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Patterns of pulmonary fibrosis in Northern Saudi Arabia

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Abstract:

***Objective**: the objective of this study was to estimate the pattern and prevalence of Pulmonary Fibrosis in Northern KSA. **Methodology:** In this study, clinical, imaging and laboratory parameters were investigated for 60 patients with pulmonary disorders suggesting replacement and focal pulmonary fibrosis in the Pulmonary Medicine Department at King Khalid Hospital. **Results**: Of the 60 patients, replacement and focal fibrosis were Identified in 42/60 (70%) and 2/60 (3.3%) patients, respectively. Of the 42 patients with replacement fibrosis, 20/42(47.6%) were with Tuberculosis (TB), 18/42(42.9%) were with pneumonia and 4/42(9.5%) with infarction. **Conclusion**: Replacement fibrosis is prevalent in Northern Kingdom of Saudi Arabia. Advanced investigations in regard to the control of causes are necessary.*

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Key words: Replacement fibrosis, Saudi Arabia, Focal Fibrosis

Introduction

Pulmonary fibrosis involves a heterogeneous group of conditions described by replacement of the lung parenchyma with fibrous tissue. Despite many years of research, its pathogenesis leftovers vague and a cure remains mysterious. The great majority of data in this subject derived from patients with idiopathic pulmonary fibrosis (IPF). Pulmonary fibrosis has also appeared as a leading source of mortality in patients with systemic sclerosis. [1,2].

IPF is a progressive, permanent disease of the lung that has no ending choice for treatment other than transplantation. It is characterized by replacement of the normal lung tissue by fibrotic scarring, honeycombing, and increased levels of myofibroblasts. The underlying causes of IPF are quiet largely obscure [3]. Patients with IPF fibrosis may be predisposed genetically to tractional injury to the peripheral lung. The consequence is recurrent damage to the epithelial-mesenchymal interface, favorably at the outer edges of the basilar lung lobules where tractional stress is high during inspiration. A distinctive "reticular network of injury" (the *fibroblast focus*) forms, joined by a extended phase of wound repair (*tear and slow repair*). Isolated areas of alveolar collapse are seen in scar at the periphery of the lung lobules. The sequence recurrences over many years resulting in progressive fibrous remodeling and replacement of the alveoli in a lobule by bronchiolar cysts surrounded by fibrous scar. Abnormalities in surfactant function are proposed as a likely mechanism of first lung damage [4,5].

Lung fibrosis is one of the main disorders that impair lung and it is being ever more recognized in Saudi Arabia in

recent years [6]). There are few published data in the literature on different aspects of lung fibrosis in Saudi Arabia. There a lack of published reports on the various etiological factors responsible for pulmonary fibrosis from Saudi Arabia, particularly from northern Saudi Arabia [7,8]. Therefore, the aim of this study was to determine the pattern and prevalence of Pulmonary Fibrosis in Northern Saudi Arabia.

Methodology

This retrospective study was conducted in King Khalid hospital involving 60 patients, who were previously diagnosed as having pulmonary fibrosis and were identified by review of admission/discharge and out patient records, during the period from January 2010 to January 2014. Diagnosis of pulmonary fibrosis was considered if clinical / pulmonary function tests were suggestive and High Resolution CT Scan (HRCT) was consistent of pulmonary fibrosis in all patients. Patients identification data were retrieved from the medical records of Pulmonary Medicine Department at King Khalid Hospital. Data was retrieved to take information on age, gender, clinical signs and symptoms as recorded by the treating physician. Patients were considered to have a Secondary cause of Pulmonary fibrosis if they were diagnosed to have collagen vascular disease. Patients without any identifiable cause for pulmonary fibrosis were considered to have idiopathic pulmonary fibrosis (IPF).

Results

This study investigated 60 patients who were previously diagnosed as having pulmonary lung disease, their ages ranging from 15 to 96 with a mean age of 58 years. Of the 60 patients, 33/60(55%) were males and 27/60(45%) were females,

giving males' females' ration of 1.22: 1.00. Out of the 60 patients with lung fibrosis, 2/60 (3.3%) were identified with focal fibrosis and 58/60 (96.7%) were with replacement fibrosis. Of the 58 patients with replacement fibrosis, 20/58 (34.5%) were found with tuberculosis, 18/58 (31%) with Pneumonia, 4/58 (6.9%) with infarction and the remaining 16/58 (27.6%) were found with unpredictable cause (idiopathic), as indicated in Fig1.

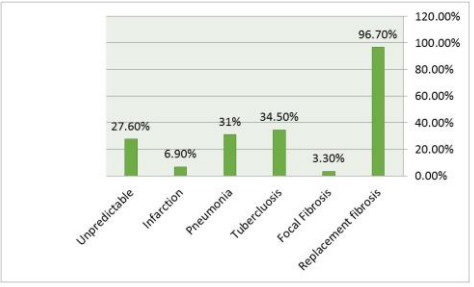

Figure1. Description of the study subjects by pattern of pulmonary lung fibrosis

Out of the 42 patients with known causes of replacement fibrosis, 21/42 (50%) were males and 21/42(50%) were females. Of the 21 males, 11/21 (52.4%), 7/21(33.3%) and 3/21(14.3%) were found with tuberculosis, pneumonia and infarction, respectively. Of the 21 females, 11/21 (52.4%), 9/21(42.9%) and 1/21(4.7%) were found with pneumonia, tuberculosis, and infarction, respectively, as indicated in Fig2, Table 1.

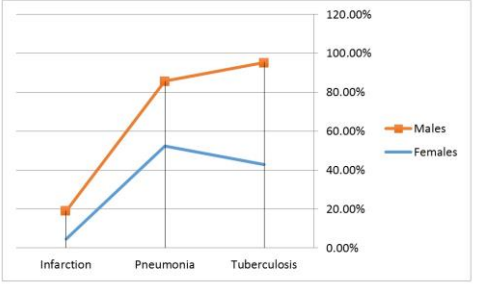

Figure2. Description of known cases of pulmonary fibrosis by sex.

As indicated in Table 1, the majority of cases of pulmonary fibrosis were found at age group 56+ constituting 38/60(63.3%). Accordingly, the risk of pulmonary fibrosis is significantly increase with the increase of age (P <0.0001). The mean age at diagnosis was 55 years. In regard to the age sex, although, relatively most cases were seen at elder age for both sex, but some younger females were found as shown in Table1.

Table 1 Distribution of the pulmonary fibrosis by sex and age

Age group	Sex		Total
	Males	Females	
<25 years	3	4	7
26-35	3	2	5
36-45	3	2	5
46-55	2	3	5
56+	22	16	38
Total	33	27	60
Tuberculosis	11	9	20
Pneumonia	7	11	18
Infarction	3	1	4
Focal fibrosis	2	0	2
Idiopathic	12	6	18
Total	33	27	60

Furthermore, some of the patients with lung fibrosis were identified with other disorders including; Arrhythmia (13.8%); Cardiovascular CVS (29.3%), Diabetes Mellitus (DM) (43%), Hepatic (10.3%), Obesity (8.6%), infection (24%), Malignancy (8.3%) as shown in Fig 3.

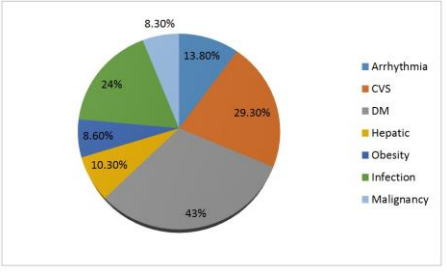

Figure 3. Description of study subjects by other accompanied conditions.

Table 2. Distribution of the replacement fibrosis by total score

Total score	TB	Pneumonia	Infarction	Idiopathic	Total
0	4	4	1	4	13
1	6	5	2	3	16
2	3	6	0	6	15
3	3	2	0	2	7
4	2	1	0	2	5
5	2	0	0	1	3
6	0	0	1	0	1
Total	20	18	4	18	60

In regard to the distribution of the replacement fibrosis by total score, most patients were identified with score one followed by score two and three representing 16/60 (26.7%), 15/60(25%) and 13/60(21.7%), respectively as shown in Table 2, Fig4.

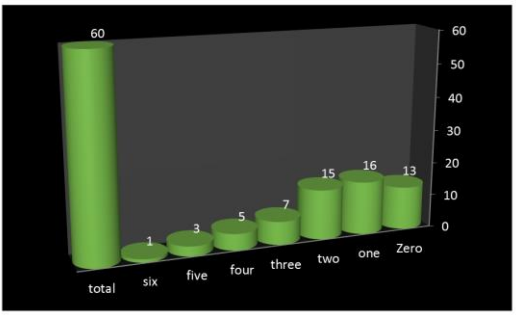

Figure 3. Description of lung fibrosis by total score

Discussion

The pulmonary fibrosis is a frequent characteristic of several autoimmune or immune mediated disorders and may be induced by inflammatory changes following inhalation of substances. In the present study, a reasonable number of cases might be attributed to certain etiological factors, such as tuberculosis, pneumonia and infraction. Notably, there is determined number of cases with idiopathic type of pulmonary fibrosis.

What is interesting is the association of some cases of pulmonary fibrosis with tuberculosis in rich country like Saudi Arabia, but this might be attributed to the fact that these cases occurred before several years when there was still poverty in some parts of the Kingdom.

Tuberculosis, which is a disease caused by infection with *Mycobacterium tuberculosis*. The inhaled bacteria into the alveoli of the lung are phagocytosed by resident macrophages that produce and secrete a number of inflammatory mediators that recruit additional inflammatory cells to the site of infection [9,10]. These intense inflammatory reactions result in massive alveolar tissue damage that is ultimately replaced by fibrous tissue. Existing data suggest that TGF-b, together with TNF-a, plays a key part in the formation of the fibrous wall that encapsulates the tuberculous granuloma [11,12].The significance of TGF-b with respect to pulmonary fibrosis has been well established [13,14]. It is believed that, TGF-b may contribute to the dys-regulation of Extracellular Matrix turnover in tuberculosis. Indeed, TGF-b may also extend fibrogenesis by inhibiting apoptosis of fibroblasts [15].

However, the prevalence of tuberculosis in this study (33.3%), is relatively higher than the reports from other regions of Saudi Arabia. I a study Riyadh and Dammam had the highest prevalence of tuberculosis with 22% and 21%, respectively, while prevalence was lowest in Jazan and Hail with an incidence of 2% and 3%, respectively [16].

In regard to the pneumonia and its association with lung fibrosis, it represented 30%, as well as those with those with idiopathic etiology. Idiopathic pulmonary fibrosis (IPF) is a chronic, progressive fibrosis of lung of unknown cause and its diagnosis comprises the careful omission of secondary causes for pulmonary fibrosis and the presence of a pattern of usual interstitial pneumonia. Despite several efforts made in

establishing specific, generally accredited diagnostic criteria for IPF, its ascertainment remains a challenge [17].

Non-specific interstitial pneumonia (NSIP) is an interstitial lung disorder that may be idiopathic or secondary to connective tissue disease, toxins or numerous other causes. Idiopathic NSIP is a rare and its diagnosis requires exclusion of many other probable causes [18]. IPF is regularly progressive, though its clinical sequence might significantly differ on an individual basis, with occurrences of severe acute respiratory deterioration (acute exacerbations) being unpredictable. A deeper understanding of the mechanisms responsible for a hastened course of the disease and the identification of biomarkers of progression would lead to an improved stratification of the disease, important for bringing personalized therapeutic strategies [17].

In study from Saudi Arabia that investigated lung fibrosis, the most frequent disease was connective tissue disease (CTD)-associated interstitial lung disease (ILD) (34.8%), followed by idiopathic pulmonary fibrosis (IPF) (23.3%), sarcoidosis (20%), and hypersensitivity pneumonitis (6.3%). Non-classifiable ILD was present in 1.8% of the total ILD cases [6]. Furthermore, in Saudi Arabia, IPF patients tended to be somewhat older and the disease progression was slightly slower than reported IPF cohorts in other populations. The impact of genetics and co-morbid diseases on the incidence and consequence of IPF should be further searched.

Replacement fibrosis is prevalent in Northern Kingdom of Saudi Arabia. Advanced investigations in regard to the control of causes are necessary.

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