A rare entity of interstitial lung disease, pleuropulmonary fibroelastosis: does it affect the chest wall geometry?

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Introduction Pleuropulmonary fibroelastosis (PPFE) is a rare type of interstitial lung disease (ILD); however, it may not be as rare as it was described. PPFE has been recognized increasingly worldwide during the past years.

Patients and methods The study was held in the Chest Department, Kasr Al-Ainy hospitals, during the period from January 2015 till June 2018. Seventy patients were included and divided into two main groups. Group 1 included 36 cases with PPFE, diagnosed either radiologically alone or combined with histopathological examination of lung biopsy. Group 2 included 34 cases of hypersensitivity pneumonitis (HP) as controls. Group 1 was further subdivided into two subgroups: group A included patients with 19 PPFE without any other pattern of ILD, and group B included 17 cases of PPFE associated with other forms of ILD. Clinical assessment, BMI, and high-resolution computed tomography chest were done. The inner anteroposterior diameter (APD) and transverse diameter (TD) of the chest wall were measured, and the ratio between them was calculated.

Results Significant female predominance was observed. Both groups of PPFE presented at earlier age than the HP group. Patients with PPFE had a lower body weight and BMI than HP group. There was a significant reduction in the APD and TD in both groups of PPFE than HP group.

Conclusion Thirty-six cases with PPFE presented either alone or in association with other forms of ILD. Significant reduction in their chest wall APD in comparison with TD was observed, giving a characteristic flat shape of the chest. Further evaluation of this phenomena and its explanation is required.

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Introduction

Pleuropulmonary fibroelastosis (PPFE) is classified under the title rare interstitial pneumonia in 2013 [1]. However, it was first described in the Japanese literature by Amitani *et al.* [2] under the name idiopathic pulmonary upper lobe fibrosis. However, it may not be as rare as it was described, and PPFE has been recognized increasingly worldwide during the past years [3]. It is mainly characterized by predominant upper lobe fibrosis [4]. PPFE could be classified into idiopathic type (no etiology encountered or underlying disease) or associated with other underlying disease [5].

Patients and methods

This is a prospective study held in the Chest Department, Kasr Al-Ainy hospitals in collaboration with Radiology Department during the period from January 2015 till June 2018.

Inclusion criteria

All ages and both sexes were included. High-resolution computed tomography (HRCT) could be performed.

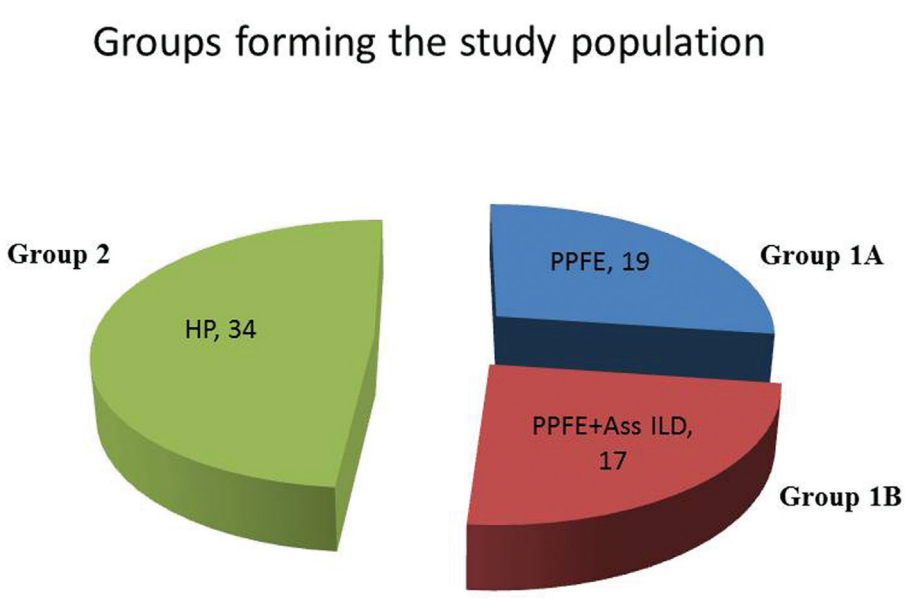
Exclusion criteria

HRCT could not be performed.

The study included three groups (Fig. 1): group 1 included 36 cases that presented to the diffuse parenchymal lung disease unit for assessment, and proved to have PPFE: 30 cases were diagnosed radiologically (definite disease fulfilling the criteria of the disease) and six cases by histopathological examination of lung biopsy for radiologically consistent cases done either surgically or by medical thoracoscopy. Group 1 is subdivided into two subgroups: group A included 19 cases diagnosed as having PPFE without any other pattern of interstitial lung disease (ILD), and group B included 17 cases presented by PPFE associated with other form of ILD [three cases were associated with nonspecific interstitial pneumonia and 14 cases associated with hypersensitivity pneumonitis (HP)]. Group 2 included 34 cases diagnosed with HP [6] as a control group. The control group was height matched.

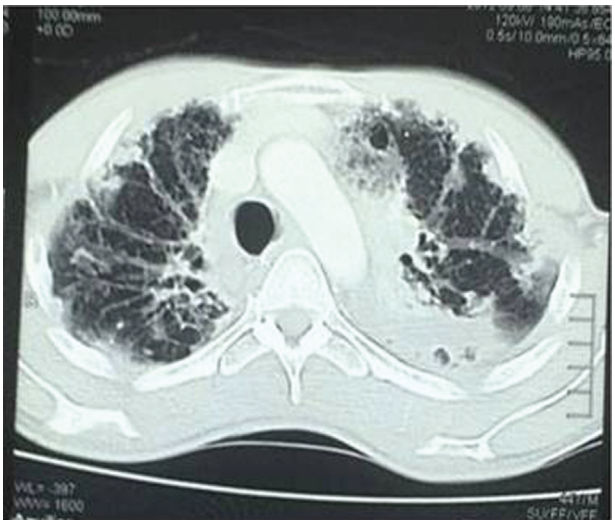
Thorough history taking, clinical examination, routine laboratory examinations, and HRCT chest were done

Figure 1



Groups forming the study population.

Figure 2



CT chest axial cuts showing classic picture of PPFE: upper lobe predominance, cervical pleura thickening, reticulations, and traction bronchiectasis. CT, computed tomography; PPFE, pleuropulmonary fibroelastosis.

to cases that formed the study population. Moreover, an informed written consent was obtained from all participating cases after ethical committee approval.

The inner anteroposterior diameter (APD) and transverse diameter (TD) of the chest wall were measured from the CT images at the level of the carina; moreover, the ratio (APD/TD) between these diameters was calculated for all cases [5].

The TD was defined as the longest transverse distance of the thoracic cage from the innermost of the ribs at the level of the carina in the axial cuts of the HRCT.

APD was determined as the longest longitudinal distance of the anteroposterior dimension of the thoracic cage measured perpendicular. In addition, TD and APD were also defined as the distances from the inside of a rib to the inside of the opposite rib. If anteroposterior diameter of the thoracic cage (APDT) in one hemithorax was different to the APDT in the other hemithorax, a mean value was calculated.

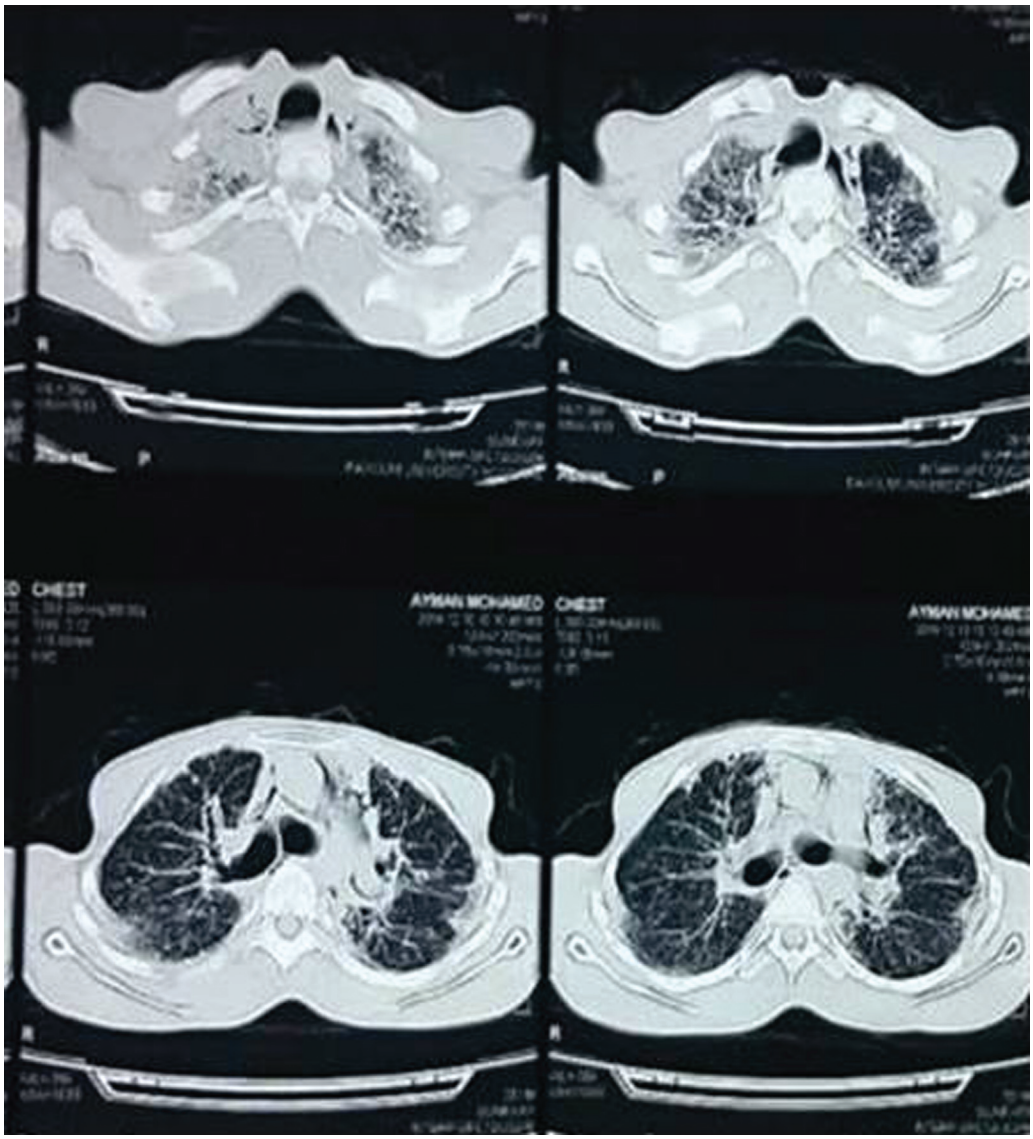
According to HRCT, the criteria [7] with which the diagnosis of PPFE depended upon included the following:

(1) Marked bilateral apical pleural thickening (Fig. 2).
(2) Bilateral irregular pleuroparenchymal thickening (Fig. 2).
(3) Upper and mid zonal distribution.
(4) Architectural distortion, associated with traction bronchiectasis, upper volume loss, or peripheral consolidation.
(5) Pneumothorax±pneumomediastinum (Figs 3 and 4).
(6) Reticular abnormalities, including thickening of interlobular septa (Figs 3 and 4).

Statistical analysis

Coding and data entering was done using the statistical package for the social sciences, version 25 (IBM Corporation, USA), and summarizing it using mean and SD for quantitative variables and frequencies (number of cases) and relative frequencies

Figure 3



CT chest axial cuts showing classic case of PPFE complicated with pneumomediastinum. CT, computed tomography; PPFE, pleuropulmonary fibroelastosis.

(percentages) for categorical variables. Groups were compared using unpaired *t* test when comparing two groups and analysis of variance with multiple comparisons post-hoc test when comparing more than two groups [8]. For comparing categorical data, χ^2 test was performed. Exact test was used instead when the expected frequency is less than 5 [9]. Correlations between quantitative variables were done using Pearson's correlation coefficient [10]. *P* values less than 0.05 were considered as statistically significant.

Results

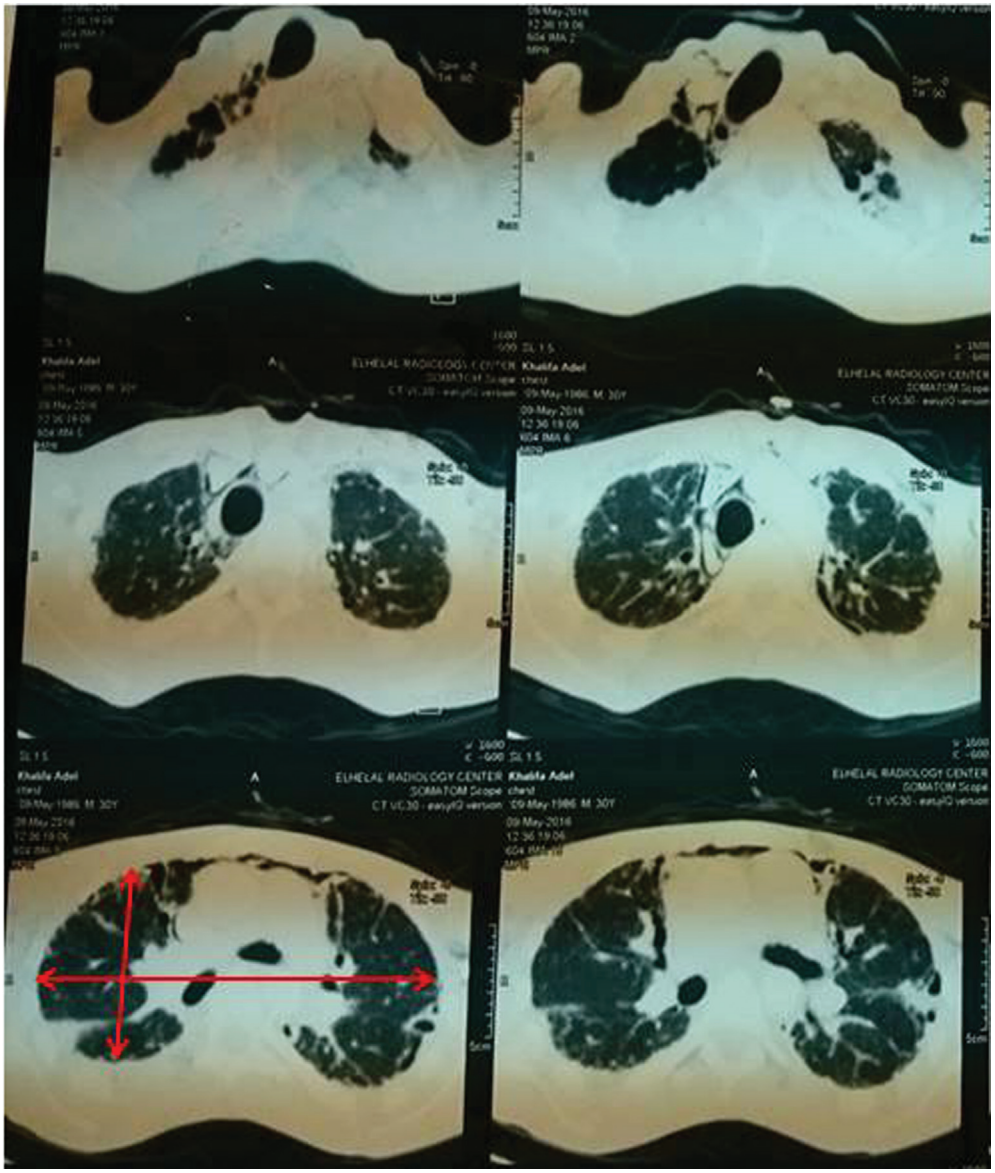
There was a statistically significant difference regarding sex distribution among different study groups, with *P* value 0.003 (Fig. 5).

The mean age was 34.68±14.09, 32.65±12.27, and 42.3 ±12.83 for PPFE, PPFE associated with ILD, and HP groups, respectively, showing statistical significance with *P* value 0.027. Both groups, PPFE and PPFE associated with ILD, presented at earlier age, as the mean decade was 3.84±1.42 and 3.76±1.25, whereas HP groups presented at higher decade, with mean±SD 4.94±1.27, with statistically significant difference, as *P* value was 0.003 (Table 1).

Moreover, the body weight and BMI (Fig. 6) were lower in patients with PPFE either alone or with associated ILD than the patients in the HP group, with statistical significance (*P* value 0.001) (Table 1).

There was a statistically significant difference regarding the measurements of the chest wall

Figure 4



CT chest axial cuts showing the way of anteroposterior and transverse diameter measurements. CT, computed tomography.

geometry. It was found that the APD and TDs were lower in patients with PPFE when presented with PPFE alone or even when associated with other forms of ILD in comparison with HP group (Table 1 and Fig. 7). Reduction in the APD was more significant than the TD in these patients, associated with significant reduction in the ratio between APD and TD.

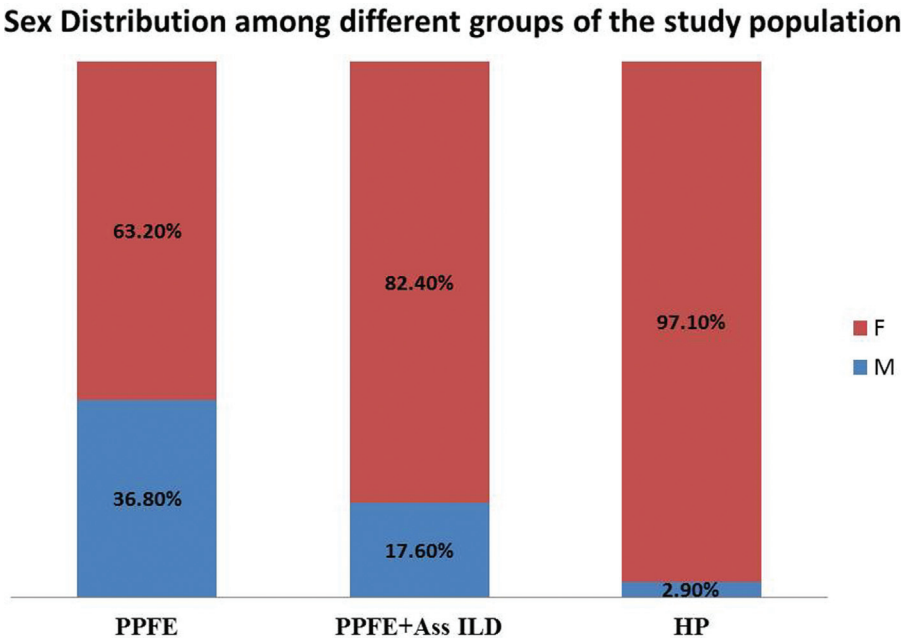
In the PPFE group, six cases presented with pneumomediastinum, one case with unilateral pneumothorax, and two cases with bilateral pneumothorax, whereas in the PPFE associated with ILD group, three cases presented with pneumomediastinum, two cases with unilateral pneumothorax, and two cases with bilateral pneumothorax (Table 2).

Discussion

The sex distribution among our study population was predominantly female, in HP group was 97.1%, in PPFE with associated ILD was 82.4%, and in PPFE group was 63.2%. However, some papers and case series published on PPFE had almost equal distribution among both sexes [11,12], with no sex predilection [13], whereas others had female predominance [14]; moreover, in HP, there was female predominance [15].

The mean decade of presentation for both groups PPFE and PPFE associated with ILD was 3.84 ±1.42 and 3.76±1.25, and this is consistent with the literature stating that most of the cases present at third and fourth decade of life. This may be attributed to hereditary or genetic factors [5]. Although HP groups presented at higher decade with mean±SD 4.94±1.27,

Figure 5



Sex distribution among the study population. ILD, interstitial lung disease; PPFE, pleuropulmonary fibroelastosis.

Table 1 Correlation between study population groups regarding demographics and chest wall measurements

	Groups						*P* value
	PPFE (*N*=19)		PPFE+associated ILD (*N*=17)		Controls (patients with HP no PPFE) (*N*=34)		
	Mean	SD	Mean	SD	Mean	SD	
Age	34.68	14.09	32.65	12.27	42.30	12.83	0.027
Decade	3.84	1.42	3.76	1.25	4.94	1.27	0.003
Weight	59.53	13.12	55.00	7.63	80.50	19.87	<0.001
Height	160.05	4.77	159.47	5.47	157.26	5.27	0.130
BMI	23.25	5.08	21.55	2.44	32.51	8.49	<0.001
APD	10.83	1.85	10.68	1.62	14.44	1.48	<0.001
Transverse diameter	19.84	1.96	20.47	1.56	21.10	1.44	0.029
AP/T ratio	0.55	0.08	0.52	0.07	0.69	0.06	<0.001

AP/T, anteroposterior/transverse diameter; APD, anteroposterior diameter; HP, hypersensitivity pneumonitis; ILD, interstitial lung disease; PPFE, pleuropulmonary fibroelastosis.

it is consistent with that of Indian registry where the mean±SD age was 56.4±13 years [16].

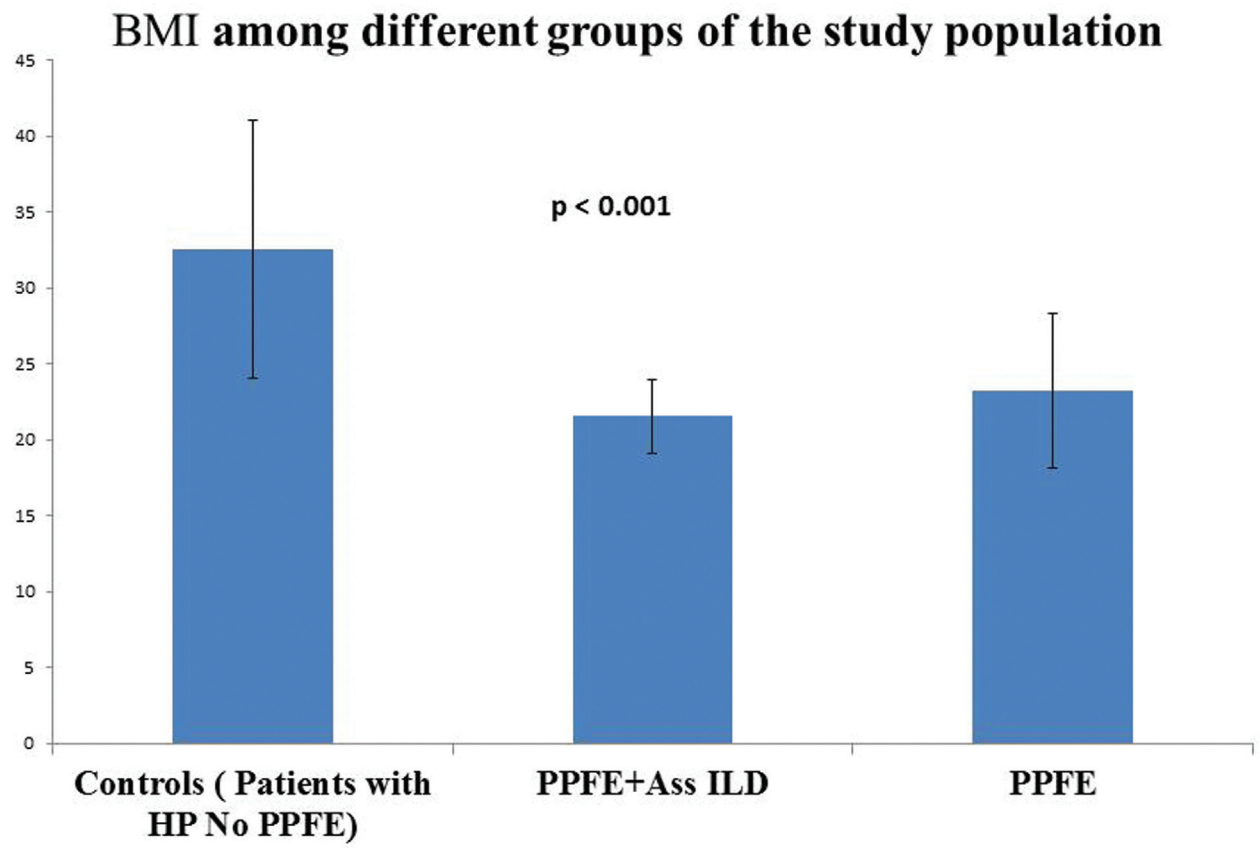
The BMI was 23.25±5.08 in PPFE group, 21.55±2.44 in the PPFE with associated ILD group, and both groups together was 22.45±4.1, which is near to that stated by Shioya *et al.* [12], which was 20.1±3.25. However, other studies had a lower BMI [14,17]. Although most cases of PPFE associated with ILD were presenting with HP, this did not lead to the increase of the ratio between the APD and TD (0.52 ±0.07). On the contrary, it was lower in this group followed by PPFE group (0.55±0.08) whereas that of HP group was 0.69±0.06. This could be explained by the elastic tissue deposition, which leads to this chest configuration or upper lobe shrinkage rather than the airway affection as a part of HP [5].

Moreover, the ratio between the APD and TD of both groups (PPFE and PPFE-associated ILD) was comparable to that described in literature [5,11,12].

In the PPFE group and PPFE associated with ILD, nine cases presented with pneumomediastinum, three cases with unilateral pneumothorax, and four cases with bilateral pneumothorax. It was almost the same as found by Shioya *et al.* [12] where 19 cases out of 29 had events in the form of pneumothorax or pneumomediastinum.

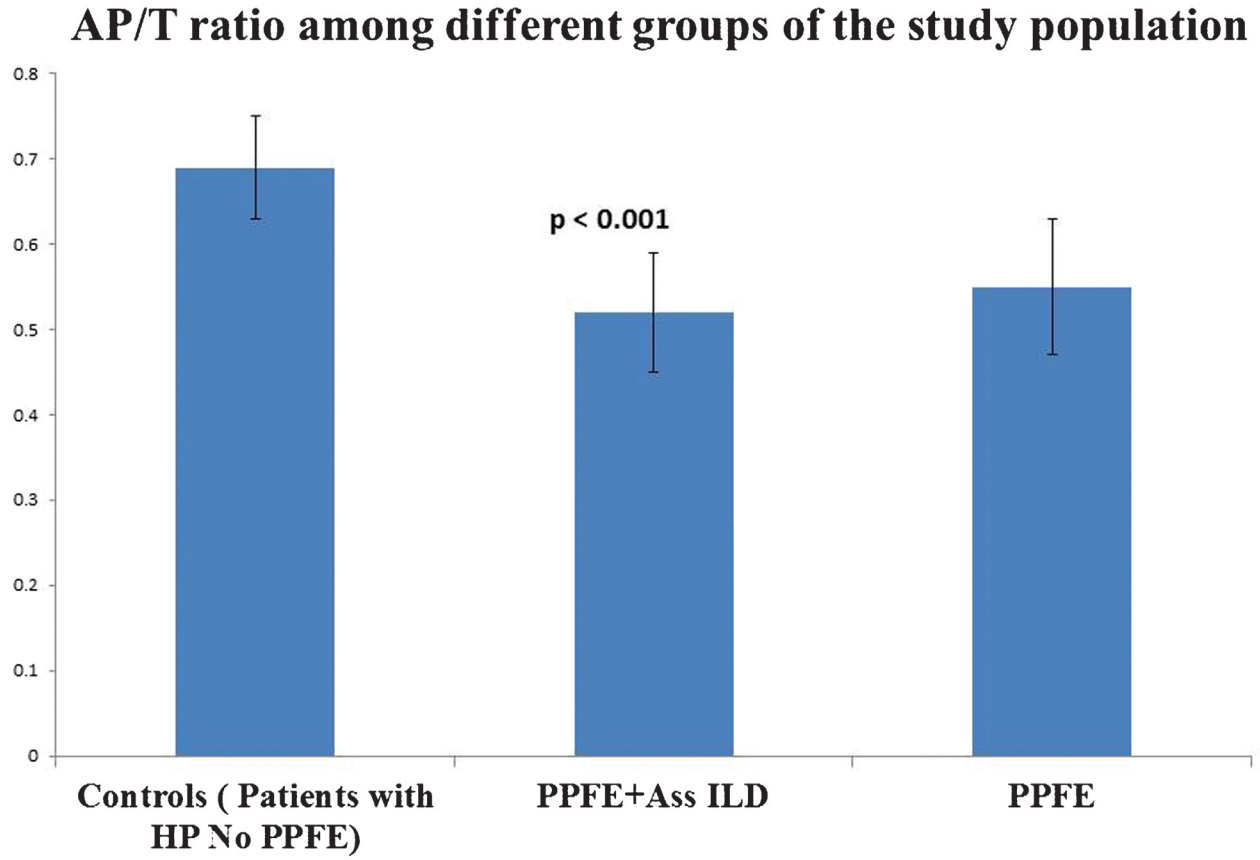
The small sample size owing to the rarity of the cases worldwide and that it is a single-center experience contributed to the study limitation. More attention and studies should be paid to this rare entity among different ILD.

Figure 6



BMI distribution among the study population. HP, hypersensitivity pneumonitis; PPFE, pleuropulmonary fibroelastosis.

Figure 7



APD/TD ratio. APD, anteroposterior diameter; TD, transverse diameter.

Table 2 Pneumothorax and pneumomediastinum among the pleuropulmonary fibroelastosis subgroups

	Groups				
	PPFE (*N*=19)		PPFE +associated ILD (*N*=17)		
	Count	%	Count	%	*P* value
Pneumomediastinum					
Yes	6	31.6	3	17.6	0.451
No	13	68.4	14	82.4	
Unilateral pneumothorax					
Yes	1	5.3	2	11.8	0.593
No	18	94.7	15	88.2	
Bilateral pneumothorax					
Yes	2	10.5	2	11.8	1
No	17	89.5	15	88.2	

ILD, interstitial lung disease; PPFE, pleuropulmonary fibroelastosis.

Conclusion

In conclusion, this study described 36 cases with PPFE, presented with radiological features of the disease, with or without its complications, particularly pneumothorax and/or pneumomediastinum. PPFE is more predominant in females and third decade of life. It has been observed that PPFE may develop either alone (idiopathic) or secondary to different forms of ILD especially HP, which takes the upper hand in our study. These patients were previously diagnosed and treated as idiopathic pulmonary fibrosis or even as pulmonary tuberculosis especially early in the disease when it affected mainly the upper lobes. PPFE may not be as rare as it was thought, and need to be considered when assessing a patient presenting with ILD. Research is still needed to reach the exact nature of PPFE and to answer the question whether it is confined to the lungs and pleura or it is a systemic disease.

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Conflicts of interest
There are no conflicts of interest.

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