation, reticular, etc.]. Fifth section: bronchoscopy results and complications, in which we determined the complications after bronchoscopy, including bleeding, pneumothorax, escalation of care, etc. Sixth section: histopathology findings.

Statistical analysis

We analyzed the data using Statistical Package for the Social Sciences (SPSS) 28. Continued data were statistically described in terms of Mean ± SD, median, and range; the categorical data were expressed as frequencies and percentages. χ^2 test was used to determine the correlation between the categorical variables, and a *P*-value below 0.05 was considered a statistically significant value.

Results

Baseline characteristics of the study sample

This retrospective study included 174 patients whose ages ranged from 40 to 70 years. The overall average age of the study patients was 53 years. The average age was 51.5 and 57 years of non-idiopathic ILDs, and idiopathic ILDs; retrospectively, patients with idiopathic ILDs were older than nonidiopathic ILDs with a statistically significant difference. Males consisted a larger proportion in our study than females, 107 (61.5%), as well as almost half of the patients (51.72%) were smokers, with an average of cigarette pack/year 33.5 ± 8.8. In addition, 31.5% of the patients had chronic diseases (Table 1).

Clinical findings of the inquired patients

The most prevalent clinical symptoms among the patients, who made up 79.12% and 78.16%, respectively, were cough and dyspnea. Night sweats, hemoptysis, and clubbing, which made

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Table 1

Baseline characteristics of the study sample.

Variable	Categories	Frequency	Percent
Age (Mean ± SD)		53 ± 7.1	
Gender	Male	107	61.5
	Female	67	38.5
Smoking	Smoker	90	51.72
	Nonsmoker	84	48.27
No. of cigarette packs/year (Mean ± SD)		33.5 ± 8.8	
Chronic diseases	Yes	55	31.5
	No	119	68.5
Previous medications	Yes	46	26.43
	No	128	73.68

up 9.77%, 6.32%, and 4.60% of the clinical findings, respectively, made up the least amount of clinical findings (Table 2).

Radiological findings of the inquired patients by HRCT

On HRCT, we found a considerable proportion of GGO as the radiological findings, which reached 102 (58.62%), as well as 74 (42.53%) for the reticular lesions. Other findings of a tree in bud and cavitation were made retrospectively in eight and seven cases, respectively (Table 3).

Histopathological findings of the inquired patients by transbronchial lung biopsy

We divided the histopathological findings according to the international criteria of the ILDs classification (Table 4) into two sections, as following idiopathic ILDs and nonidiopathic ILDs (Table 5).

Table 2

Histopathological findings.

Nonidiopathic interstitial lung diseases (ILDs)	Number	Percent
Tuberculosis	19	10.92
Sarcoidosis	15	8.62
Hypersensitivity pneumonitis	13	7.47
Bronchoalveolar ca (Adenoma carcinoma)	8	4.60
Lymphangitis carcinomatous	7	4.02
Pneumonia	6	3.45
Silicosis	3	1.72
Eosinophilic pneumonia	2	1.15
Radiation pneumonitis	2	1.15
Lymphoma	1	0.57
Metastasis breast cancer	1	0.57
Alveolar microlithiasis	1	0.57
Sum nonidiopathic ILDs	78	44.83
Idiopathic ILDs		
Unclassified ILD	58	33.33
Nonspecific interstitial pneumonia	14	8.05
Respiratory bronchiolitis-associated interstitial lung disease	13	7.47
Idiopathic pulmonary fibrosis	9	5.17
Cryptogenic organizing pneumonia	1	0.57
Acute interstitial pneumonia	1	0.57
Sum idiopathic ILDs	96	55.17
Total	174	100.00

Table 3

Clinical findings of the study sample.

Symptoms	Number	Percent
Cough	138	79.12
Dyspnea	136	78.16
Weight loss	57	32.76
Sputum	54	31.03
Fever	44	25.29
Chest pain	21	12.07
Night sweats	17	9.77
Hemoptysis	11	6.32
Clubbing	8	4.60

Nonidiopathic ILDs

A large group of patients with nonidiopathic ILD illness (19.54%) included patients who had TB and sarcoidosis. Additionally, there were seven, six, three, and two instances of individuals with nonidiopathic ILD disease among those with lymphangitis carcinomatous, pneumonia, silicosis, and eosinophilic pneumonia abnormalities.

Idiopathic ILDs

Of the patients with idiopathic ILDs, 58 cases (33.33%) were unclassified ILD (UILD) patients. Additionally, 14 cases (8.05%) were NSIP, 13 cases (7.47%) were RB-ILD patients, and 9 cases (5.17%) were IPF.

Complications after performing of TBLB among the sample study

We defined 43 patients with complications after performing TBLB to diagnose ILD. The complications consisted of 40 patients with bleeding, of which 24 patients had minor bleeding, and 11 patients had major bleeding, as well we had 3 patients with pneumothorax (Table 6).

Diagnostic accuracy of the TBLB in ILD patients

We defined 58 (33.33%) patients as unclassified (UILD) or undiagnosed cases of ILD, so the diagnostic yield of the TBLB in our ILD patients was 66.66%.

Predominant CT findings among histopathological subgroups of the study population

We defined a highly significant correlation between the histopathological findings and ground-glass opacity and reticular opacity ($P < 0.001$). In our study, we detected 102 cases with

Table 4

Radiographic findings.

Radiographic	Number	Percent
GGO	102	58.62
Reticular lesions	74	42.53
NO 0	67	38.51
Consolidation	33	18.97
Tree in bud	8	4.60
Cavitation	7	4.02

GGO, ground-glass opacity; NO 0, Nodular opacities.

Table 5

Classification of interstitial lung diseases.

Idiopathic			Nonidiopathic		
	Rare	Granulomatous	Exposure	Systemic illness	Variety illness
UIP	PLCH	Sarcoidosis	Occupational	CD-ILD	Infections
NSIP	EG		Environmental	Vasculitis	Tumors
DIP	TS		Drug		
RB-ILD	LAM		Radiation exposure		
AIP	H-PS				
COP	LIP				
UILD					

AIP, acute interstitial pneumonia; CD-ILD, connective tissue disease-associated interstitial lung disease; COP, cryptogenic organizing pneumonia; DIP, desquamative interstitial pneumonia; DPLD, diffuse parenchymal lung disease; EG, eosinophilic granulomas; H-PS, Hermansky–Pudlak syndrome; LAM, lymphangioleiomyomatosis; LIP, lymphoid interstitial pneumonia; NSIP, nonspecific interstitial pneumonia; PLCH, pulmonary Langerhans cell histiocytosis; RB-ILD, respiratory bronchiolitis-associated interstitial lung disease; TS, tuberous sclerosis; UILD, unclassified interstitial lung disease; UIP, usual interstitial pneumonia.

ground-glass appearance and 74 cases with reticular opacities, where in UILD patients, 18 patients had ground-glass appearance and, in addition, 32 patients had reticular opacities (Table 7).

Discussion

To our knowledge, this is the first study in Syria that determine the histological findings of TBLB in ILD, and detects the diagnostic accuracy of this procedure for the diagnosis of ILDs, with the observed complications. Clinicians have a great deal of difficulty in correctly diagnosing the different ILD forms. However, a thorough clinical examination coupled with suitable imaging and diagnostic methods may provide a reliable diagnosis of a particular kind of ILD, and invasive testing such as rigid bronchoscopy or surgical lung biopsy (SLB) may not be necessary[14]. The sooner the diagnosis is made in diffuse parenchymal lung disease DPLD, the higher their chances of survival. In this case, bronchoalveolar lavage, mainly when guided by HRCT scan results conducted a few hours previously, is often useful in identifying opportunistic infections, alveolar proteinosis, alveolar hemorrhage and capillaritis, lymphomatous or leukemic lung infiltration, carcinomatous lymphangitis, disseminated hematogenous lung metastases, and hypersensitivity pneumonitis. When bronchoalveolar lavage fluid analysis fails to provide a definite diagnosis, or in most individuals who develop DPLD, TBLB, or even open lung biopsy may be explored. The TBLB forceps allow lung tissue collection through bronchial pathways, and the specimens thus collected often come from the centrilobular areas. As a result, illnesses concentrated on the terminal and respiratory bronchioles (respiratory bronchiolitis,

Table 6

Complications after transbronchial lung biopsy.

Complication	Number	Percent
Pneumothorax	3	1.72
Bleeding	40	22.99
Minor bleeding	29	16.67
Major bleeding (need adrenalin infusion)	11	6.32

tuberculosis, lobular infectious pneumonia, cellular bronchiolitis) or that substantially affect these structures (organizing pneumonia) or that are dispersed along lymphatic channels (sarcoidosis, carcinomatous lymphangitis) may be sampled often by forceps. TBLB is a common diagnostic tool utilized by almost all bronchoscopists nowadays, and the flexible bronchoscope is the tool of choice for performing the procedure. Bleeding is the most common complication of TBLB; less common complications include pneumothorax, hypoxemia, or cardiac arrhythmias during the treatment. In terms of clinical symptoms, we note that the two main symptoms in the patients of our study are cough in 138 (79.12%) patients and dyspnea in 136 (78.16%) patients. It was stated in the article by Spagnolo et al.[15] that cough and dyspnea were the most important symptoms in patients with ILDs; cough was a characteristic symptom of ILDs with a sensitivity of more than 80%, but with low specificity, while dyspnea was neither sensitive nor specific to ILDs. Age and MUC5B genotype were significantly associated with the progression of ILD[16]. Our study pointed out the role of advanced age in increasing the prevalence of fibrotic cases in patients with ILD due to disease progression until after the cellular inflammatory stage has been passed. And the disease has progressed to the fibrotic stage, where at this stage, the result of biopsies is fibrosis, and it is difficult to know the etiologic cause of the disease. Also, in the Framingham study[17], it was indicated that increasing age is associated with the progression of ILD. A HRCT scan has high sensitivity and specificity for ILDs and is believed to give a macroscopic description of these diseases. ILA is defined on a HRCT scan of the chest as a lesion that includes more than 5% of the lung tissue[18]. The progression of the disease has been defined as the increase in the affected area on HRCT imaging. Reticular radiographic signs increased disease progression more than sixfold[19]. In our study, we found a considerable proportion of GGO as the radiological findings, which reached 102 (58.62%), as well as 74 (42.53%) for the reticular lesions. Johkoh[20] noted that serial CT reveals an increase in the extent of honeycombing and reticulation and a decrease in the extent of areas with ground-glass attenuation. In our study, it was clear that the radiographic reticular appearance was more prevalent in patients with idiopathic diseases compared with patients with nonidiopathic ILDs, with a significant statistical difference because it indicates fibrosis and progression of the interstitial lesion. This can be logically linked with patients with idiopathic interstitial diseases being older in our study, with a statistically significant difference. In the advanced fibrotic stage, it is difficult to know the causal etiological diagnosis of the lesion. The recommendations indicated that some of the radiological features of the CT scan might eliminate the need for lung biopsy because it indicates the diagnosis[21,22]. It was suggested[23,24] to keep the lung biopsy for cases before fibrosis or at an early stage where complications are logically acceptable, but in advanced fibrotic stages, even surgical biopsy will not provide a curative solution. Since the ground-glass appearance indicates the inflammatory cellular stage, we often direct the biopsies to the sites of ground-glass appearance radiologically to increase the diagnostic yield[25]. Lynch et al. indicated a better prognosis and the degree of GGO predictor of therapy response[21]. According to multivariate logistic regression analysis, the visual amount of fibrosis on CT scans was the only significant predictor of death during follow-up[26]. The extra predictive ability provided by the more quantitative indicators was minimal. These findings concur with previous research by

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Table 7

Predominant computed tomography findings among histopathological subgroups of the study population.

Histopathological findings

Predominant CT finding	BA ca	TB	SI	LC	LYM	MBC	EP	HP	SAR	PNEU	RP	AM	COP	IPF	NSIP	RB-ILD	UILD	AIP	Total	P value
Number	8	19	3	7	1	1	2	13	15	6	2	1	1	9	14	13	58	1	174	
Ground-glass opacity	5	11	2	6	1	1	2	11	11	4	2	1	1	4	10	11	18	1	102	< 0.001
Percent	62.5	57.9	66.7	85.7	100	100	100	84.6	73.3	66.7	100	100	100	44.4	71.4	84.6	31.0	100	58.6	
Reticular opacity	0	3	1	4	0	0	0	3	4	0	0	1	0	9	13	4	32	0	74	< 0.001
Percent	0.0	15.8	33.3	57.1	0.0	0.0	0.0	23.1	26.7	0.0	0.0	100	0.0	100	92.9	30.8	55.2	0.0	42.5	

AIP, acute interstitial pneumonia; AM, alveolar microlithiasis; BA ca, bronchoalveolar ca (Adenoma carcinoma); COP, cryptogenic organizing pneumonia; CT, computed tomography; EP, eosinophilic pneumonia; HP, hypersensitivity pneumonitis; IPF, idiopathic pulmonary fibrosis; LC, lymphangitis carcinomatosis; LYM, lymphoma; MBC, metastasis breast cancer; NSIP, nonspecific interstitial pneumonia; PNEU, pneumonia; RP, radiographic pneumonia; RB-ILD, respiratory bronchiolitis-associated interstitial lung disease; SAR, sarcoidosis; SI, silicosis; TB, tuberculosis; UILD, unclassified interstitial lung disease.

Lynch et al.[21], which identified lung fibrosis visual extent as the greatest independent predictor of death. Ground-glass attenuation in individuals with UIP should only be taken into account as an active process when there are no concurrent findings, according to research by Remy-Jardin et al.[25]. Intralobular reticular opacities, honeycombing, and traction bronchiectasis are signs of fibrosis in UIP patients[27]. Although we excluded the UIP pattern compatible with the IPF diagnosis, we had a final histological diagnosis of IPF in nine (5.17%) of the study patients. This was also shown in the Indian[28] study that was also conducted on cases of ILDs after exclusion of the radiographic UIP pattern; they had a histological IPF of 6.1%, and they concluded suggesting that despite a 'non-IPF pattern' on HRCT thorax, histological evidence of UIP may be found. Also, this study shows the spectrum of ILDs among patients attending Aleppo University Hospital. A large prevalence of pulmonary TB is noted, as it constituted 10.9% of ILD patients, which indicates a large prevalence of pulmonary TB in the Aleppo Governorate. Rates of TB in Syria are increasing, and recent figures show that one-third of all TB cases in the country are found in the Aleppo governorate. After evaluating the diagnostic yield and considering the UILD undiagnosed, we find that the diagnostic yield is 66.66%. UILDs represent 33.33% of our study patients. Patients with unclassifiable fibrotic ILDs were defined as[29] those without a specific ILD diagnosis following a multidisciplinary review of their clinical, radiologic, and pathologic data approximately (17.5%) of all ILDs. Hunninghake et al.[30] conclude that in ILD, a specific diagnosis might be difficult to obtain in ~15–20% of the cases, even with a surgical biopsy. Unclassifiable cases are considered[31] to represent a heterogeneous collection of fibrotic ILDs such as IPF, idiopathic NSIP, chronic hypersensitivity pneumonitis, and connective tissue disease-associated ILD. Hyldgaard et al.[32] suggested that 'unclassifiable ILD' were used in cases where the diagnostic examinations and the re-evaluation failed to meet the 2011 criteria for IPF or any other specified subtype of ILDs. In comparison with the results of international studies shown in Table 8, we note that the diagnostic yield is low for us, and this is due to two reasons: The first reason is the small size of the biopsies and their insufficiency in making the final diagnosis, and this problem is fundamental in the transbronchial lung biopsy with a flexible endoscope and is often mentioned in international studies[39,41].The second reason is that ILD's basic symptoms (cough and dyspnea) are nonspecific[42]. Therefore, patients are late in reviewing the thoracic section in the hospital, where most of them are reviewed at an advanced stage, as the fibrotic stage is difficult to reach the final diagnosis. Comparing our research to other worldwide studies, the incidence of problems is low and acceptable, as the table illustrates. In the medical literature, the most significant complications in transbronchial biopsy procedures are major bleeding (0.58–2.8%) where most cases are minor, and pneumothorax (0.97–4%), with tension pneumothorax being rare[43,44]. Our study has some limitations, the most significant of which is that we did not complete the diagnostic study of unclassified cases by either SLB or transbronchial cryobiopsy, and we did not perform molecular tests on samples taken by bronchoscopy in patients with ILD. It is clear that SLB is no longer the gold standard for diagnosing ILDs[45]. As SLB has morbidity and mortality risk. However, the interdisciplinary discussion[46] has emerged as the gold standard where the medical and occupational history, clinical symptoms, the outcomes of laboratory titrations, genomic approaches, and

Table 8

Literature review of similar studies.

References	Publish date	Country	Diagnostic yield (%)	Tuberculosis (%)	Complications, n (%)	Major bleeding, n (%)	Pneumothorax, n (%)	Need chest tube, n (%)
Sindhwani et al.[28]	2015	India	85.7	18.4	5 (10.2)	0	5 (10.2)	3 (6.1)
Arya et al.[33]	2021	USA	91	0	3 (8.5)	1 (2.85)	2 (5.7)	1 (2.85)
Milman et al.[34]	1994	Denmark	66.7	1.9	27 (6)	1 (0.22)	26 (5.8)	17 (3.8)
Youssef et al.[35]	2018	Egypt	73.1	0	6 (23)	2 (7.7)	4 (15.4)	0
Vahedi et al.[36]	1990	Iran	66	3.7	2 (4)	0	2 (4)	1 (2)
Almadani et al.[37]	2018	Ireland	35	0	23 (28.75)	10 (12.5)	3 (3.75)	0
Ibrahim et al.[38]	2005	Qatar	64	5.4	8 (11.2)	0	7 (9.8)	0
Loube et al.[39]	1993	USA	33.3	0	3 (11.1)	2 (7.4)	1 (3.7)	0
Jabbardarjani et al.[40]	2010	Iran	47.7	0	5 (11.3)	2 (3.4)	3 (6.8)	2 (4.5)

molecular phenotypes, as well as radiographic observations and pathological results, are examined.

Conclusion

The TBLB had an appropriate diagnostic accuracy (66.66%) in confirming the diagnosis of ILDs, and bleeding was the most common complication of this treatment. More interventional studies are required to evaluate this procedure's diagnostic efficacy to that of other invasive and noninvasive diagnostic techniques. Pulmonologists should be aware of the precise examination of ILD patients, and promising biological research should be performed to examine the possibility of setting a speedy and appropriate diagnosis using TBLB in the early stages of ILD to prevent severe complications owing to the delay in diagnosis.

Ethical approval

The protocol of this study was approved by the Scientific Research Council in Aleppo (IRB: 1263).

Ethics approval and consent to participate

The ethical approval was taken from the dean of the Faculty of Medicine, Aleppo, and the president of the Pulmonology Department and the Aleppo Hospital.

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Author contribution

All authors have contributed to writing and reviewing the manuscript and have approved the final draft of the manuscript.

Conflicts of interest disclosure

There are no conflicts of interest.

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Data availability

The datasets used and analyzed during the current study are available from the corresponding author at reasonable request.

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