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Pleuropulmonary Involvement in Connective Tissue Disorders in A Tertiary Care Hospital in Africa

Marie Doualla-Bija[1,2*], Bertrand Hugo Mbatchou Ngahane[2], Kingue A Djam Lucien[2], Ayeah Mark Chia[2], Suh Jude Moutchia[2]

[1]Faculty of Medicine and Biomedical Sciences, University of Yaounde I, Yaoundé, Cameroon

[2]General Hospital Douala, Cameroon

[*]**Corresponding author:** Doualla-Bija Marie, Faculty of Medicine and Biomedical Sciences, University of Yaounde I, Yaoundé, Cameroon. Tel: +237677934648; Email: marie.doualla@gmail.com

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Abstract

Background: Pleuropulmonary manifestations are very common and associated with high mortality in patients with Connective Tissue Disorders (CTDs). Their frequency and patterns are variable depending on the type of CTD. Limited data is available in these patients in Sub-Saharan Africa.

Aim: To study the spectrum of pleuropulmonary manifestations of CTDs in a tertiary hospital in Douala, Cameroon.

Methods: This was a cross sectional hospital-based study, including CTD patients recruited in the Douala general hospital Rheumatology and Chest Medicine clinics. CTD was defined according to the American College of Rheumatology and European League against Rheumatism (ACR/EULAR) criteria. Between January and August 2016, all consenting adult patients with various CTDs were assessed for pleuropulmonary involvement using a clinical examination, Chest X-Ray (CXR), Pulmonary Function Tests (PFT) and High Resonance Computed Tomography (HRCT).

Results: We included 54 CTD patients, 29 had Rheumatoid Arthritis (RA), 16 Systemic Lupus Erythematosus (SLE), 7 scleroderma (SSc) and 2 Mixed Connective Tissue Disease (MCTD). Pulmonary clinical signs and symptoms were present in 18 patients (33.3%) with dyspnea (27.8%) and cough (13.0%) being more predominant. Chest HRCT revealed mostly Interstitial Lung Disease (ILD) patterns in 16 patients (29.6%) with honeycombing lesions occurring in 9.3% of CTD patients, (10.3% of RA patients and 28.6% of SSc patients) and Ground glass lesions occurring in 5.6% of CTD patients [1/29 RA (3.4%) and 2/7 scleroderma patients (28.6%)]. PFTs abnormalities were seen in 51.9% of CTD patients (28/54) and restrictive defect was the most common abnormality as seen in 41.4% of RA patients,71.4% of scleroderma patients, 56.2% of SLE patients and 50.0% of MCTD patients. Pulmonary hypertension was a rare finding as seen only in 1 RA patient (3.4%). Seven out of 16 (43.8%) CTD patients with radiographic lesions and 15 out of 28 (53.6%) CTD patients with abnormal PFTs were asymptomatic. There was a significant association between pleuropulmonary involvement and methotrexate use, (p=0.046), and corticosteroid use (p=0.033).

Conclusion: One third of CTDs patients have clinical involvement. Half of the asymptomatic patients have radiographic and/or PFTs abnormalities. CTDs should be systematically screened for pulmonary involvement.

Keywords: Africa; Connective Tissue Disorders; Pleuropulmonary

Introduction

Connective Tissue Diseases (CTDs) are a heterogeneous group of immunologically mediated inflammatory disorders with multi-organ involvement [1]. They include Systemic Lupus Erythematosus (SLE), Rheumatoid Arthritis (RA), Sjögren syndrome, ankylosing spondylitis, Systemic Sclerosis (SSc), Dermatomyositis (DM), Polymyositis (PM) and Mixed Connective-tissue Disease (MCTD) [1]. Pleuropulmonary manifestations are

frequent and may be asymptomatic or symptomatic, with varied degrees of severity [2-4]. Symptoms commonly include pleuritic chest pain, coughing, and dyspnea which are often the first clues to make the diagnosis. The pattern, spectrum and frequency of the pleuropulmonary involvement depend on the specific type of collagen vascular disease and may include one or more compartments such as alveolus, interstitium, vessels, lymphatic tissue, airways and pleura [5,6]. Pleuropulmonary abnormalities in patients with connective tissue diseases may not only be due to the CTD, but may result from the immunosuppressive treatment of the disease. As a result of immunosuppression, infection by bacteria or opportunistic organisms, such as Pneumocystis jirovecii, and atypical mycobacteria may occur [5,6]. The most frequent pulmonary manifestations are diffuse interstitial pneumonias [5-7] and pulmonary hypertension which represents the main causes of mortality and morbidity in these patients [5,6,8]. Chest X-rays (CXRs), most of which are usually of fairly good quality in settings with limited resources, have low sensitivity and specificity. High-Resolution Computed Tomography (HRCT) is the method of choice for assessment of pulmonary abnormalities in connective tissue diseases since it offers the best correlation with histologic findings, disease severity, prognosis, evaluation of disease progression and differential diagnosis [5,9].

It has been reported that pleuropulmonary manifestations are seen in approximately 50-70% of adult SLE patients with the pleura being the most affected [10,11]. In Saudi Arabia, a study showed that the most common presenting symptoms of lung disease in SLE patients were cough, dyspnea and pleuritic chest pain while the most common presenting signs were crackles, pleural rub, chest dullness and ronchi [12]. Yet another study in Saudi Arabia, found that the prevalence of pleuropulmonary involvement was 33.2% amongst which 85% with HRCT scan abnormalities [13]. The most common HRCT findings were pleural effusion, consolidation and atelectasis [13]. In RA, the majority of pulmonary manifestations occur within the first 5 years of the disease and pulmonary symptoms may precede onset of articular symptoms in 10–20% of cases [14,15]. Respiratory symptoms in RA can be due to a variety of conditions that affect the parenchyma, pleura, airways or vasculature with Interstitial Lung Disease (ILD) being the most common pulmonary manifestation of RA lung disease [16,17]. Evidence of pulmonary disease has been shown in 50% of RA patients using HRCT [18,19]. In SSc, most patients will present with direct pulmonary involvement, indirect pulmonary complications or as combinations of direct and indirect pulmonary manifestations; and other lung diseases not related to SSc such as chronic obstructive pulmonary disease, emphysema, asthma and lung nodules [20]. Pulmonary involvement is common in patients with SSc and most often comprises of fibrosis or ILD, and pulmonary vascular disease leading to Pulmonary Arterial Hypertension (PAH) [21]. Pulmonary manifestations are the leading cause of disease-related morbidity and mortality in patients with SSc [22]. The pattern and spectrum of pleuropulmonary manifestations in black Africa has received scant attention in world literature. The objective of this study was to review the pattern, frequency and spectrum of pleuropulmonary manifestations in patients with connective tissue diseases in a tertiary hospital in Douala, Cameroon.

Methods and Patients

Patients and Study Design

This was a cross sectional hospital-based study including all consenting adult patients who fulfilled the American College of Rheumatology and European League against Rheumatism (ACR/EULAR) criteria for CTDs attending a tertiary health care Rheumatology clinic in Douala, Cameroon. We used the 1997 ACR classification criteria for lupus diagnosis, the 2010 ACR/EULAR classification criteria for RA and 2013 ACR/EULAR classification criteria for SSc. This study was approved by the Institutional Ethics Committee of Research on Human Health of the University of Douala and the study hospital. The identity of patients was concealed and confidentiality of information preserved. We excluded all pregnant women and patients with established diagnoses of lung pathologies such as emphysema, chronic bronchitis, pulmonary edema, asbestosis, silicosis and pneumoconiosis.

Data Collection and Statistical Analysis

Data was collected from patients' medical records included socio-demographic data (age, sex, disease duration), past medical history (hypertension, diabetes mellitus and smoking), drug history (cumulative steroid and methotrexate dose) and the presence of co-morbidity (HIV status, previous infectious or non-infectious lung disease). Some relevant findings such as Erythrocyte Sedimentation Rate (ESR), C-reactive protein (CRP) and immunological data were also recorded. Patients were called via telephone and invited for a clinical examination and paraclinical assessments. After providing informed consent to participate in the study, the presence of the following chest clinical symptoms was recorded: cough, dyspnea, and chest pain and a chest clinical exam performed. Every patient had a CXR and HRCT scan done. We recorded the following radiology findings: the presence of interstitial opacities (reticular, linear, micro-nodular, ground glass, honey comb, edema or milliary opacities), parenchymal lesions (nodular lesions and masses), pleural anomaly (pleurisy, pleuritis, pleural effusion and masses) and finally the site of the lesion on the lung parenchyma. These patients also underwent pulmonary function tests (PFT) before and after bronchodilatation according to the American Thoracic Society (ATS) and European Respiratory Society (ERS) guidelines for subject maneuver, techniques and quality control, using Spirobank II (Medical International Research, Roma, Italy) [23-27]. Three tests with values within 5% were defined as being acceptable, and the best of three values was used to grade pulmonary function. Forced Expiratory Volume in the first second (FEV1), Forced Vital Capacity (FVC) and FEV1/FVC ratio were measured. Three additional acceptable tests were recorded. Airflow obstruction was defined as a FEV1/FVC ratio <70% with FVC >80%, restrictive defects defined as an FEV1/FVC ratio >70% with an FVC <80% predicted, and mixed defects as FVC of <80% predicted and an FEV1/FVC ratio of <70% [23-27]. Lung function impairment was

defined by the presence of at least one of these three abnormalities. The severity of lung function impairment was classified as per the FEV1-based criteria agreed by the ERS and the ATS [23-27]. The findings of the CXR, PFT and HRCT scan were all interpreted with the collaboration of a chest physician, rheumatologist and a radiologist with diagnoses reached by consensus.

Delay in disease diagnosis was defined as the period from onset of symptoms, to date of diagnosis. Disease duration was defined as the period from diagnosis to time of study. Dyspnea was classified according to the New York Heart Association (NYHA) functional classification as follows: stage I was defined as no dyspnea on normal physical exertion, stage II was defined as mild dyspnea on normal physical exertion, stage III was defined as marked dyspnea on exertion with no dyspnea at rest and stage IV was defined as dyspnea at rest. Pleuropulmonary involvement was defined as the presence of one or more abnormalities in the clinical examinations, chest radiography, PFT and HRCT findings.

Data was recorded and analyzed using the Statistical Package for Social Sciences (SPSS) Standard version, Release 20.0 (IBM Inc. 2012). Mean with standard deviation were calculated for continuous (scale) variables. Categorical variables are reported as proportions, which were compared using the chi-square test and Fisher's exact test. A P-value of < 0.05 was considered to be significant.

Results

We reviewed 54 CTD patients (92.6% females); 29 had RA (53.7%), 16 had SLE (29.6%), 7 had SSc (13.0%) and 2 had MCTD (3.7%). The mean age amongst all CTDs patients was 45.5±12.4 years.

The mean duration of CTD was 10.1±6.6 years. Sixteen patients (29.6%) presented with a known past history of lung disease amongst which were 5 patients with pulmonary tuberculosis, one with sarcoidosis and 9 with bacterial pneumonia. Fifty-three (98%) patients were on corticosteroids.

The prevalence of pleuropulmonary involvement in our study participants was 68.5% (37/54), amongst which 17/29 RA patients (58.6%), 12/16 SLE patients (75.0%), 6/7 SSc patients (85.7%) and all 2 MCTD patients (100%) presented with pleuropulmonary manifestations [Table 1].

Variables	Total (n=54)	RA (n=29)	SLE (n=16)	SSc (n=7)	MCTD (n=2)
Female, n (%)	50 (92.6)	25 (86.2)	16 (100.0)	7 (100.0)	2 (100.0)
Sex ratio (female to male ratio)	13 :1	6 :1	All females	All females	All females
Age, mean ± SD	43.8±12.4	47.7±11.0	39.7±11.9	33.3±11.4	56.0±9.9
Age groups (years)					
15-29 years n (%)	7 (13.0)	1 (3.4)	4 (25.0)	2 (28.6)	0 (0.0)
30-44 years n (%)	16 (29.6)	8 (27.6)	4 (25.0)	4 (57.1)	0 (0.0)
45-59 years n (%)	26 (48.1)	17 (58.6)	7 (43.8)	1 (14.3)	1 (50.0)
60-74 years n (%)	5 (9.3)	3 (10.3)	1 (6.2)	0 (0.0)	1 (50.0)
Disease duration, mean ± SD	10.1±6.6	9.5±5.2	10.2±8.0	12.6±9.2	8.0±5.7
Extra-articular involvement, n (%)	21 (51.7)	4 (13.8)	10 (62.5)	7 (100.0)	0 (0.0)
Muscular involvement	2 (3.7)	1 (3.4)	1 (6.2)	0 (0.0)	0 (0.0)
Cutaneous involvement	14 (25.9)	3 (10.3)	5 (31.2)	6 (85.7)	0 (0.0)
Raynaud phenomenon	1 (1.9)	0 (0.0)	0 (0.0)	1 (14.3)	0 (0.0)
Past history of lung disease, n (%)	16 (29.6)	5(17.2)	6 (37.5)	4 (57.1)	1 (50.0)
History of chest infections, n (%)	10 (18.5)	3 (10.3)	3 (18.7)	3 (42.9)	1 (50.0)
History of PTB, n (%)	5 (9.3)	1 (3.4)	3 (18.8)	1 (14.3)	0 (0.0)
Non-specific lung disease, n (%)	1 (1.9)	1 (3.4)	0 (0.0)	0 (0.0)	0 (0.0)
Sarcoidosis, n (%)	1 (1.9)	1 (3.4)	0 (0.0)	0 (0.0)	0 (0.0)
HIV Seropositive	3 (5.6)	2 (6.9)	0 (0.0)	1 (14.3)	0 (0.0)
Elevated CRP	24 (82.8)	18 (94.7)	3 (42.9)	1 (100.0)	2 (100.0)

Elevated ESR	41 (95.3)	23 (95.8)	12 (92.3)	4 (100.0)	2 (100.0)
Hydroxychloroquine	30 (55.6)	12 (41.4)	15 (93.8)	1 (14.3)	2 (100.0)
Azathioprine	12 (22.2)	1 (3.4)	7 (43.8)	3 (42.9)	1 (50.0)
Penicillamine	4 (7.4)	0 (0.0)	0 (0.0)	4 (57.1)	0 (0.0)
Cyclophosphamide	1 (1.9)	0 (0.0)	0 (0.0)	1 (14.3)	0 (0.0)
Corticosteroids	53 (98.1)	29 (100.0)	16 (100.0)	6 (85.7)	2 (100.0)
Methotrexate	25 (46.3)	4 (13.8)	13 (81.2)	7 (100.0)	1 (50.0)
Pleuropulmonary manifestations, n (%)	**37 (68.5)**	**17 (58.6)**	**12 (75.0)**	**6 (85.7)**	**2 (100.0)**

Table 1: Baseline characteristics of connective tissue disease patients (n=54).

On clinical assessment, 18 patients (33.3%) had pulmonary symptoms with dyspnea (27.8%) and cough being the most frequent symptoms (13.0%) [Table 2].

Radiographic findings revealed mainly ILD patterns in 16 cases (29.6%) with linear opacities (20.4%), micronodular opacities (13.0%), Honey comb opacities (9.3%), Ground glass opacities (5.6%). Amongst the different radiographic findings, honey comb and ground glass opacities were both diffuse and bilateral.

Pulmonary function tests were abnormal in 28 patients (51.9%). Restrictive defect was observed 27 (50%) of CTD patients [Table 2].

Variables	Total (n=54)	RA (n=29)	SLE (n=16)	SSc (n=7)	MCTD (n=2)	P value
Presence of signs/symptoms, n (%)	**18 (33.3)**	**7 (24.1)**	**7 (43.8)**	**3 (42.9)**	**1 (50.0)**	**0.490**
Dyspnea, n (%)	15 (27.8)	4 (13.8)	7 (43.7)	3 (42.9)	1 (50.0)	0.105
Stage I	2 (13.3)	0 (0.0)	0 (0.0)	1 (33.3)	1 (100.0)	0.053
Stage II	6 (40.0)	3 (75.0)	3 (42.9)	0 (0.0)	0 (0.0)	
Stage III	3 (20.0)	0 (0.0)	3 (42.9)	0 (0.0)	0 (0.0)	
Stage IV	4 (26.7)	1 (25.0)	1 (14.3)	2 (66.7)	0 (0.0)	
Cough, n (%)	7 (13.0)	4 (13.8)	0 (0.0)	2 (28.6)	1 (50.0)	0.105
Productive	4 (57.1)	2 (50.0)	0 (0.0)	1 (50.0)	1 (100.0)	0.649
Unproductive	3 (42.9)	2 (50.0)	0 (0.0)	1 (50.0)	0 (0.0)	
Chest pain, n (%)	2 (3.7)	0 (0.0)	2 (12.5)	0 (0.0)	0 (0.0)	0.177
Crackles (Crepitations), n (%)	2 (3.7)	1 (3.4)	1 (6.2)	0 (0.0)	0 (0.0)	0.636
Wheezing, n (%)	2 (3.7)	0 (0.0)	1 (6.2)	1 (14.3)	0 (0.0)	0.636
CXR/HRCT abnormality, n (%)	**16 (29.6)**	**9 (31.0)**	**2 (12.5)**	**4 (57.1)**	**1 (50.0)**	**0.156**
Linear opacities, n (%)	11 (20.4)	5 (17.2)	1 (6.2)	4 (57.1)	1 (50.0)	0.029
Micronodular opacities, n (%)	7 (13.0)	2 (6.9)	1 (6.2)	3 (42.9)	1 (50.0)	0.023
Honey comb opacities, n (%)	5 (9.3)	3 (10.3)	0 (0.0)	2 (28.6)	0 (0.0)	0.173
Fibrosis, n (%)	5 (9.3)	3 (10.3)	0 (0.0)	2 (28.6)	0 (0.0)	0.173
Ground glass opacities, n (%)	3 (5.6)	1 (3.4)	0 (0.0)	2 (28.6)	0 (0.0)	0.039
Alveolar opacities, n (%)	1 (1.9)	1 (3.4)	0 (0.0)	0 (0.0)	0 (0.0)	0.831
Nodules, n (%)	1 (1.9)	1 (3.4)	0 (0.0)	0 (0.0)	0 (0.0)	0.831
Pleurisy, n (%)	1 (1.9)	0 (0.0)	1 (6.2)	0 (0.0)	0 (0.0)	0.490
Pulmonary hypertension, n (%)	1 (1.9)	1 (3.4)	0 (0.0)	0 (0.0)	0 (0.0)	0.831
Upper 1/3 lung field involvement	8 (14.8)	3 (10.3)	1 (6.2)	3 (42.9)	1 (50.0)	0.052
Middle 1/3 lung field involvement	5 (9.3)	1 (3.4)	1 (6.2)	3 (42.9)	0 (0.0)	0.012
Lower 1/3 lung field involvement	12 (22.2)	6 (20.7)	2 (12.5)	4 (57.1)	0 (0.0)	0.093
Diffuse lung involvement	5 (9.3)	1 (3.4)	1 (6.2)	3 (42.9)	0 (0.0)	0.012

Unilateral lung involvement	7 (13.0)	5 (17.2)	1 (6.2)	1 (14.3)	0 (0.0)	0.225
Bilateral lung involvement	9 (16.7)	4 (13.8)	1 (6.2)	3 (42.9)	1 (50.0)	0.225
PFT abnormality, n (%)	**28 (56.0)**	**13 (50.0)**	**9 (56.2)**	**5 (83.3)**	**1 (50.0)**	**0.526**
Restrictive airway disease, n (%)	27 (55.1)	12 (48.0)	9 (56.2)	5 (83.3)	1 (50.0)	0.480
Obstructive airway disease, n (%)	1 (1.9)	1 (3.4)	0 (0.0)	0 (0.0)	0 (0.0)	
Mixed airway disease, n (%)	1 (1.9)	1 (3.4)	0 (0.0)	0 (0.0)	0 (0.0)	
Severity of obstruction						
Mild obstruction	32 (62.7)	19 (70.4)	10 (62.5)	2 (33.3)	1 (50.0)	0.290
Moderate obstruction	15 (29.4)	7 (25.9)	5 (31.2)	2 (33.3)		
Severe obstruction	4 (7.8)	1 (3.7)	1 (6.2)	2 (33.3)	0 (0.0)	
Reversibility of obstruction						
Mild	34 (68.2)	18 (69.2)	12 (75.0)	2 (33.3)	2 (100.0)	0.234
Moderate	12 (24.0)	7 (26.9)	3 (18.8)	2 (33.3)	0 (0.0)	
Severe	4 (8.0)	1 (3.8)	1 (6.2)	2 (33.3)	0 (0.0)	

Table 2: Pleuropulmonary manifestations in CTD patients.

There were significant associations between the presence of radiologic and spirometry features with clinical symptoms. Overall, significant associations were observed between CTD patients with pleuropulmonary manifestations and the presence of radiographic lesions (p = 0.025) or abnormal PFTs (p=0.019). [Table 3]. Seven out of 16 (43.8%) CTD patients with radiographic lesions had no clinical symptoms. Also, 15 out of 28 (53.6%) CTD patients with abnormal PFT had no clinical symptoms.

CTD patients	Pleuropulmonary involvement	Radiological features				Spirometry findings			
		Abnormal	Normal	Total	P value	Abnormal	Normal	Total	P value
RA	Yes	5 (55.6)	2 (10.0)	7 (24.1)	**0.016**	5 (38.5)	1 (7.7)	6 (23.1)	0.16
	No	4 (44.4)	18 (90.0)	22 (75.9)		8 (61.5)	12 (92.3)	20 (76.1)	
	Total	9 (31.0)	20 (69.0)	29 (100)		13 (50.0)	13 (50.0)	26 (100)	
SLE	Yes	1 (50.0)	6 (42.9)	7 (43.8)	1.000	5 (55.6)	2 (28.6)	7 (43.8)	0.358
	No	1 (50.0)	8 (57.1)	9 (56.2)		4 (44.4)	5 (71.4)	9 (56.2)	
	Total	2 (12.5)	14 (87.5)	16 (100)		9 (56.3)	7 (43.8)	16 (100)	
SS	Yes	3 (75.0)	0	3 (42.9)	0.143	2 (40.0)	0	2 (33.3)	1.000
	No	1 (25.0)	3 (100)	4 (57.1)		3 (60.0)	1 (100)	4 (66.7)	
	Total	4 (57.1)	3 (42.9)	7 (100)		5 (83.3)	1 (16.7)	6 (100)	
MCTD	Yes	0	0	0		0	0	0	-
	No	1 (50.0)	1 (50.0)	2 (100)		1 (50.0)	1 (50.0)	2 (100)	
	Total	1 (50.0)	1 (50.0)	2 (100)		1 (50.0)	1 (50.0)	2 (100)	
All CTD	Yes	9 (56.2)	9 (23.7)	18 (33.3)	**0.025**	13 (46.4)	3 (13.6)	16 (32.0)	**0.019**
	No	7 (43.8)	29 (76.3)	36 (66.7)		15 (53.6)	19 (86.4)	34 (68.0)	
	Total	16 (29.6)	38 (70.4)	54 (100)		28 (56.0)	22 (44.0)	50 (100)	

Table 3: Associations between the presence of radiological and spirometry findings with pleuropulmonary involvement.

In RA patients, there was a relation between the presence of clinical symptoms and the presence of radiographic lesions (p=0.016); but no association between the presence of clinical symptoms and abnormal PFTs (p=0.160).

As for SLE, no significant associations were observed between CTD patients with clinical symptoms and the presence of radiographic lesions or abnormal PFTs (p=1.000 and p=0.358 respectively.

One out of four (25.0%) SSc patients with radiographic lesions and 3 out of 5 (60.0%) SSc patients with abnormal PFT were asymptomatic.

There was a significant association between pleuropulmonary involvement and methotrexate use, (p=0.046), and corticosteroid use (p=0.033). [Table 4].

Variables	Category	Present (n=37)	Absent (n=17)	Total (n=54)	OR (95% CI)	P value
Sex	Male	3 (75.0)	1 (25.0)	4	1.412 (0.136-14.655)	0.772
	Female	34 (68.0)	16 (32.0)	50		
Disease duration	≥10 years	20 (76.9)	6 (23.1)	26	2.157 (0.659-7.064)	0.200
	<10 years	17 (60.7)	11 (39.3)	28		
Extra-articular Involvement	Present	15 (71.4)	6 (28.6)	21	1.250 (0.379-4.116)	0.713
	Absent	22 (66.7)	11 (33.3)	33		
History of PTB	Yes	3 (50.0)	3 (50.0)	6	0.412 (0.074-2.292)	0.300
	No	34 (70.8)	14 (29.2)	48		
HIV seropositive	Yes	2 (66.7)	1 (33.3)	3	0.914 (0.077-10.834)	0.943
	No	35 (70.8)	16 (31.4)	51		
HRCT scan findings	Abnormal	16 (100.0)	0 (0.0)	16	Undefined	**0.001***
	Normal	21 (55.3)	17 (44.7)	38		
Hydroxychloroquin use	Yes	24 (80.0)	6 (20.0)	30	3.385 (1.017-11.261)	**0.042**
	No	13 (54.2)	11 (45.8)	24		
Azathioprine use	Yes	9 (75.0)	3 (25.0)	12	1.500 (0.345-6.431)	0.584
	No	28 (66.7)	14 (33.3)	42		
Penicillinamine use	Yes	4 (100.0)	0 (0.0)	4	Undefined	0.159
	No	33 (66.0)	17 (34.0)	50		
Cyclophosphamide use	Yes	1 (100.0)	0 (0.0)	1	Undefined	0.688*
	No	36 (67.9)	17 (32.1)	53		
Corticosteroid use	Yes	36 (67.9)	17 (32.1)	53	Undefined	0.688*
	No	1 (100.0)	0 (0.0)	1		
MTX use	Yes	18 (62.1)	11 (37.1)	29	0.517 (0.158-1.691)	0.272
	No	19 (76.0)	6 (24.0)	25		
Rheumatoid factor#	Positive	6 (46.2)	7 (53.8)	13	0.514 (0.085-3.109)	0.466
	Negative	5 (62.5)	3 (37.5)	8		
PFT findings#	Abnormal	28 (80.0)	0 (0.0)	28	Undefined	**<0.001**
	Normal	7 (20.0)	15 (100.0)	22		

Table 4: Factors associated with pleuropulmonary manifestations in CTDs.

Discussion

Pleuropulmonary involvement was found in two third of CTD patients, and half of patients with no clinical symptoms had radiographic and/or PFTs abnormalities.

The prevalence of pleuropulmonary manifestations amongst RA patients was 58.6% and 24.1% presented with clinical findings [dyspnea (13.8%), cough (13.8%) and crackles (3.4%)], as in many studies [18,28]. In our RA patients, the radiographic findings were abnormal in 31.0% similar to the 33.8% obtained by Fatima et al., in North India [28], but lower than findings by Correa Soto et al. [18]

in Spain and Liote [19] in France who both showed radiographic evidence of pulmonary disease in half of RA patients. About 44.4% of RA patients with HRCT evidence of pulmonary disease were asymptomatic in our study lower than in Liote's study wherein 90% of patients presented with no clinical symptoms. This lesser prevalence of HRCT evidence of pulmonary disease and lesser patients with no clinical symptoms could be due to prompt diagnosis of CTDs in the developed countries compare to our patients with a median (IQR) delay in disease diagnosis of 3.0 (1.0-7.0) years. ILD is the commonest pulmonary manifestation in RA patients [15-17,28] confirmed by our findings confirmed by the presence of linear opacities (17.2%), honey comb (10.3%), micronodular (6.9%) and ground glass opacities (3.4%). These HRCT lesions of ILD or pulmonary fibrosis were diffused and or bilaterally located in RA patients with past history of lung disease particularly pulmonary tuberculosis. PAH was observed in one RA patient and could be due to underlying severe interstitial fibrosis and restrictive lung disease, although a subgroup of patients may develop isolated PAH independent of the degree of interstitial fibrosis [29]. About 44.8% of RA patients had abnormal findings on PFTs and more than half with these abnormal PFT were asymptomatic. The majority of RA patients presented with a restrictive pattern (41.4%) which once again highlights the presence of an underlying interstitial lung disease and pulmonary fibrosis [28,30]. In our study, a mixed pattern was observed in only one RA patient and no RA patient had the obstructive pattern on PFTs as may be observed in RA patients having bronchiectasis, bronchiolitis obliterans, chronic airway obstructive or cricoarytenoid arthritis [31].

Pleuropulmonary involvement in SLE occurred in 75% of our cases. This is similar to reports that show approximately 50-70% [10,11]. Clinical features were present in 43.7%, predominantly dyspnea (43.7%) and pleuritic chest pain (12.5%). These observations are similar to those obtained by Mohammad et al in Egypt who reported that a prevalence of 48% with dyspnea and chest pain being amongst the common respiratory symptoms [32]. Our findings were however slightly higher than those in Saudi Arabia and India with prevalence of 33% and 23.68% respectively [13,33]. Our patients had longer disease duration as it is described in lupus-related lung disease, which is usually one of the first extraarticular presentation in lupus patients. Approximately 12.5% of the SLE patients had radiographic evidence of pleuropulmonary involvement. This differs from studies done in Egypt, Saudi Arabia and India who reported a higher prevalence of pleuropulmonary involvement in 64%, 85% and 55.26% respectively [13,32,33]. Furthermore, Felon HM et al., and Sant SM et al. also reported HRCT abnormalities in 70% and 72% of SLE patients respectively [34,35]. The most predominant pattern of HRCT lesions in our study were linear (6.2%) micronodular opacities (6.2%) and pleurisy (6.2%) indicating the fact that ILD and pleural disease are equally common amongst SLE patients with pleuropulmonary involvement than previously suggested [13,32,33,36]. More than half of SLE patients (56.2%) had an abnormality on PFTs; As in other studies we found a high frequency of restrictive pattern and high frequency of asymptomatic presentation [32,33].

The prevalence of pleuropulmonary involvement in SSc patients was 85.7% amongst which about half presented with respiratory symptoms. Dyspnea (42.9%) and cough (28.6%) were the most common respiratory symptoms. These findings are similar to those reported by Deepa et al. in India who reported a prevalence of pleuropulmonary involvement in SSc patients of 90% with over 2/3rd being asymptomatic for respiratory complaints [37]. HRCT revealed evidence of pleuropulmonary involvement in 57.1% (4/7) of SSc patients, with honey comb opacities (fibrosis) and ground glass opacities (ILD) each occurring in 28.6% (2/7) of SSc patients. However our findings slightly differ from those reported by Santos et al. in Brazil [38] who observed honeycombing in 39.1%, ground-glass opacities associated with reticular opacities in 34.7% and observed abnormalities suggestive of fibrosis (honeycombing and reticular opacities) in 60.8% of their patients[38]. PFTs abnormality was seen in 71.4% (5/7) of SSc patients amongst which all had a restrictive pattern which is common finding in patients with pulmonary fibrosis as reported by Steen et al. in the United States [22,39].

The prevalence of pleuropulmonary involvement in MCTD patients was 100%. A prospective study evaluating patients with MCTD over time emphasizing lung involvement reported that 85% of 34 patients with MCTD had evidence of pulmonary involvement[40]. In our study, we had 2 MCTD patients amongst which one of them (50%) presented with dyspnea associated with cough and HRCT abnormalities such as linear and micronodular abnormality while the other asymptomatic MCTD patient (50%) had a restrictive pattern on PFTs. These findings are slightly similar to those reported by Sylvain et al. which revealed that 73% of their asymptomatic patients had evidence of pulmonary disease on chest x-ray or pulmonary function testing with dyspnea being the most common respiratory symptom [40].

Conclusion

About one third of CTD patients have pleuropulmonary involvement. Half of these patients have no pulmonary symptoms, hence all patients with CTDs should be systematically screened for pulmonary involvement as soon as the definitive diagnosis of CTD is established. Further studies are therefore needed to identify the determinants of pleuropulmonary involvement amongst CTD patients in black Africa.

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