Prevalence of Significant Pulmonary Diseases in Chinese Adult Patients Presenting with Persistent Cough in Primary Care in Hong Kong-A Pilot Study

Hong Kiu Queenie Wong*, Pang Fai Chan and Kit Ping Loretta Lai

Department of Family Medicine and Primary Health Care, The University of Hong Kong, Hong Kong, China

Abstract

Objectives: To evaluate the prevalence of significant pulmonary diseases among Chinese adult patients presenting with persistent cough lasting for 3 weeks or more in primary care in Hong Kong.

Methods: Based on the data generated from the hospital authority clinical data analysis and reporting system, 880 Chinese adult patients who presented with cough as the predominant symptom lasting for 3 weeks or more in two general out-patient clinics in Hong Kong from 1st January 2017 to 31st December 2017 were included in this study. We have evaluated the prevalence of significant pulmonary diseases including lung cancer, non-tuberculosis pneumonia, pulmonary tuberculosis, asthma, bronchiectasis, chronic obstructive pulmonary disease and interstitial lung diseases among the subjects. The proportions of positive pulmonary investigation findings arranged in the study sites and the associated factors for significant pulmonary diseases were also analysed.

Results: The prevalence of significant pulmonary diseases among the studied subjects was 19.2% (169/880). The proportions of positive investigation findings among those with investigations done were 32.0%, 24.7%, 6.2% and 36.7% for chest radiograph, sputum for bacterial culture, sputum for acid-fast bacilli culture and spirometry respectively. The presence of red flag symptoms (OR 3.01, $p<0.001$), history of other chronic lung diseases (OR 6.82, $p<0.001$) and older age (OR 1.02, $p=0.010$) had strong associations with significant pulmonary diseases.

Conclusion: One fifth of the studied subjects had significant pulmonary diseases. Comprehensive clinical evaluation was warranted in these patients for timely detection and intervention of underlying significant pulmonary diseases.

Keywords: Pulmonary diseases; Subacute cough; Chronic cough; Primary care; Asthma; Chronic obstructive pulmonary disease; Bronchiectasis, Pneumonia; Pulmonary tuberculosis; Lung cancer

For the evaluation of patients with subacute cough, the American College of Chest Physicians (ACCP) guidelines recommend to first determine whether it is a post infectious cough (e.g. pneumonia, acute bronchitis or tuberculosis), a new onset or exacerbation of pre-existing conditions (e.g. asthma, chronic bronchitis, upper airway cough syndrome and GERD) or a non-infectious cough. According to the American thoracic society and the Infectious Diseases Society of America (IDSA) guidelines, chest radiography is required as a routine evaluation for the diagnosis of community acquired pneumonia [18]. Although sputum for bacterial culture is optional for patients who are being managed as outpatients, obtaining sputum for culture can optimize the selection of an appropriate antibiotic [19]. For patients presented with chronic cough, both the British Thoracic Society (BTS) and ACCP guidelines suggest chest radiography and spirometry as initial investigations. Sputum smears and cultures for Acid Fast Bacilli (AFB) should be obtained for patients who live in areas with a high prevalence of pulmonary tuberculosis. If the initial investigations are normal, referral to a specialist centre for further evaluations such as bronchoscopy and high resolution computed tomography of the thorax is indicated.

Studies have consistently shown that smoking is the most important risk factor for significant respiratory tract disorders including lung cancer, COPD, pulmonary tuberculosis, pneumonia, ILD and other chronic lung diseases [20-23]. Alcoholism increases the risk of community acquired pneumonia and pulmonary tuberculosis but whether alcohol consumption increases the risk of lung cancer remains controversial [24]. Older age was shown to be a risk factor of significant pulmonary diseases in patients with chronic cough, in particular pneumonia, pulmonary tuberculosis and ILD [25]. Female has increased risk for asthma whereas male gender has increased risk for pulmonary tuberculosis and ILD [26]. Socioeconomic status is inversely related to the risks of developing COPD and pulmonary tuberculosis [27]. Patients with neurological disorders (*i.e.* stroke, dementia, age P ı ulmona x [M in t`a f
p p' pa1 p M0]

respiratory causes with the diagnoses documented. The identified significant pulmonary diseases would be further categorized into newly diagnosed or exacerbation of underlying chronic lung diseases. For patients with no diagnosis established, their outcomes would also be recorded.

The findings of investigations arranged in both primary and secondary care would be reviewed for the establishment of diagnosis. Non-tuberculosis pneumonia was diagnosed when the clinical or investigations findings were suggestive of chest infection. Patients with chest radiographs showing infective changes along with positive sputum culture for non-tuberculous mycobacteria were also classified as non-tuberculosis pneumonia. Patients with positive sputum culture for mycobacterium tuberculosis were diagnosed with pulmonary tuberculosis. The diagnoses of COPD needed to be confirmed by spirometry whereas bronchiectasis and ILD by computed tomography of the thorax [35,36]. Asthma was diagnosed when patients exhibit respiratory symptoms consistent with asthma combined with confirmative spirometry findings [37]. The diagnosis of lung cancer was established by histopathology or imaging studies in patients who refused invasive investigations.

Positive chest radiography findings were defined as chest radiographs suggestive of any of the following conditions: Active pulmonary tuberculosis, pneumonia, emphysema, bronchiectasis, lung cancer or other new onset lung diseases as reported by the radiologists. Positive sputum culture results were defined as a positive growth of bacteria. Positive spirometry results were those demonstrating an obstructive pattern, defined as post bronchodilator Forced Expiratory Volume in one second (FEV_1)/Forced Vital Capacity (FVC) ratio smaller than 0.70 with or without bronchodilator reversibility or a restrictive pattern, defined as FEV_1/FVC ratio equals to or greater than 0.70 and FVC less than 80% predicted.

Outcomes

Primary outcome was the prevalence of significant pulmonary diseases including lung cancer, non-tuberculosis pneumonia, pulmonary tuberculosis, asthma, bronchiectasis, chronic obstructive pulmonary disease and interstitial lung diseases among Chinese adult patients presenting with persistent cough lasting 3 weeks or more in the two GOPCs. Secondary outcomes were the proportions of patients with positive pulmonary investigation findings, namely chest radiograph, sputum for bacterial and AFB culture and spirometry arranged in the study sites and the associated factors for significant pulmonary diseases.

Sample size calculation

The prevalence of significant pulmonary diseases among Chinese adult patients with persistent cough in primary care was lacking both locally and internationally. Hence, we opted to employ the data from a multicenter survey published in China in 2013 where the population was ethnically similar to our population though the study was carried

chronic lung diseases in which near half of the patients had asthma (4.5%).

	Mean 61.1 (SD 13.5)	**Number (%)**
Age (years)		
<30		26 (2.9)
30-39		37 (4.2)
40-49		82 (9.3)
50-59		227 (25.8)
60-69		297 (33.8)
70-79		139 (15.8)
≥ 80		72 (8.2)
Sex		
Male		363 (41.2)
Female		517 (58.8)
Duration of cough (weeks)	**Median 4**	
3-7 (sub-acute)		551 (62.6)
≥ 8 (chronic)		329 (37.4)
Smoking status		
Non smoker		679 (77.2)
Ex-smoker		106 (12)
Current smoker		92 (10.5)
Unknown		3 (0.3)
Drinking status		
Non-drinker		737 (83.8)
Ex-drinker		6 (0.7)
Social drinker		82 (9.3)
Chronic drinker		23 (2.6)
Unknown		32 (3.6)
Socioeconomic status		
Not on CSSA		752 (85.5)
On CSSA		125 (14.2)
Unknown		3 (0.3)
Presence of red flag symptoms		
Yes		201 (22.8)
Haemoptysis		60 (6.8)
Shortness of breath		80 (9.1)
Fever		51 (5.8)

Weight loss		37 (4.2)
No		674 (76.6)
Not documented		5 (0.6)
History of chronic lung disease		
Yes		85 (9.7)
Asthma		40 (4.6)
Bronchiectasis		13 (1.5)
COPD		8 (0.9)
Lung cancer		3 (0.3)
ILD (Pneumoconiosis)		1 (0.1)
Pulmonary fibrosis		2 (0.2)
Pulmonary tuberculosis		18 (2.1)
No		795 (0.3)
History of chronic kidney disease		
Yes		51 (5.8)
No		829 (94.2)
History of chronic liver disease		
Yes		48 (5.5)
No		832 (94.5)
History of diabetes		
Yes		138 (15.7)
No		742 (84.3)
History of malignancy		
Yes		60 (6.8)
No		820 (93.2)
History of neurological disease		
Yes		39 (4.4)
No		841 (95.6)
Note: CSSA: Comprehensive Social Security Allowance, COPD: Chronic Obstructive Pulmonary Disease, ILD: Interstitial Lung Diseases		

Prevalence of significant pulmonary diseases and other conditions

169 (19.2%) patients with persistent cough lasting 3 weeks or more were found to have significant pulmonary diseases in which 16.1% were newly diagnosed. The majority of patients were diagnosed with non-tuberculosis pneumonia (10.8%). The prevalence of asthma, bronchiectasis, COPD and ILD (pneumoconiosis) was 3.3%, 2.2%, 1.9% and 0.1% respectively. 0.3% of our patients were confirmed to have pulmonary tuberculosis and 0.6% was diagnosed to have lung cancer (Table 2).

About one fourth (22.2%) of patients was clinically diagnosed to have other pulmonary diseases in which most of them were diagnosed with bronchitis (12.3%) followed by post viral cough (6.5%). 2.4% had abnormal chest radiograph undergoing work up in secondary care. Non respiratory causes were clinically diagnosed in 15.9% patients and most of them were diagnosed with allergic rhinitis with post nasal drip (9.8%). 42.7% (376) of patients had no diagnosis established in which majority (32.0%) had their cough subsided during the review period.

Diagnosis	No. of patients (%)
Significant pulmonary diseases	169 (19.2)
Newly diagnosed significant pulmonary diseases	142 (16.1)
Non tuberculosis pneumonia	95 (10.8)
COPD	16 (1.8)
Bronchiectasis	12 (1.4)
Asthma	11 (1.2)
Lung cancer	5 (0.6)
Pulmonary tuberculosis	3 (0.3)
Exacerbation of underlying chronic lung diseases	27 (3.1)
Asthma	18 (2.1)
Bronchiectasis	7 (0.8)
COPD	1 (0.1)
ILD (Pneumoconiosis)	1 (0.1)
Other pulmonary diseases	195 (22.2)
Bronchitis	108 (12.3)
Post viral cough	57 (6.5)
Allergic airways	4 (0.5)
Post pneumonia cough	3 (0.3)
Smoker’s cough	2 (0.2)
Lung opacity on chest radiograph[#]	14 (1.6)
Lung nodule on chest radiograph[#]	5 (0.6)
Pleural effusion[#]	2 (0.2)
Non respiratory causes	140 (15.9)
Allergic rhinitis with post-nasal drip	86 (9.8)
ACEI induced cough	37 (4.2)
Gastro esophageal reflux syndrome	12 (1.3)
Congestive heart failure	5 (0.6)
No cause established	376 (42.7)
Patients with cough subsided	282 (32.0)
Patients lost to follow up	53 (6.0)

Factors associated with significant pulmonary diseases

846 patients with no missing demographic or clinical data were included for analysis of factors associated with significant pulmonary diseases in the logistic regression.

The results revealed that the presence of red flag symptoms (OR 3.01, p<0.001), a history of other chronic lung diseases (OR 6.82, p<0.001) and older age (OR 1.02, p=0.010) had strong associations with significant pulmonary diseases (Table 4).

Associated factors	**OR**	**95% CI**	**P value**
Age	1.02	1.01-1.04	0.010*
Male	0.85	0.55-1.32	0.477
Duration of cough	1.00	1.00- 1.01	0.457
Smoking status			
Ex-smoker	1.12	0.65-2.39	0.514
Current smoker	1.78	0.91-3.35	0.093
Drinking status			
Social drinker	0.93	0.46-1.91	0.852
Chronic drinker	2.55	0.92-7.12	0.074
Socioeconomic status			
On CSSA	1.56	0.93-2.60	0.092
Presence of red flag symptoms	3.01	2.01-4.50	<0.001*
History of chronic lung disease	6.82	4.02-11.58	<0.001*
History of chronic kidney disease	1.28	0.60-2.76	0.527
History of chronic liver disease	1.33	0.61-2.92	0.479
History of diabetes	0.99	0.59-1.67	0.980
History of malignancy	0.97	0.46-2.04	0.925
History of neurological disease	0.75	0.31-1.81	0.520

Note: OR: Odd Ratio; CI: Confidence Interval; CSSA: Comprehensive Social Security Assistance

Discussion

of breath after active infection was excluded and some patients with mild symptoms might not attend our clinic for follow up after the active infection was treated. Moreover, some patients who fit into these criteria were already known to have asthma or COPD; hence, spirometry was not rearranged. The proportion of patients with positive sputum bacterial and AFB culture was 24.7% and 6.2% respectively among patients with sputum saved. 10.6% (93/880) of all patients with persistent cough had positive sputum bacterial culture results. This implied that the test was warranted as a positive result together with the sensitivity test could guide physicians for appropriate antibiotic treatment. Although a relatively smaller proportion (2.5%) of all patients with persistent cough had positive AFB culture results, early diagnosis of *Mycobacterium tuberculosis* and non-tuberculous mycobacteria is crucial as they could both cause significant morbidity and mortality with the former being highly contagious. This supported the need of performing the test for patients with persistent cough in our locality. 6.0% and 0.1% of all patients were lost to follow up and refused workup respectively; this might result in an underestimationn of the proportion of positive investigation results and prevalence of significant pulmonary diseases.

In keeping with the findings of various studies, older age, a history of chronic lung diseases and the presence of red flag symptoms were significantly associated with significant pulmonary diseases. Thus, particular attention should be paid with the presence of the above clinical history during the evaluation of patients with persistent cough. Other factors including smoking, alcoholism, gender, socioeconomic status, history of neurological disease, diabetes mellitus, chronic kidney disease, chronic liver disease and malignancy were not found to be associated with significant pulmonary diseases as compared with other studies. This could be attributed to the fact that only a small number of our patients were smokers, drinkers or had a history of the above chronic diseases and therefore a significant association could not be generated in the analysis. Different gender was observed to have increased risks of different significant pulmonary diseases in former studies. This could explain the discrepancy when compared with our results as our study analysed significant pulmonary diseases collectively. The differences in living standard and general health status of the CSSA and non-CSSA recipients might not solely depend on whether the patients were receiving CSSA due to current financial adversity but also other socioeconomic factors which were not retrievable in this retrospective study. Besides, the majority of our diabetic patients had good diabetic control; they might not be more prone to significant infectious pulmonary diseases which were caused by weakened immunity.

Our study was the first study to show the prevalence of significant pulmonary diseases in Chinese adult patients presenting with persistent cough in primary care in Hong Kong. We have demonstrated that about one fifth of patients with persistent cough had Bæm ˈu had