Epidemiology of interstitial lung disease in Palestine: first national data

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Abstract

Significant progress has been made in recent years in understanding the epidemiology of interstitial lung diseases (ILD) across the world, but the amount of information available is still small compared to other respiratory diseases like obstructive lung diseases or lung cancer. In this study we tried to explore the epidemiology of ILD in a virgin area of the world (Palestine), by describing a retrospectively collected cohort of newly diagnosed ILD cases in a single – and the only – Pulmonology center in Palestine over two years.

Introduction

Interstitial lung diseases, also called diffuse parenchymal lung diseases are a large and diverse group of fibrotic and non-fibrotic conditions that affect the bronchioles, alveoli and interstitium of the lungs. Several factors play role in the pathogenesis of these diseases including genetics, drug and radiation toxicities, smoking, environmental and occupational exposures. They could also be idiopathic. DPLD are classified based on etiology into four groups: DPLD of known cause (like drugs or CTD associated), Idiopathic interstitial pneumonias (like IPF), Granulomatous DPLD (like sarcoidosis), and others (like Lymphangioleiomyomatosis). The incidence of these diseases has been increasing based on population based analyses.[1,2] Most of these studies came from the Western hemisphere, with few Mediterranean studies. Unfortunately there are no data about the epidemiology of ILD in Palestine. In this study we examined all cases of newly diagnosed ILD presented to our Hospital (which is the first Pulmonology center in Palestine), between the years 2014-2015.

Materials and Methods

This is a retrospective analysis of all 82 undiagnosed patients, who were suspected to have ILD, and who presented to our hospital, in the period between January 1st 2014 and December 31st 2015.

Data were collected from Bronchoscopy unit records over that period, which means we included only patients who required a bronchoscopic procedure in order to make a diagnosis, regardless of DPLD classification. A total of 83 diagnostic procedures were used, including 82 Bronchoalveolar lavages (BAL) with transbronchial biopsies, and only one surgical lung biopsy. Each case was discussed by a pulmonologist and a radiologist and a pretest differential diagnosis list was generated. The pathologist reviewed the clinical and radiologic information, and then examined pathologic specimens in light of the most likely differential diagnosis.

The combination of clinical-radiologic-pathologic correlation yielded confident and accurate diagnosis in 86% of all the bronchoscopic procedures and in the one surgical lung biopsy performed.

Results

We identified 82 patients with suspected ILD, including 36 males (44%) and 46 females (56%), with a mean age of 49.3 years (50.5 for males, 49 for females). Most patients were never smokers 48 (58.5%), 11 (13.4%) were ex-smokers and only 10 patients (12%) were active smokers at the time of diagnosis. Data about smoking status could not be retrieved in 13 patients (15.8%) (Table 1).

A history of relevant occupational or environmental exposure was documented in 25 patients (30%). These included 11 patients (44%) who were exposed to construction dust, 5 patients (20%) who were exposed to chemicals, other exposures included farm dust, tobacco farming, asbestos, metals, tear gas and others (Table 2). Patients were also distributed geographically according to their place of residence. Most patients came from Hebron (23%), Jerusalem (12%), Ramallah (11%), Nablus (9.7%), and Gaza (7.3%), these numbers were probably biased by the ease of access to our hospital from surrounding cities compared to others and by different population sizes of these cities (Table 3).

As stated previously, a final diagnosis was made in 68 out of 82 patients (diagnostic accuracy of 86%), more than 15 different interstitial lung diseases were identified. The most common ILD in Palestine was Sarcoidosis, diagnosed in 22 patients (26.8%), this was also the most common diagnosis in males (25%) and females (28.2%) alone, being slightly more common in females.

The second most common diagnosis made was Non-specific interstitial Pneumonitis (NSIP), surprisingly NSIP was more common in males than in females at 19.4% in males compared to 17.3% in females. The third most common ILD was Occupational lung disease in males (16.6%) and Vasculitis, LIP, Bronchiolitis and Alveolar proteinosis in females, each making up to 6.5% of diagnoses. all 4 Alveolar proteinosis cases were diagnosed in 2014,and none in 2015. See table4 for other diagnoses (Table 4).

All patients underwent Chest x-ray and Ct chest as part of their evaluation, the most common finding was bilateral interstitial infiltrates in more than 89% of patients.

Discussion

As expected interstitial lung diseases were more common in females compared to males (1.27:1), probably because of higher incidence of associated diseases, like vasculitis and connective tissue diseases in females. The most common diagnosis made was Sarcoidosis, followed by NSIP in both genders. While Sarcoidosis was more common in females (1:0.69), NSIP was slightly more common in males compared to females (1.16:1). The third most common diagnosis was Occupational lung disease in males-mostly due to exposure to construc-

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Table 1. Demographics of patients.

	2014			2015			2014-2015		
	Total	Males	Females	Total	Males	Females	Total	Males	Females
Number of patients	44	21 (47%)	23 (53%)	38	15 (39.5%)	23 (60.5%)	82	36 (44%)	46 (56%)
Mean age	47.9	50.8	47.9	51	52.7	50.2	49.3	50.5	49
Smoking status									
Smoker	3 (6.8%)			7 (18.4%)	6 (40%)	1 (4.3%)	10 (12%)		
Exsmoker	8 (18%)			3 (7.8%)	3 (20%)	0	11 (13.4%)		
Not Mentioned	8 (18%)			5 (13%)	2 (13%)	3 (13%)	13 (15.8%)		
Non-smoker	25 (56.8%)			23 (60.5%)	4 (27%)	19 (82%)	48 (58.5%)		
History of exposure	18 (40.9%)			7 (18.4%)	6 (40%)	1 (4.3%)	25 (30%)		

tion dust in the workplace- where as in females LIP, Vasculitis, Bronchiolitis and Alveolar proteinosis came third, each making up 6.5%.

Of note, all four Alveolar proteinosis cases were diagnosed in 2014, and none in 2015. We believe these cases were non-diagnosed left over cases from previous years (Table 4). It is not until 2016 when another case of Alveolar proteinosis gets diagnosed. (Not included in this analysis).

These data represent the first and only available data on ILD in Palestine, however they are still not enough to accurately calculate the incidence or prevalence of ILD in the country, for several reasons.

First, the data were collected from archives of only one medical center in the country (though the only well-structured one), while many Palestinians still seek medical care in surrounding countries, this represents a potential loss of data. Second, the data were a retrospective analysis of all bronchoscopy-derived ILD diagnoses, this means that interstitial lung diseases that usually get diagnosed -based on clinical presentation and typical imaging- without invasive procedures were not be included in this analyses, for example patients with diseases like Idiopathic pulmonary fibrosis, Lymphangioleiomyomatosis, or Pulmonary Langerhans cell histiocytosis were unlikely to undergo a bronchoscopic procedure in our department. Additionally, patients who were sick enough not undergo diagnostic procedures were not included in this registry.

Data about the epidemiology of interstitial lung diseases are still scarce compared to other pulmonary diseases, especially in the Mediterranean region. Karakatsani *et al.*[3] studied the incidence and prevalence of various interstitial lung diseases among 967 Greek patients, they found that the annual incidence of ILDs was 4.63 new cases per 100,000 inhabitants, and the estimated prevalence was 17.3 cases per 100,000 inhabitants. The most frequent diagnoses were Sarcoidosis at (34.1%), followed by IPF at (19.5%) and CTD related ILD at (12.4%).

Table 2. Relevant occupational or environmental exposure of patients.

Exposure	Number of patients	Percentage
Construction dust	11	44%
Metalworker	1	4%
Asbestos	1	4%
Farm dust	2	8%
Tobbaco industry	1	4%
Chemicals	5	20%
Others	4	16%

In Italy Agostini[4] provided the first look into the Italian register for diffuse infiltrative lung disorders (RIPID), his report spanned the period 1998-2000 and showed that the most frequent disorders were IPF at (37.6%), followed by sarcoidosis at (29.2%), and Langherans' cell hystiocytosis at (6.6%). A second look at the same register by Tinelli[5] from 2001 to 2005 included 3152 patients and showed that the most frequently reported diagnoses were Sarcoidosis (33.7%) and IPF (27.4%).

In a report from the southern regions of Spain that included 744 patients, López-Campos[6] studied the incidence of ILD over a 3-year period 1998-2000, the most common diseases were Idiopathic interstitial pneumonias (39%) followed by sarcoidosis (12%). The annual incidence of ILD was 3.62 cases per 100,000 inhabitants. Another study from Spain by Xaubet[7] calculated the incidence of ILD at 7.6 cases per 100,000 inhabitants, again the most common diseases were IPF (38.6%), followed in decreasing order by sarcoidosis (14.9%), cryptogenic organizing pneumonia (10.4%), ILD associated with collagen vascular diseases (9.9%) and hypersensitivity pneumonitis (6.6%).

Finally in a study from Saudi Arabia by Alhamad *et al.*[8] CTD related ILD was the most common diagnosis at (34.8%), followed by IPF (23.3%) and Sarcoidosis (20%).

The results of this study are comparable to data from other Middle Eastern and Mediterranean countries, taking in consideration that our data were derived from bronchoscopy archives and did not include IPF patients in the current study. In all these studies sarcoidosis was the most common or second most common interstitial lung disease encountered.

Although we studied a small number of patients (83 patients) over a short period of time -only two years- our results are invaluable, because they represent the first and only data about ILD in Palestine, we hope this study will lay the ground for more extensive research of ILD in Palestine.

Conclusions

Sarcoidosis is the most common ILD in Palestine (26.8%)in both males (25%) and females (28.2%), followed by Non-specific Interstitial Pneumonia (NSIP) at (15.8%). ILD in general is more common in females compared to males (1.27:1), and in none smokers or ex-smokers compared to current smokers (5.9:1). The mean age at diagnosis was comparable in both males and females at (50.5 years) and (49 years) respectively. Nearly one third of patients had an occupational or an environmental exposure, the most common was exposure to construction

Table 3. City of provenance of patients.

	2014		2015		2014-2015	
	Number of patients	Percentage	Number of patient	Percentage	Number of patients	Percentage
Jenin	2	4.50%	4	10.50%	6	7.30%
Nablus	4	9.00%	4	10.50%	8	9.70%
Tulkarm	3	6.80%	1	2.60%	4	4.80%
Ramallah	5	11.30%	4	10.50%	9	11%
Jericho	0	0	1	2.60%	1	1.20%
Jerusalem	4	9.00%	6	15.70%	10	12%
Beithlehem	4	9.00%	3	7.90%	7	8.50%
Hebron	9	21%	10	26.30%	19	23%
Gaza	5	11.30%	1	2.60%	6	7.30%
Not Mentioned	8	18%	4	10.50%	12	14.60%

Table 4. Diagnoses of patients.

	2014			2015			2014-2015		
	Total (44 pts)	Males	Females	Total (38 pts)	Males	Females	Total (82 pts)	Males	Females
IPF	1 (2.27%)	1 (4.7%)	0	0	0	0	1 (1.2%)	1 (2.7%)	0
NSIP	6 (13.6%)	4 (19%)	2 (8.7%)	7 (18.4%)	3 (20%)	4 (17.3%)	13 (15.8%)	7 (19.4%)	6 (17.3%)
LIP	2 (4.5%)	0	2 (8.7%)	1 (2.6%)	0,00%	1 (4.3%)	3 (3.6%)	0	3 (6.5%)
DIP	0	0	0	1 (2.6%)	1 (6.6%)	0	1 (1.2%)	1 (2.7%)	0
Sarcoidosis	11 (25%)	7 (33.3%)	4 (17.3%)	11 (28.9%)	2 (13.3%)	9 (39%)	22 (26.8%)	9 (25%)	13 (28.2%)
Occupational lung disease	2 (4.5%)	2 (9.5%)	0	4 (10.5%)	4 (26.6%)	0	6 (7.3%)	6 (16.6%)	0
Drug induced lung disease	1 (2.27%)	0	1 (4.3%)	1 (2.6%)	0,00%	1 (4.3%)	2 (2.4%)	0	2 (4.3%)
AEP	0	0	0	1 (2.6%)	1 (6.6%)	0	1 (1.2%)	1 (2.7%)	0
Bronchiolitis	1 (2.27%)	0	1 (4.3%)	3 (7.9%)	1 (6.6%)	2 (8.7%)	4 (4.8%)	1 (2.7%)	3 (6.5%)
Vasculitis	2 (4.5%)	1 (4.7%)	1 (4.3%)	3 (7.9%)	1 (6.6%)	2 (8.7%)	5 (6%)	2 (5.5%)	3 (6.5%)
Alveolar proteinosis	4 (9%)	1 (4.7%)	3 (13%)	0	0	0	4 (4.8%)	1 (2.7%)	3 (6.5%)
HSP	2 (4.5%)	1 (4.7%)	1 (4.3%)	0	0	0	2 (2.4%)	1 (2.7%)	1 (2.1%)
BOOP	2 (4.5%)	0	2 (8.7%)	0	0	0	2 (2.4%)	0	2 (4.3%)
Aspiration pneumonia	2 (4.5%)	0	2 (8.7%)	0	0	0	2 (2.4%)	0	2 (4.3%)
Not diagnostic	8 (18%)	4 (19%)	4 (17.3%)	6 (15.8%)	2 (13.3%)	4 (17.3%)	14 (17%)	6 (16.6%)	8 (17.3%)

IPF, idiopathic pulmonary fibrosis; NSIP, non-specific interstitial pneumonia; LIP, lymphocytic interstitial pneumonia; DIP, desquamative interstitial pneumonia; AEP, acute eosinophilic pneumonia; HSP, hypersensitivity pneumonia; BOOP, bronchiolitis obliterans organising pneumonia.

dust. Most patients (89%) had bilateral interstitial infiltrates on imaging. Also the diagnostic yield of clinical-radiologic information combined with bronchscopic transbronchial procedures was excellent at 86%. These results were comparable to epidemiologic data from other Mediterranean and Middle Eastern countries.

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