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Proportion of occupational progressive fibrosing interstitial lung diseases in the tertiary hospitals of Thailand

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Abstract

Idiopathic pulmonary fibrosis (IPF)-the prototypical progressive fibrosing interstitial lung diseases (PF-ILDs)-is associated with occupational exposure. Other unidentified PF-ILDs may also be work-related. This study aimed to evaluate the magnitude of occupational related causes in unknown aetiology PF-ILDs. We conducted a descriptive study with a sample of 112 patients in two tertiary hospitals in Khon Kaen, Thailand, between 2016 and 2020. Descriptive statistics were used to analyse the findings. The response rate was 26.8% (30/112). Demographic data and clinical information were reviewed from medical records. Telephone interviews were used to explore occupational histories. A multi-disciplinary team (MDT) was held to reach a consensus on the final diagnosis of 8 participants who had significant exposure per their respective interview. The result demonstrated that 16.7% (5/30) of respondents were possible occupational related PF-ILDs and the majority (3/5) were due to metal dust exposure. The result is inconsistent with the occupational burden related to the IPF but resembles the proportion of occupational ILDs in USA and Europe. Moreover, we found that only 23.7% (7/30) had occupational histories taken by their treating physician. Therefore, a multi-disciplinary approach with an occupational physician in the team was used to precisely diagnose occupational related unknown ILDs.

Keywords: Occupational interstitial lung disease, Occupational exposure, Progressive fibrosing interstitial lung disease, Multidisciplinary team diagnosis

1. Introduction

Interstitial lung diseases (ILDs) comprise various lung conditions caused by injury to the lung interstitium. Most patients are asymptomatic, but patients may experience dyspnea, cough, and/or chest tightness after years of occasional acute inflammatory events. A previous study reported that 13-40% of ILDs were estimated to gradually develop scars in the lung parenchyma called progressive fibrosing interstitial lung diseases (PF-ILDs) [1]. Once lung scarring occurs, it is primarily irreversible and can cause diminishing lung function, impaired quality of life, and early mortality [2,3]. The ILD subtypes which are at risk of developing a progressive fibrosing phenotype comprise connective tissue disease-associated interstitial lung disease, sarcoidosis, hypersensitivity pneumonitis, exposure-related ILDs (e.g., asbestosis and complicated silicosis) and idiopathic interstitial pneumonia. Idiopathic pulmonary fibrosis (IPF) was regarded as a prototypical PF-ILDs. Previous studies have demonstrated evidence of an association between IPF and occupational exposure [4-8]. It is possible that other unknown causes of PF-ILDs may be a work-related disease as well.

Occupational exposure can be associated with various diffuse parenchymal lung diseases [9]. Accordingly, history-taking regarding job(s) and their respective hazards are essential. A high degree of suspicion in work-relatedness is the first step to the identification of occupational ILDs. However, since physicians lack knowledge on the relationship between disease and occupational exposure, under-reporting of occupational diseases is common. Multi-disciplinary team approaches—comprising occupational physicians, pulmonologists, radiologists, and pathologists—may help identify definite occupational ILDs [10-12].

Previous studies have presented evidence that the respective occupational burden of ILDs in the USA is 14% [13] and in Europe is about 4-18% [14]. As for IPFs, the evidence is around 26% of occupational relatedness [15]. Occupational parenchymal lung disease in Thailand has focused on pneumoconiosis, so valuable data of other ILDs is limited, especially in groups with unknown aetiology. Perhaps by understanding the magnitude of the problem and defining risky jobs would be beneficial for establishing proper prevention strategies for same exposure groups of employees. The current study aimed to evaluate the proportion of possible occupational related causes in patients with unknown PF-ILDs in tertiary hospitals of Khon Kaen, Thailand.

2. Material and methods

2.1 Study design

We conducted a descriptive study of two tertiary hospitals in Khon Kaen, Thailand.

2.2 Study population and sample

The study involved patients diagnosed with ICD-10 codes J84.1 (other interstitial pulmonary diseases with fibrosis) and J84.9 (interstitial pulmonary disease, unspecified). The patients were without underlying conditions affecting pulmonary fibrosis (i.e., connective tissue diseases, HIV, and/or active or old pulmonary tuberculosis) between January 2016 and December 2020. The total target population from the two tertiary hospitals in Khon Kaen was 262 patients. The study populations included participants (a) 20 years of age or over and (b) documented chest imaging using computed tomography techniques with evidence of interstitial lung abnormalities suggesting lung fibrosis confirmed by a thoracic radiologist. The exclusion criteria were (a) any history of using drug(s) associated causing pulmonary fibrosis documented at www.pneumotox.com (b) inability to communicate due to medical or psychological conditions (e.g., hearing loss). The study population comprised 112 unknown aetiology PF-ILDs patients. The sample size was calculated using the Windows Program for Epidemiologists (WINPEPI) version 11.65. The applied formula was based on estimating a proportion with following indicators: a confidence level of 95%, a precision of 0.05, assumed proportion of occupational ILDs from previous studies [13-15] at 20%, and size of population as 112 participants. Based on this formula, the required sample size was 72 participants (Figure 1). We then adjusted the sample size for an estimated 15% data loss, so all eligible 112 study populations were included in the sample. The response rate to the posted letters of consent was 26.8% (30/112) (Figure 1). The 82 non-respondents comprised 43 males and 39 females (Figure 1).

2.3 Data collection

After ethical approval, we sent a letter to both hospital directors requesting permission to access the electronic database and paper records. Addresses of participants were retrieved first. A clarification form and informed consent form were sent to each potential participant. We asked if they would complete the informed consent and requested their call-back information and the best time for a call. Respondents were asked to return the forms by post to the researcher by a set date. An occupational medicine resident interviewed participants by telephone within a week of receiving the consent letter. The resident was trained and experienced in occupational history taking.

The telephone interview was used to collect the following data: working status, started working age, full retirement age, job(s) ever held, job description(s), and history of occupational and environmental dust exposure. The latter included related processes, frequency of exposure, and duration of exposure.

Clinical information was gained from hospital medical records. The following data were reviewed: (a) demographics (age at diagnosis, sex, and smoking status) (b) presenting signs and symptoms (c) lung function (forced expiratory volume in 1 sec (FEV1), forced vital capacity (FVC) and FEV1/FVC ratio) (d) result of bronchoalveolar lavage fluid (e) the chest CT appearance and (f) occupational history recorded by a treating physician.

A multi-disciplinary team (MDT) consensus meeting was convened to confirm occupational related PF-ILDs diagnosis.

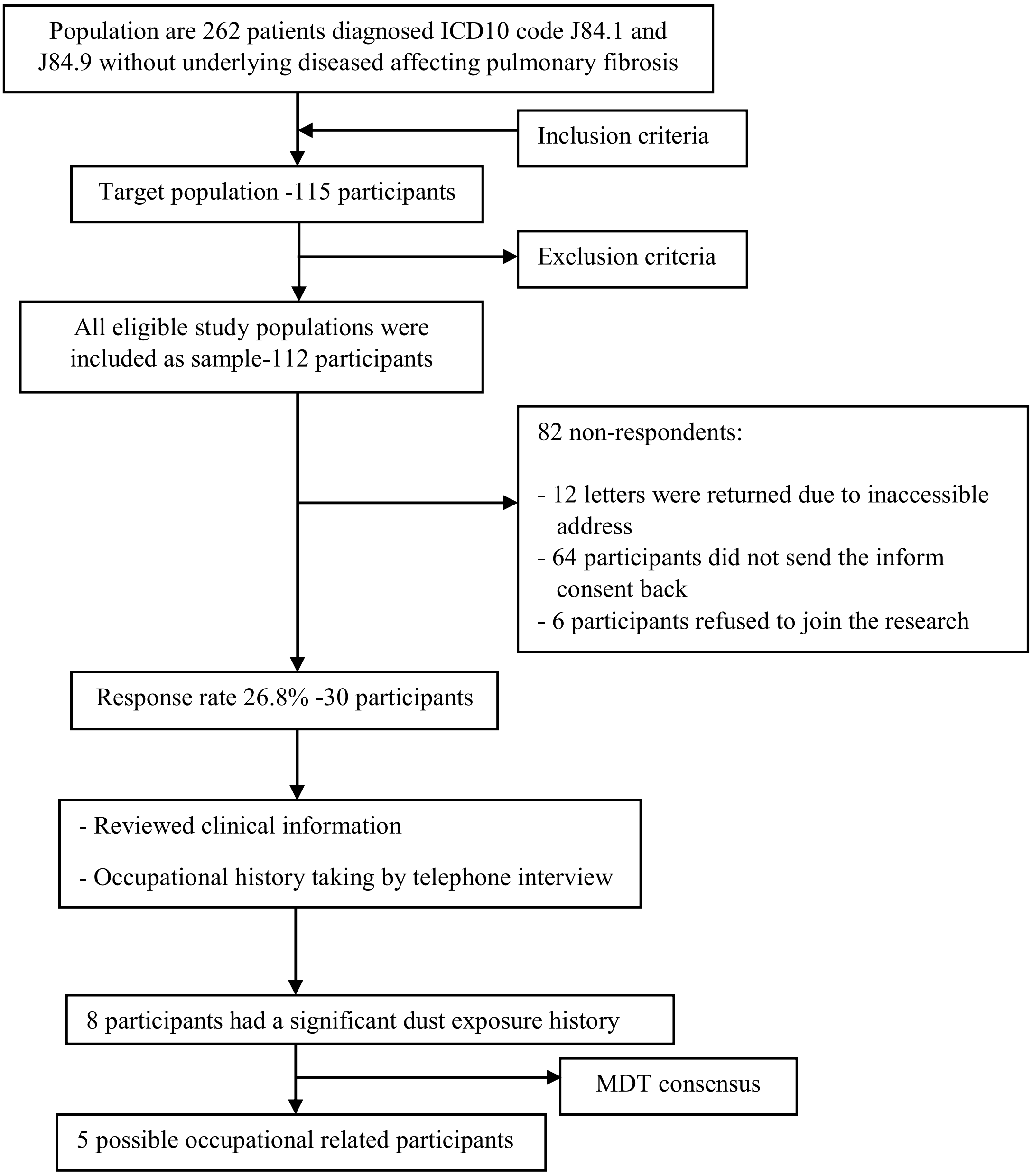

Figure 1 Sample and result.

2.4 Multi-disciplinary team consensus

In the current study, the evaluation of participants took place in two steps. The first step aimed to confirm the diagnosis of fibrotic ILDs and identify participants who had significant occupational exposure, which could cause the disease. The second step was the multi-disciplinary discussion. Researchers reviewed all of the retrieved clinical information from the medical database, including age, sex, smoking habit, underlying diseases, family history, drug intake, and respiratory and other related systemic symptoms as well as those suggestive of connective tissue diseases. If available, the MDT also reviewed any related investigation(s) such as lung function test, chest CT images, autoimmune profile, and BAL. In addition, the occupational history of the participants throughout their life was explored during the telephone interview. We defined significant occupational exposure if there were any history of 1) exposure to metal dust causing lung fibrosis [16] more than 1.1 work years (estimated 2600 h of working hours) [6]; 2) exposure to organic dust as well as wood dust more than 10 h per week continuedly 5 years [4]; or, 3) exposure to mineral dust (e.g., silica and asbestos) more than 10 h per week continually for 5 years [4]. Participants who had significant occupational exposure would be selected for the second step, the multi-disciplinary team discussion.

The multi-disciplinary team on the diagnosis of occupational related PF-ILDs comprised two occupational physicians, a pulmonologist and a thoracic radiologist. The MDT synthesised all the information to confirm a diagnosis. The diagnosis was categorised into three groups depending on the degree of confidence in the diagnosis: "Definite" ≥ 90% diagnostic confidence having compatible history, CT features, and suggestive laboratory test; "Possible" 50-89% diagnostic confidence, having evidence of history and CT appearance with more likely compatible but without histological test confirmation; and, "Unclassifiable" if the percentage of confidence was < 50%.

2.5 Data analysis

Descriptive statistics, including frequencies, percentages, and 95% confident interval (95% CI), were used to analyse the data. All analyses were performed using SPSS version 26.0 (IBM SPSS Inc, Chicago, IL, USA).

3. Results

The response rate was 26.8% (30/112). The majority of participants were female (56.7%). The mean age was 68.5 years (SD = 8.1; range 48-83). Hypertension was the most common underlying disease (64.7%), followed by diabetes mellitus and dyslipidaemia, respectively. Most of the participants who had a family history related to lung diseases had non-infectious pulmonary diseases. Most of the participants never smoked, but half of the non-smokers had a history of second-hand smoke. Almost one-fourth had a history of traditional charcoal making for household use but usually less than 5 years (Table 1).

Table 1 General characteristics of participants. (n=30).

Characteristic	n	%
Sex		
Male	13	43.3
female	17	56.7
Underlying diseases	17	56.7
Hypertension	11	64.7
Diabetes mellitus	4	23.5
DLP	3	17.6
Hyperthyroidism	2	11.8
Asthma	2	11.8
COPD	2	11.8
Others	4	23.5
Family history of lung diseases	6	20.0
Pulmonary tuberculosis	1	16.7
Asthma	2	33.3
COPD	2	33.3
Lung cancer	1	16.7
Smoking habit		
Never smoked	16	53.3
Current smoker	1	3.3
Ex-smoker	13	43.4
History of second-hand smoker	8	26.7
History of traditional charcoal making	7	23.3
Less than 5 years	5	71.4
More than 5 years	2	28.6
Mean age (SD)	68.5 (8.1)	

A physician took the occupational history for a few of the participants (23.3%; 7/30). Typically, work history recorded only one job title. Half of the participants had undergone spirometry which mainly indicated a restrictive pattern (26.6%). A small number of participants had undergone bronchoscopy and BAL for histological study. The proportion of participants who had HRCT was greater than those done chest CT (Table 2).

Table 2 Data obtained from medical records. (n=30).

Item	n	%
Occupational history recorded by treating physicians		
One job title	5	16.7
More than one job with job description	2	6.7
No	19	63.3
Missing data	4	13.3
Pulmonary function test		
Restrictive pattern	8	26.6
Obstructive pattern	3	10.0
Mixed pattern	2	6.7
Normal	2	6.7
Not done	15	50.0
Bronchoscopy		
BAL	8	26.7
Not done	22	73.3
Imagine modality (n=30)		
HRCT	21	70.0
Chest CT	9	30.0

One-third of the participants reported that they were presently working. The estimated age for starting work was around 18 years of age (mean = 17.9, SD = 3.6; range 12-24), and participants retired at age around 62 (Mean = 61.9, SD = 4.0; range 53-68). Throughout all participants' lifetime, most had more than one occupation (63.3%). Extra jobs were regularly related to animal raising. The longest-held occupation each participant ever did was mostly agricultural-related occupations. According to the interview, eight participants were identified with a significant dust exposure history (Table 3).

Table 3 Occupational history obtained from telephone interview. (n=30).

Item	n	%
Work status		
Working	10	33.3
Retired	20	66.7
Occupation(s) in lifetime		
One Occupation	11	36.7
Two Occupations	16	53.3
Three Occupations or more	3	10.0
Extra job		
Poultry raising	4	13.4
Hog raising	1	3.3
Street food selling	1	3.3
None	24	80.0
Longest-held occupation classified by major group of ISCO-08		
Group 1 - managers	1	3.3
Group 2 - professionals	4	13.3
Group 3 - technicians and associate professionals	0	0
Group 4 - clerical support workers	0	0
Group 5 - services and sale workers	2	6.7
Group 6 - skilled agricultural, forestry and fishery workers	15	50.0
Group 7 - craft and related trades workers	1	3.3
Group 8 - plant and machine operators and assemblers	3	10.0
Group 9 - elementary occupations	2	6.7
Group 0 - armed forces occupation	2	6.7
Significant dust exposure history		
Yes	8	26.7
No	22	73.3
Mean age starting work (SD)	17.9 (3.6)	
Mean age of retirement (SD)	61.9 (4.0)	
Mean years of the longest-held occupation (SD)	36.9 (10.7)	

According to the multi-disciplinary team discussion, most of the participants who were diagnosed as possible occupational related PF-ILDs were male and used to smoke. The majority experienced metal dust exposure. All participants experienced cough, and some who had chest CT abnormalities in more than 10% of total lung involvement developed dyspnea. All metal dust-related participants had traction bronchiectasis in their chest CT features. Nonspecific interstitial pneumonia (NSIP) feature was found in the chest CT of participants exposed to organic and inorganic dust. Almost all occupational related cases (4/5) had pulmonary lesions distributed in both lower lungs (Table 4).

Table 4 Participants diagnosed as possible occupational related causes. (n=5).

No	Sex	Age	Smoking habit	Possible job	Occupational dust	Job description	Years of exposure	Clinical presentation	Chest CT		
									Features	Distribution	Total of lung involvement
1	male	59	ex-smoker	artillery soldier	metal dust	firing and cleaning artillery 1-2 hours per day	32	productive cough and dyspnea	traction bronchiectasis, reticulation, centrilobular nodules, mild ground glass opacities	upper and middle both lungs	10-20%
2	female	55	never	production worker in firework factory	metal dust	mixing of raw material such as aluminium powder 3-4 hours per day	12	productive cough	traction bronchiectasis, centrilobular nodules	middle and lower both lungs	10-20%
3	male	81	ex-smoker	welder	metal dust and fume	cutting and welding alloy 1-3 hours per day	18	productive cough	traction bronchiectasis	lower both lungs	<10%
4	female	63	never	rice milling worker	organic dust	pouring rice grain to grading machine and cleaning rice chuff in working environment 6-8 hours per day	20	progressive dyspnea and dry cough	NSIP	lower both lungs	10-20%
5	male	66	ex-smoker	constructi on worker	inorganic dust	demolish buildings, roofing, flooring and tiling 7-9 hours per day	20	dyspnea and productive cough	NSIP	lower both lungs	>20%

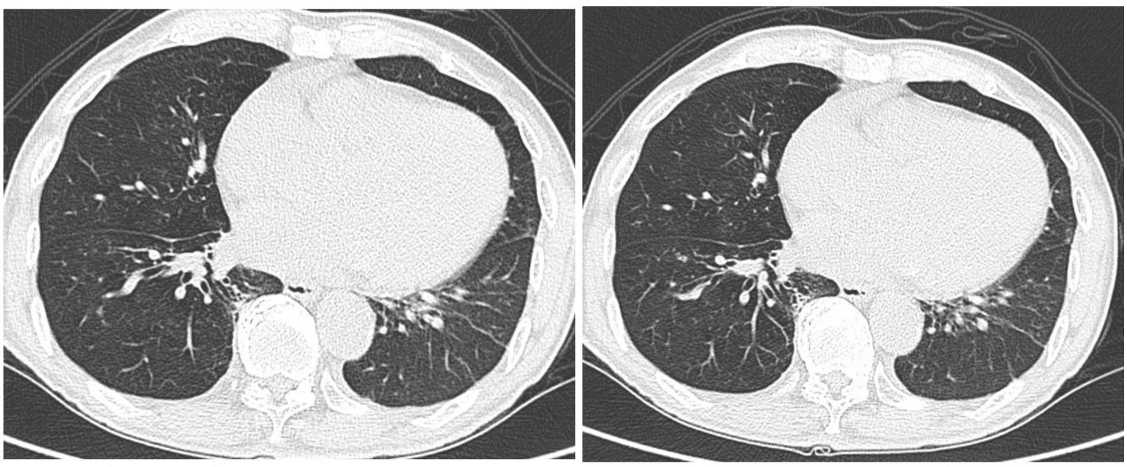

Figure 2 Axial chest computed tomography (CT) of participant No.3—an 81-year-old male who used to work as a welder and considered exposed to metal dust. Lesions predominate in both lower lobes and consist of traction bronchiectasis.

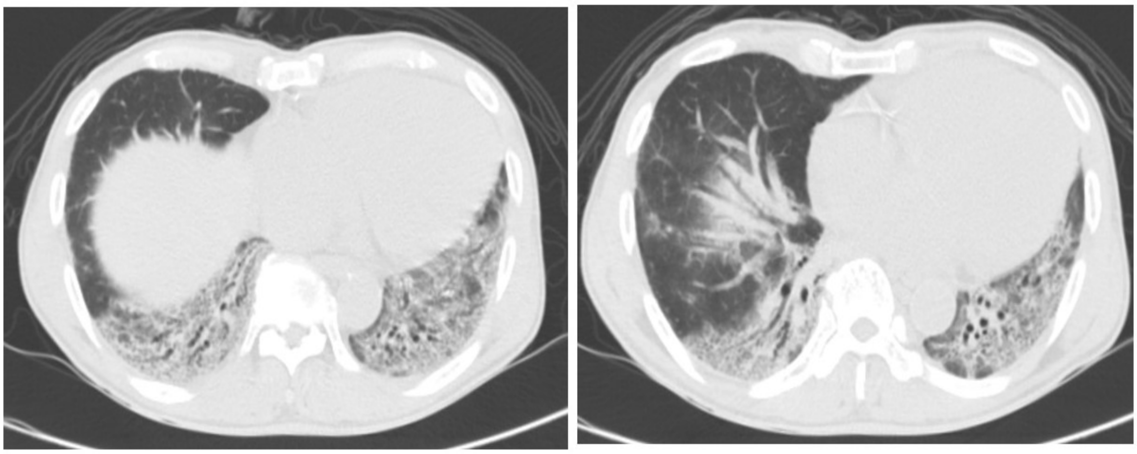

Figure 3 Axial chest CT demonstrates a pattern suggestive of nonspecific interstitial pneumonia (NSIP) in participant No.5—a 66-year-old male with history of exposure to inorganic dust (suspected silica and asbestos) while working in construction for about 20 years.

4. Discussion

The study summarises the proportion of patients (16.7%) diagnosed as possible occupational related PF-ILDs in 30 participants from two tertiary hospitals in Khon Kaen, Thailand. A previous study argued that multi-disciplinary discussions are an essential process for assuring the accuracy of interstitial lung disease diagnosis [11]. We, thus, held MDT consensus discussion in order to reach a consensus diagnosis. The MDT discussed the clinical information of the eight participants with a significant dust exposure history. The two occupational physicians in the MDT played roles in exploring the participants' occupational history, a chronology of all jobs, job description, job hazards, specific symptoms during and after exposure to specific dust, fumes, chemical substances, and similar illness among co-workers. A pulmonologist then reviewed the clinical manifestations, pulmonary function tests, and associated laboratory investigations. All of the selected participants had assessable radiography images—six had HRCT, and two had chest CT. A thoracic radiologist reviewed all computed radiography, and the results classified according to the AST/ERS/JRS/ALAT guidelines [17] vis-à-vis UIP pattern, probable UIP, and inconsistent with UIP patterns. This MDT did not include any pathologist as there was just one case that had undergone bronchoscopy to evaluate pulmonary histology. In conclusion, no case was diagnosed as a definite case since there was inadequate pathological or histological confirmation. Besides, five cases were diagnosed as possible occupational related PF-ILDs; however, three of the eight cases were diagnosed as unclassifiable because the CT showed evidence of intrathoracic esophageal dilatation, which suggested an association with systemic sclerosis [18].

The study revealed five participants from two different tertiary hospitals in Khon Kaen, Thailand who could be identified as possible occupational related cases. Most of these participants (3/5) had a history of metal dust exposure. Similarly, many prior studies identified a strong association between metal dust and idiopathic pulmonary fibrosis, the prototype disease of PF-ILDs [4,6,19-21]. Chest CT features of participants with metal dust exposure in the current study presented non-specific features classified by a thoracic radiologist as inconsistent with UIP patterns (Figure 2). All three participants had traction bronchiectasis in chest CT, which can happen after hard metal exposure, as indicated in prior studies where a radiologic pattern of parenchymal abnormalities in hard metal ILDs has bilateral ground-glass opacities, reticulation, and in advanced disease, parenchymal distortion and traction bronchiectasis [22,23]. As for other possible occupational related cases, one of them was exposed to rice grain and rice chuff in a rice milling factory, which can be described as organic dust. Previous evidence suggests that rice milling's grinding process can produce respirable particles [24], which may cause chronic inflammation in the lungs and eventually fibrotic hypersensitivity pneumonitis. This participant's CT chest revealed NSIP, which is compatible with the radiographic features of chronic hypersensitivity pneumonitis [25]. The last case was a male construction worker who was exposed to silica and asbestos (Figure 3). In Thailand, occupational exposure to asbestos typically occurs in workers during the manufacturing of asbestos-containing products i.e., roof tile and cement pipe. Besides that, asbestos exposure occurs during working with asbestos and coping with asbestos products being breaking such as demolishing buildings. Owing to the long duration of exposure, the chest CT abnormalities presented more than 20% of total lung involvement, and features showed an NSIP appearance associated with a history of exposure to mineral dust and more likely to asbestos [23,25].

The proportion of possible occupational related unknown PF-ILDs in the current study was 16.7% (95% CI: 7.3-33.6), which is quite low; perhaps because some respondents tended to overlook previous occupational exposure, particularly when the exposure was a long time ago. Since there was no prior report on the prevalence of ILDs and occupational ILDs in Thailand, we compared our outcome with previous existing studies from western countries. The result was similar to the prevalence of occupational causes in ILDs in the USA [13] and Europe [14]. Nonetheless, it is lower than a previous study suggesting that occupation has a population-based attributable fraction for IPF of about 26% [15]. Previous research investigated the association between occupational exposure and IPF by using a case-control study. By comparison, our study identified occupational causes through a MDT discussion which might have increased the precision of diagnosis since this method is one of the best ways to identify the causes of ILDs.

The current study demonstrated that only 23.3% (7/30) of participants had an occupational history taken by their treating physician. This low proportion is like previous studies [26,27]. The reason might be that physicians were not trained in occupational history taking [28] or had insufficient awareness of occupational related conditions. Thus, improving physician skill [29, 30] and developing assistive tools for exploring occupational histories would help find work-related lung diseases.

The study had some limitations (a) it had a small sample size, and (b) lacked pathological data and a contribution by a pathologist in MDT so that definite diagnoses of occupational PF-ILDs could not be confirmed. A more extensive study with more detail on the histological aspects of disease should be done to assess the real impact of occupation on developing unknown aetiology of PF-ILDs as well as other ILDs.

5. Conclusion

Among previously thirty unknown PF-ILDs patients, the proportion of possible occupational related patients at two tertiary hospitals in Khon Kaen, Thailand, was 16.7%. Therefore, a multi-disciplinary approach with an occupational physician in the team is suggested for precisely diagnosis occupational related unknown ILDs. Increasing documented occupational ILDs will promote proper prevention strategies and monitoring of health effects among co-workers who have similar job and exposure histories.

6. Ethical approval

The study was conducted according to the guidelines of the Declaration of Helsinki and approved by Khon Kaen University Ethics Committee for Human Research (KKUEC) of the Faculty of Medicine, Khon Kaen University, Thailand with series number HE631048 in 7th April 2020. and Khon Kaen Hospital Institutional Review Board (IRB) in Human Research with series number KEF63037 in 21st October 2020.

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