ESTIMATION OF IgG AND IgG/ALBUMIN RATIO IN BRONCHOALVEOLAR LAVAGE AND SERUM OF PATIENTS WITH INTERSTITIAL PULMONARY FIBROSIS

THESIS

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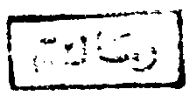

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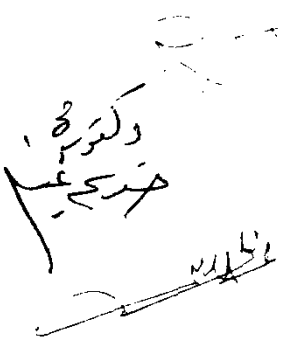

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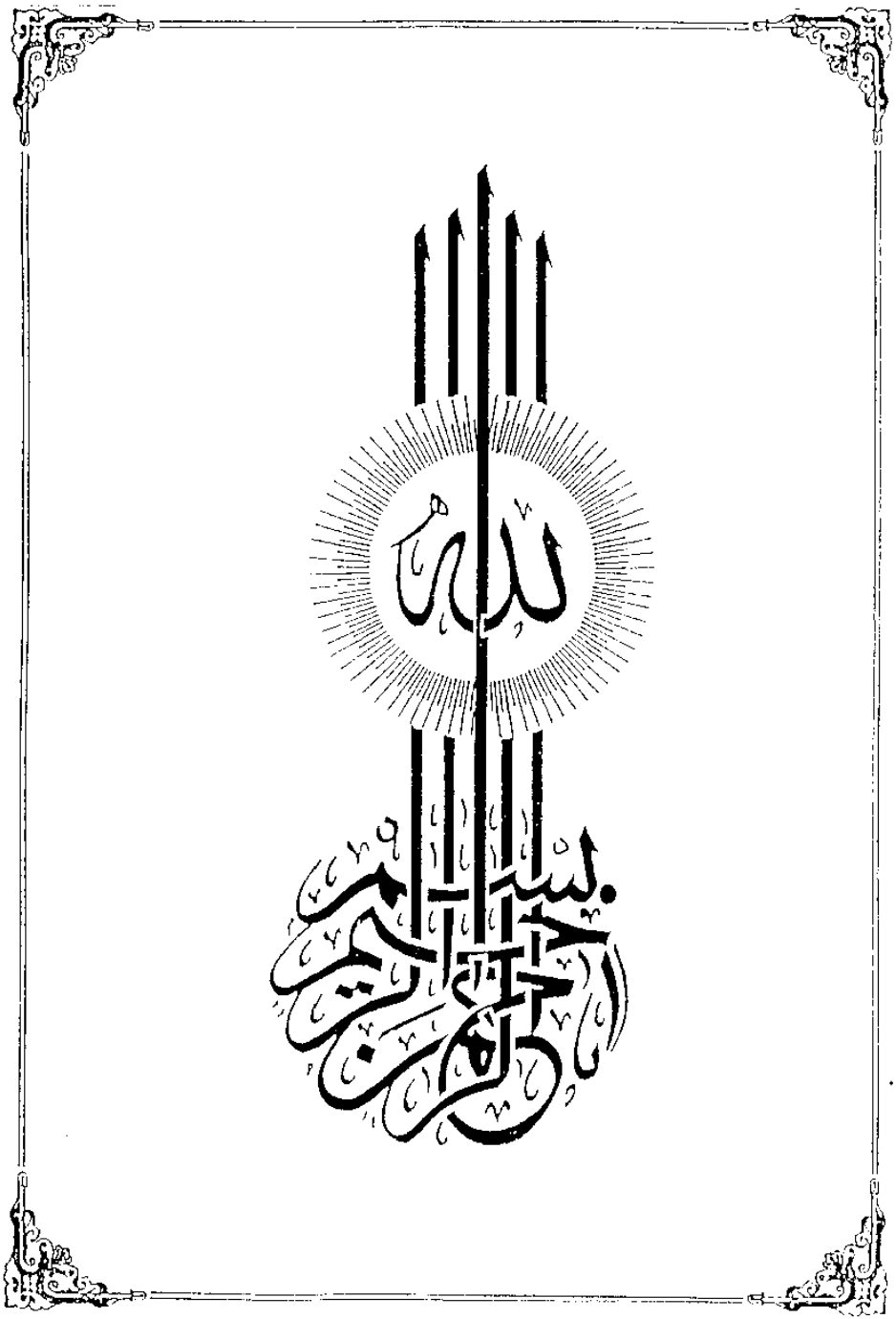

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INTRODUCTION

The fibrotic lung diseases are a heterogeneous group of chronic, sometimes fatal disorders, characterized radiographically by a pattern of interstitial infiltration and physiologically by loss of lung volume and a decrease in diffusing capacity. Histologically there is cellular infiltration of alveolar septa and an apparent increase in parenchymal collagen.

Although some patients with pulmonary fibrosis can be grouped according to etiology (e.g., occupational, environmental, infectious, tumor, or drug) or by characteristic lung pathology (e.g., granulomatous or granulomatous), many can be classified only as having idiopathic pulmonary fibrosis (IPF). While the term IPF implies that the etiology and pathogenesis of the disorder is unknown, there are clues which suggest that inflammatory and or immune-mediated mechanisms are related to the continued activity of the disease.

In contrast to IPF, chronic hypersensitivity pneumonitis is a group of fibrotic lung diseases in

which the etiology is often known. With chronic inhalation of certain organic antigens, susceptable individuals develop a granulomatous interstitial disease which often leads to significant parenchymal fibrosis. Studies have suggested that in hypersensitivity pneumonitis local immune reaction in the lungs, involving both humoral and cellular mechanisms are intimately related to the pathogenesis & activity of the disease process (Reynolds et al., 1977).

Our understanding of these diseases, however, is restricted by limitations in technology available for their study. Lung tissue is not accessible for repeated studies and radiographical, physiological and peripheral blood studies do not give a true assessment of the dynamic inflammatory and immune mechanisms operating in the local environment of the lung. The present study attempts to evaluate these mechanisms through an analysis of protein component in bronchoalveolar lavage fluid from a representative portion of the epithelial surface of the lower respiratory tract in patients with interstitial pulmonary fibrosis of different etiology.

AIM OF THE WORK:

The aim of this work is to estimate the IgG level, IgG albumin ratios in bronchoalveolar lavage and in the serum of patients with interstitial pulmonary fibrosis and to evaluate the degree and extent of lung fibrosis with the level of IgG in BALF and serum of that patients.

REVIEW OF LITERATURE

The term interstitial was originally applied to these disorders because they are associated with thickening of the alveolar septum. In a sense, however, the term "interstitial" is a misnomer, since the interstitial lung disorders are not confined to the alveolar interstitium, but generally involve alveolar epithelial and endothelial cells as well.

Anatomically, the "interstitium" is that part of the alveolar structures bounded by the alveolar epithelial and endothelial basement membranes [Weinberger & Crystal, 1979]. The normal alveolar interstitium is composed of connective tissue components (collagen, elastic fibers, proteoglycans and fibronectin) [Hance & Crystal, 1975 and Bray, 1978], mesenchymal cells (fibroblasts, pericytes and rare smooth muscle cells) [Bradley et al., 1980], and inflammatory and immune effector cells (monocytes, macrophages and lymphocytes) [Bunnlnghake et al., 1979 (1)].

A typical patient with interstitial lung disease presents with the insidious onset of breathlessness, occasionally associated with non-productive cough [Scadding, 1974]. On physical examination, the most common clinical finding is bibasilar end-expiratory dry rales [Epler et al., 1978], often associated with

The disease has been reported in all ages from infancy to old age but the majority are middle aged or elderly. It seems that the sex representation is equal. There appears to be no particular geographical distribution.

CAUSES:

A-Drugs:

1-Chemotherapeutic agents: Busulphan, Bleomycin, Cyclophosphamide, Methotrexate, Nitrosoureas, Procarbazine and Mitomycin.

2-Antibiotics: Nitrofurantoin, Sulphonamide and Penicillin.

3-Other drugs: Diphenylhydantoin, drugs inducing lupus-like syndrome, Gold salts, Hexamethonium, Mecamylamine, Methylsergide, Pentolinium, Propranolol & Carbamazine [Crystal et al, 1981 (1)].

B-Inorganic dusts:

Silica, Silicates (Asbestos, Talc, Kaolin), Sillimanite, Diatomaceous earth, Nephline, Mica, Aluminum, Antimony, Carbon, Beryllium and hard metal dust.

C-Organic dusts:

Extrinsic allergic alveolitis (inhaled fungal, avian or other protein) [Stein & Ruad, 1987]. Farmer s lung, Bagassosis, Mushroom worker's lung, Asperg- illosis, Humidifier lung, Air-condition lung and Bird breeder,s lung.

D-Gases: Oxygen, Sulfur dioxide and Chlorine.

E-Fumes: Oxides of Zinc, Copper, Manganese, Cadmium, Iron and Nickel.

F-Vapors: Mercury, Thermosetting resins and Toluene di-isocyanate.

G-Aerosols: Fats and Pyrethrum.

H-Poisons: Paraquat.

I-Radiation.

J-Infectious agents: Residue of active infection of any type.

K-Interstitial disease caused by disorders of organs other than lung: chronic pulmonary edema, chronic uremia and pulmonary venous hypertension [Crystal et al., 1981 (1)].

L-Autoimmune conditions associated with fibrosing alveolitis as Rheumatoid arthritis, Systemic lupus erythematosus, progressive systemic sclerosis, Mixed connective tissue disease, Sjogren's syndrome, Polymyositis/Dermatomyositis, Chronic active hepatitis, Autoimmune thyroid disease, Ulcerative colitis and Pernicious anemia.

M-Unknown etiology:

1- Idiopathic pulmonary fibrosis.

2- Histiocytosis-X.

3- Eosinophilic granuloma.

4- Tuberous sclerosis.

5- Pulmonary sarcoidosis.

6- Goodpasture s syndrome.

7- Familial pulmonary fibrosis.

8- Neurofibromatosis.

9- Pulmonary vero-occlusive disease.

10-Whipple s disease [Winberg et al., 1978].

11-Weber-Christian disease [Federman et al.,1976].

12-Hermansky-Pudlak syndrome [Garay et al., 1979].

The spectrum of disease included under this heading is enormous - at least 130 different interstitial lung diseases - have been described. Most of these diseases are relatively rare, the common interstitial disorders are those resulting from inhalation of

inorganic or organic dusts, sarcoidosis, idiopathic pulmonary fibrosis and the interstitial lung diseases associated with the collagen vascular disorders [Keogh et al., 1981 (1)].

While diagnosis is not usually a major problem, the management of patients with interstitial lung disease presents a different challenge. These diseases are generally progressive, often intermittent, stop-start fashion. More importantly, it is now apparent that conventional clinical, radiological and physiological assessments bear little relationship to staging the activity of these disorders, thus frustrating the clinician s attempt to make rational therapeutic decisions [Crystal et al., 1981 (1)].

EXTRINSIC ALLERGIC ALVEOLITIS

(Hypersensitivity pneumonitis)

It results from an immunological reaction in the pulmonary alveoli and terminal bronchioles. Many antigens can produce the disease. The most common antigens are the spores of micro-organisms and avian protein.

Causes of allergic alveolitis:

	Antigen source	Disease
Microbial	Thermophilic actinomycetes	Farmer's lung
		Bagassosis
		Mushroom workers lung
		Air conditioner lung
	Aspergillus clavatus	Maltworkers' lung
	Aspergillus fumigatus	Allergic aspergillosis
	Aspergillus versicolor	*Doghouse disease*
	Alternaria spp.	Wood-pulp workers' lung
	Aurobasidium pullulans/Graphium spp.	Sequoiosis
	Cryptostroma corticale	Maple bark strippers' lung
	Penicillium frequentens	Suberosis
	Merulius lacrimans	Dry rot lung
	Mucor spp.	Paprika splitters' lung
	Penicillium casei,P.roqueforti	Cheeseworkers' lung
	Lycoperdon spp.	Puff-ball lung
	Trichosporon cutaneum	Summer pneumonitis
	Bacillus subtilis	Washing powder lung
	Bacillus cereus	Humidifier lung
Animal	Budgerigar)	
	Pigeon)	Bird fanciers' lung
	Hen)	
	Turkey)	
	Fish	Fish meal lung
	Animal pituitary	Pituitary snuff-takers lung
	Animal pancreas	Enzyme workers' lung
	Podents	Podent handlers' lung
	Wheat weevil	Weevil alveolitis
Chemicals	Bordeau mixture	Vineyard sprayers' lung
	Cobalt	Hard metal disease
	Isocyanates	Isocyanate alveolitis
	Pauli's reagent	Pauli's reagent alveolitis
	Pyrethrum	Insecticide lung
	Trimellitic anhydride	TMA lung
Uncertain	Lake water	Sauna lung
	Hut thatch	New Guinea lung
	Boxwood	Pamin lung

[Seaton et al., 1989]