A HOSPITAL BASED STUDY ON PULMONARY MANIFESTATIONS OF SYSTEMIC LUPUS ERYTHEMATOSUS

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CERTIFICATE

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DECLARATION

I solemnly declare that the dissertation entitled **"A HOSPITAL BASED STUDY ON PULMONARY MANIFESTATIONS OF SYSTEMIC LUPUS ERYTHEMATOSUS"** is done by me at Madras Medical College and Hospital, during 2003-2006 under the guidance and supervision of **Prof.K.CHANDRA, M.D.** This dissertation is submitted to The Tamil Nadu Dr.M.G.R. Medical University towards the partial fulfilment of requirements for the award of **M.D. DEGREE IN GENERAL MEDICINE (BRANCH I)**.

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CONTENTS

INTRODUCTION

Systemic Lupus Erythematosus (SLE) is an autoimmune disease in which organs, tissues, and cells undergo damage mediated by tissue-binding auto-antibodies and immune complexes.

Many of its clinical manifestations are secondary to the trapping of antigen-antibody complexes in capillaries of visceral structures or to auto antibody-mediated destruction of host cells. The clinical course is marked by spontaneous remission and relapses. The severity may vary from a mild episodic disorder to a rapidly fulminant, life -threatening illness.

The lungs may conveniently be considered in six main regions: the pleural space, the parenchyma, the pulmonary vasculature, the airways, the diaphragm, and the chest wall including the ribs and respiratory muscles. Systemic Lupus Erythematosus (SLE) and the adverse effects of various therapies may affect all these regions of the chest.

Pulmonary involvement is common in SLE and will affect half of patients during the disease course and is part of the spectrum of presenting symptoms in 4% to 5% of patients[1].

Primary involvement of the lung and pleurae is common in SLE. The clinical presentation are protean and sometimes are presenting feature of the disease. Subclinical involvement also is prevalent, as shown

by the high frequency of the abnormal pulmonary function test results in patient who are free from respiratory complaints.

Furthermore, other complications of lupus such as cardiac failure or nephritic syndrome may lead to lung involvement with the development of pleural effusions. Pulmonary involvement may increase the risk of mortality; in one study, lung involvement was one of several factors that was predictive for increased mortality[2].

The prevalence of pulmonary manifestations in SLE depends on the referral pattern to the unit where patients are studied, the population under scrutiny, and the methods used to detect pulmonary involvement.

This study has been conducted to evaluate the pulmonary manifestations in SLE patients and to correlate the clinical features with radiographic findings and pulmonary function tests. The usefulness of the high resolution computed tomography (HRCT) , which is reported to be promising in the diagnosis, and the disease activity in the lung parenchyma , needs a special mention.

AIM OF THE STUDY

1. To study the prevalence of respiratory abnormalities in Systemic Lupus Erythematosus .

2. To correlate the clinical features with Plain radiographs, Pulmonary function tests(PFT) and high resolution computed tomography (HRCT).

REVIEW OF LITERATURE

HISTORICAL PERSPECTIVE

The combinations of Osler and Jadasson established that SLE was a distinct syndrome, and in 1904 Osler[3] described the occurrence of pneumonia in SLE . Further reports in the 1930s and 1940s described polyserositis , patchy lung consolidation , and other pulmonary changes including "atelectizing pneumonitis" in patients with SLE[4,5]. Autopsy of these patients showed diffuse lung consolidation with hyaline alveolar thickening and marked obliterating cellular infiltration. Baggentoss entended these observations and observed a peculiar basophilic, mucinous edema of the alveolar walls and the peribronchial and perivascular tissues in association with interstitial pneumonitis and alveolar hemorrhage. These pathologic changes were distinct from the ordinary pyogenic and fibrinous bronchopneumonia that frequently complicates the terminal stages of SLE, but they were not pathognomonic of SLE[6]. In atelectizing pneumonitis ,the alveolar walls as well as the peribronchial and perivascular connective tissues appeared to be the primary sites of an inflammatory process that obliterated alveolar spaces.

In 1953 and 1954, two patients of radiographic studies in SLE emphasized the high frequency of pulmonary involvement. Israel[7] showed. That non specific pneumonia occurred frequently, not only

during the terminal stages of SLE but throughout the course of the disease. Garland and Sisson[8] reported lung parenchymal changes in one third of their patients and observed both pleural and cardiac abnormalities to be prevalent .Comprehensive reviews of the pulmonary manifestations of SLE in adults[9-11] and in children[12] have appeared.

PATHOLOGY

A wide variety of lesions have been described in the lungs, but none are specific for SLE .For example ,an autopsy study of 54 patients showed the following pathologic abnormalities in more than 50% of cases: bronchopneumonia, hemorrhage, pleural effusion, edema, interstitial pneumonia, and congestion[6]. Fibrinoid necrosis and hemotoxylin bodies were seen[13], where as bronchiolar dilation and foci of panacinar emphysema were found[14]. Fayemi[15] 1 noted the high frequency of occlusive vascular changes of varying severity in the lungs of 7 of 20 patients with SLE; these affected arterioles, arteries and veins. The acute lesion consist of fibrinoid necrosis and vasculitis , and the chronic lesions included intimal fibrosis, medial hypertrophy, alteration of the elastic laminae and periadventitial fibrosis. Haupt et al.,[16] examined pathological changes in the lungs of 120 patients seen in the autopsy and correlate with the clinical features .In contrast to the high frequency lung involvement in clinical series[9], they showed many of the pathological changes are not caused by SLE itself, but rather by the secondary factors, such as congestive heart failure ,infection, aspiration and oxygen toxicity.

Only 18% of the lung parenchymal lesion were directly attributable to SLE. Although informative, analyse of the autopsy cases may not represent a cross-section of the general population of lupus patients and probably underestimate the prevalence of lung involvement. Certainly in the clinical setting, pulmonary abnormalities can change rapidly and subside either spontaneously or with drug therapy, so anatomic lesions may not be evident later at autopsy.

THE CLINICAL ASSESSMENT OF PULMONARY INVOLVEMENT

As with any other branch of medicine the clinical assessment of pulmonary disease in lupus patients is based on careful history, thorough examination , and appropriate further investigations.

A useful screening question is, have you been shortness of breath or had chest pain ? The most early symptom of serositis is chest pains, which occur on both inspiration and expiration. There is nothing particular about the pain that differentiates lupus from other causes of pleurisy such as infection or pulmonary embolism. resolution of pleuritic pain does not always imply improvement since pain at a particular site of the chest may disappear if a significant pleural effusion develops. Dyspnoea may be the presenting symptom of many of the other complications of lupus to affect the lung. A sudden onset is more likely to be due to pulmonary embolism, but the more usual presentation is an

insidious onset of breathlessness. An estimate of patients walking distance may is a useful guide to exercise tolerance and the extend of lung involvement. Hemoptysis may be the presenting feature of infection , infarction ,cardiac failure, or very rarely pulmonary hemorrhage. Clinically a thorough cardiac assessment is essential, with particular attention to signs of cardiac valve disease , left or right ventricular failure, and pointer towards pulmonary hypertension.

INVESTIGATION OF PULMONARY INVOLVEMENT

CHEST RADIOGRAPH

The chest radiograph is a simple and useful extension of the clinical Examination of the patient with SLE. Previous films, when available, may give valuable information on disease progression or the appearance of new lesions.

Abnormalities on chest radiographs are reasonably common in patient with SLE. For example, in a prospective study of 50 unselected patients, abnormalities were found in 38%[17], and in a study of 43 patients who were examined specifically for pulmonary dysfunction, 23% had abnormal chest radiographs[18]. In contrast , none of 70 nonsmoking patients with SLE who were free of respiratory complaints and enrolled in a study of pulmonary function had abnormal chest radiographs[27].

A wide array of abnormalities can be seen in chest radiographs. Early studies thoroughly and meticulously documented radiographic changes in the pleura ,lung parenchyma and heart. Pleural changes as an isolated abnormality or in combination with cardiac or parenchymal lesions are the most common radiographic changes[19,20]. The pleura may appear as a shaggy thickening of the pleural surface. Pleural effusions are small, and in 50% of patients, bilateral. Parenchymal lesions are characterized by ill defined focal patches, linear bands, infiltrates, small nodules, or plagues in the bases. Diffuse, granular, reticular, or reticulonodular lesions throughout the lung fields, but more prominent at the bases, are found in a small number of patients with SLE and chronic interstitial fibrosis. Cardiomegaly in minimal to moderate . Elevated diaphragms are found in 5-18% of patients[21].

In 111 patients with SLE, Levin[22] found that radiographic parenchymal changes (infiltrates or small nodules) were mostly result of secondary complications, such as infections, uremic pulmonary edema, and basilar atelectasis . Primary lupus pneumonitis was relatively rare, being found only three patients (2.7%) patients, and the diagnosis therefore became one of the exclusion.

PULMONARY FUNCTION TEST

Simple spirometry gives useful information on the pattern of pulmonary involvement. The ratio of 1 – sec Forced Expiratory Volume

to Forced Vital Capacity (FEV1/FVC) distinguishes restrictive patterns , most often due to the interstitial lung disease, from obstructive patterns due to lesions that may affect the larger airways as well as documenting lung volumes .

PFT abnormalities are exceeding common in patients with SLE, even in those without history of respiratory complaints and with normal chest radiographic findings. An impaired diffusing capacity, reduction in lung volume and hypoxia are the common abnormalities.

In 1996, Gold and Jennings[23] carried out PFT since 20 patients with SLE and respiratory symptoms and found evidence for three major changes:(1)restrictive disease, (2) airway obstruction and (3) pulmonary vascular obstruction. Twelve of the patients had evidence of restrictive disease, 3 had severe airway obstruction without pulmonary restriction, and 5 had pulmonary vascular obstruction. Three patients died and the pathologic findings in the lungs correlated with the physiologic abnormalities observed during life.

Wohlgelernter et al.,[24] found PFT abnormalities in 90% of their patients with SLE and a previous history of pleuritis and/or pneumonitis and in 71% of their without pulmonary complaints. The most common abnormalities were a decreased % Diffusion Capacity of carbonmonoxide (DLCO), lack of response to breathing helium , restrictive ventilatory defect , and arterial hypoxemia. None of their patients with chronic

discoid LE had an abnormal PFT, which is a finding consistent with the limited disease process in this condition. In a prospective study of 43 ambulatory, consecutive patients with SLE.

Silberstein et al.,[25] attempted to correlate PFT abnormalities with other measures of lupus activity. Pulmonary dysfunction was noted in 88% of the patients. An impaired % DLCO(72% of all patients) ,reduction in lung volume(49%) ,and hypoxia(44%) were the most common abnormalities that were found. No Correlation was found among the type and severity of the abnormality and with serum complement levels, anti DNA antibody , lupus-band test and nephritis. Patients with SLE and abnormal PFT results did not differ from those with normal PFT results in regard to their clinical features and immunologic findings .

In contrast, Holgate et al.,[26] reported that the patients with SLE and prominent pleuro-pulmonary disease had a lower prevalence of lupus nephritis, suggesting that this is partly a result of the low frequency of anti-DNA antibodies in this group of patients.

Andronopoulos et al[27].,conducted the largest controlled study of PFTs in patients with SLE to date. They studied 70 lifelong nonsmoking patients with SLE and an equal number of age and sex matched, non-smoking healthy subjects. None of the patients had active pulmonary disease, and all had normal chest radiographs at the time of the study. An

isolated reduction in the %DLCO was the most prevalent abnormality found in the patients with SLE (31%), but it was not found in the controls. Isolated small airway disease, which was defined as less than 60% of the predicted value of the maximal flow at 25% of vital capacity, was common in both patients with SLE (24%) and controls (17%).Restrictive and obstructive patterns were uncommon in SLE , being seen in only 5.7% of patients. Overall, only 33% of the patients with SLE had normal PFT results, compared with 83% of controls.

Eichacker et al.,[28] evaluated the PFT's of 25 patients with SLE serially over a period of 2 to 7 years. Reduction in diffusing capacity, FVC, and TLC did not change significantly with time. In contrast, small airway function decreased significantly with time and appeared not to be related to smoking history. The significance of this finding is not clear, however, in view of the finding by Andronopoulos et al[27], that the prevalence of small airway disease in patients with SLE is same as that in healthy controls. In the absence of respiratory symptoms, isolated abnormalities in PFT such as a reduced DLCO do not require treatment but should be monitored, and further investigation with HRCT chest scanning should be considered.

HIGH RESOLUTION COMPUTED TOMOGRAPHY (HRCT)

High resolution CT (HRCT) is an essential tool in the evaluation of lung disease in SLE. Early inflammatory lesion may be visualized as

alveolar or ground glass shadowing, and later in the disease course fibrotic lesions may be visible as fixed reticular honeycombing. These finding of late inspiratory crackles at the lung bases.

The radiographic findings is acute lupus pneumonitis consist of patchy unilateral or bilateral areas of ground –glass opacity or air-space consolidation , often associated with pleural effusions.

Alveolar hemorrhage is manifested radio logically by bilateral, patchy, ill-defined areas of consolidation involving mainly the lower lung zones. Radiographic evidence of interstitial fibrosis is seen in a small percentage of patients who have SLE. It was reported in 3 or 28 patients in one series[29].

Horizontal lines shadows are seen relatively common in patients who have SLE. They are usually present in the lung bases, are usually migratory, and are attributable to subsegmental atelectasis. Cavitary pulmonary nodules are rare. The lesion can be as a result of infection or infarction.

In a prospective study of 48 patients who had serologically confirmed disease but no prior clinical evidence of pulmonary involvement, chest radiographs demonstrated evidence of fibrosis in 6% and were normal in 94%[30] . Of these who had normal radiographs, 38% had abnormal findings on HRCT. The most common abnormalities were interlobular septal thickening, intralobular interstitial thickening, small

rounded areas of consolidation and areas of ground-glass attenuation. The abnormalities occurred mainly in the lower lobes. The fibrosis involved mainly the subpleural lung regions.

In another prospective study, 34 patients who had SLE were assessed using chest radiography, HRCT, and pulmonary function tests[31]. The plain chest radiograph was abnormal in 8 patients (24%), Pulmonary function abnormalities were present in 14 (41%), and HRCT abnormalities were identified in 24 (70%). The authors reported that 11 patients (32%) had definite evidence of interstitial lung disease, which was mild in 5 patients and moderately advanced in 6. Nine of the 11 patients who had evidence of interstitial lung disease on HRCT were asymptomatic, 7 had normal chest radiographs, and 4 had normal pulmonary function tests. Airway disease-defined as bronchial dilation or bronchial wall thickening-was observed in 12 patients (9 of whom had never smoked cigarettes).

As might be expected, the prevalence of parenchymal abnormalities is highest in patients who have long standing SLE and chronic respiratory symptoms . In one study of 10 patients who had mean duration of SLE of 7.5% years and who had respiratory symptoms for a mean of 2.5 years, all patients had abnormal pulmonary function tests and HRCT scans (4 had normal chest radiographs)[32] . The most common abnormalities on HRCT were areas of ground glass attenuation (seen in 8 patients), honeycombing (in 7), and pleural thickening (in 8). Two

patients had airway abnormalities, consisting of bronchial dilation in one and centrilobular nodular and branching linear opacities (“tree in bud” appearance) in the other.

NUCLEAR MEDICINE IMAGING

Ventilation Perfusion (VIQ) Scans

In any patient with SLE presenting with breathless and pleuritic pains, the possibility of pulmonary embolism should be considered. V/Q scans offer a simple and reasonably reliable screening test for pulmonary embolism that can be used with CT pulmonary angiography where the results are indeterminate .V/Q scans may also be abnormal in the absence of pulmonary embolism, and severe pulmonary hypertension may produce an appearance of hypoperfusion in the peripheral areas of the lung. The combined use of D-dimer assays, V/Q scanning, and where the appropriate, CT pulmonary angiography may raise the accuracy in diagnosing pulmonary embolism[33] Gallium-67 scans have been useful in the diagnosis and monitoring of patients with sarcoidosis, but there is little data on their use in the assessment of pulmonary disease in the lupus.

Witt et al.[34] studied lupus patients with interstitial lung disease and found an association between the presence of late inspiratory crackles clinically and increased uptake on Gallium–67 scanning and abnormal broncho alveolar lavage. However, abnormal Gallium–67 scans were

seen in only 37% of SLE patients compared to a prevalence of 74% with late inspiratory crackles and 95% of patients with abnormal CT chests, making the scans somewhat insensitive at picking up interstitial lung disease.

ARTERIAL BLOOD GASES

Arterial blood gases give an accurate estimate of alveolar ventilation .It is essential in the assessment of pulmonary embolism, extensive pulmonary infiltration, severe pneumonia, pulmonary hemorrhage, and acute reversible hypoxemia where (type I respiratory failure) may occur.

BRONCHOSCOPY AND BRONCHOALVEOLAR LAVAGE (BAL)

These techniques may be useful when evaluating the etiology of interstitial pulmonary shadowing in patients with lupus. BAL fluid may be examined to exclude opportunistic infections especially in immuno suppressed patients. In patients with suspected interstitial lung disease where CT chest images show ground–glass shadowing with a honey comb appearance, elevated cell counts in BAL fluid may suggest alveolar inflammation and direct treatment with immunosuppressive agents once infection has been excluded.

The technique of BAL facilitates the analysis of cellular and soluble components from the epithelial surface of the lower respiratory tract. BAL has yielded valuable information about immune responses and

the pathogenesis of lung injury in the connective tissue diseases, especially Systemic sclerosis and Rheumatoid arthritis (RA) .BAL findings may be diagnostic in some diseases, such as infections; in others, however, findings are nonspecific but may contribute to the management of these diseases. For example, an increased of BAL eosinophils were associated with progressive lung disease in Idiopathic Interstitial pulmonary fibrosis, and Scleroderma[35].

In a multicenter study designed to standardize the test procedure, BAL was performed in 24 patients with diffuse ILD, secondary to rheumatic disorders, including SLE[36]. The total number of cells in the BAL fluid was increased with the percentage increase in neutrophils and decrease in macrophages. Total protein, Immunoglobulin M (IgM), IgG, and IgA, but not albumin, increased in concentration in the BAL fluid. Wataert et al.[37] studied BAL fluid in 61 patients with collagen vascular disease without symptoms, and included in their study were 11 patients with SLE, all of whom had normal PFT results. An abnormal differential count of BAL fluid leukocytes was found in 48 of patients, including three with SLE .In contrast to patients with RA and systemic sclerosis, who had a predominant polymorphonuclear alveolitis, patients with SLE showed a lymphocytic predominance. An increased percentage of BAL fluid eosinophils was also found in two patients with SLE and ILD[35]. Similarly, Witt et al[34] found elevated lymphocyte and neutrophil counts in the BAL fluid from 19 lupus patients.

Alveolar macrophages in BAL fluid from 17 patients with inactive SLE were found to be normal in number, viability, and respiratory burst activity, but had severely impaired antibacterial function[37]. This dysfunction, which was observed in both steroid –treated and untreated patients, may contribute to the increased frequency of pulmonary infections in this disease.

Wataert et al.[38] introduced the concept of subclinical alveolitis in SLE and in other systemic rheumatic diseases, which is characterized by the accumulation of inflammatory and immune cells in the BAL fluid of patients without respiratory with a normal chest radiograph, and with or without significant PFT abnormalities. The clinical significance of subclinical alveolitis, however is not clear since it is not known how many of these patients will develop overt interstitial lung disease.

Higher concentrations of soluble immune complexes have been observed in BAL fluid compared to the corresponding serum specimen from patients with ILD associated with rheumatic diseases, including SLE[39] .Immune complexes were also seen within the cytoplasm of BAL neutrophils ,indicating that locally formed immune complexes may induce an inflammatory response in the lungs of these patients.

Increased numbers of activated CD8: T lymphocytes and natural killer (NK) cells were found in the BAL fluid of lupus patients with abnormal Pulmonary function tests and correlated with reduced carbon

monoxide transfer factor and diffusing capacity values[40]. In contrast the number of CD19+ B cells in the BAL fluid was lower than that seen in the fluid of healthy controls, despite the high percentage of these cells in SLE peripheral blood .The observations suggest a cell-mediated immune response in the lungs in SLE[40].

BAL, therefore may be a potentially useful technique in the assessment and follow –up of patients with SLE and pulmonary involvement, especially in those with acute lupus pneumonitis and chronic diffuse ILD.

CLINICAL MANIFESTATIONS OF PULMONARY INVOLVEMENT IN LUPUS

Respiratory tract involvement occurs in about half of the lupus patients over their disease course. The following sections describe the main features of lung disease in SLE.

The various pulmonary manifestations are classified as follows:

PLEURAL DISEASE

- Pleuritis with and without effusion.

PARENCHYMAL DISEASE

- Acute lupus pneumonitis
- Interstitial pneumonitis and fibrosis
- Pulmonary hemorrhage

VASCULAR DISEASE

- Pulmonary artery thrombosis
- Pulmonary thromboembolism
- Pulmonary hypertension

AIRWAY DISEASE

- Obliterative Bronchiolitis
- Bronchiolitis obliterans organizing pneumonia

NEUROMUSCULAR DISEASE

- Diaphragmatic dysfunction

THE PLEURA IN SLE

Pleurisy

Pleurisy is the most common manifestations of pulmonary involvement in SLE, and the pleura is involved more commonly in lupus than in any other connective tissue disease. Several early studies documented the prevalence of pleural involvement. For example, in Dubois and Tuffanelli's[41] 520 patients, the cumulative incidence of recurrent pleuritic pain was 45% and that of pleural effusions was 30%. McGehee Harvey et al.[42] reported pleurisy in 56% of their patients with recurrent pleuritic episodes in 13% , while 16% had associated pleural effusions .

Several other studies have documented high prevalences of pleuritis, ranging from 41% to 56% [19,43], being found more commonly in blacks than whites[44]. Perhaps the largest study to date, that of 1000 European lupus patients, found a prevalence at disease onset of serositis (including) both pleural and pericardial inflammation) of 17% with a cumulative incidence of 36% ,with pleuritis occurring more commonly in men than in women[45]. Lung involvement defined as acute or chronic lupus pneumonitis was much less common, with a prevalence at disease onset of 3% and cumulative incidence of 7%-almost certainly an underestimate. The highest prevalence comes from a postmortem study:

Ropes[46] described pleural changes in 93% of 58 patients with SLE at autopsy, with fluid in the pleural cavity in 33 cases.

CLINICAL FEATURES

Pleurisy as the initial manifestations of SLE was noted by Dubois[47] in 13 of 520 patients. Pleuritic symptoms may antedate other manifestations of lupus by months or even years, resulting in a delay in the diagnosis of SLE[48].

Pleuritic chest pain may be unilateral or bilateral, and is usually located at the costophrenic margins, either anteriorly or posteriorly. Attacks of pleuritic pain often last for several days, and when associated with effusions, the pain may persist for weeks often accompanied by cough, dyspnea, or fever. The effusion generally occurs on the side of the

chest pain. Pleural effusions may also occur in patients with SLE and nephrotic Syndrome; infections such as tuberculosis; or cardiac failure[18]. Massive bilateral pleural effusion is a rare presenting feature of the disease[49]. It is important to remember that the differential diagnosis of pleuritic pain in a patient with lupus may include infection and pulmonary embolism, especially in the presence of antiphospholipid antibodies.

PLEURAL FLUID

The volume of pleural effusions usually is small to moderate (400 to 1000 ml) and may be unilateral or bilateral. Large pleural effusions are uncommon[9,50]. Thoracocentesis is not always necessary in lupus patients unless the cause of the pleural effusion is uncertain and infection is suspected. The pleural fluid is SLE is usually exudative in character, although transudates have also been reported[9]. The fluid can be yellow, amber, or slightly turbid in color. In a study of 14 patients with lupus pleuritis[50], the white cell count in the pleural fluids ranged from 325 to 14,950 cells/ml (mean 4,895 cells/ML). Half the specimens showed a predominance of polymorphonuclear leukocytes, with cell counts ranging from 10% to 100% (mean, 57%). Kelley et al.[51] examined pleural effusions from ten patients with SLE and found atypical cells resembling plasma cells. The presence of these cells with other inflammatory cells, fibrinoid debris, erythrocytes and few mesothelial cells and in the absence of pathogenic organisms or malignant cells constituted a pattern that was characteristic of SLE in eight of the ten patients studied.

In most patients with lupus pleuritis, the pleural fluid glucose concentration is greater than 60 mg/dl, with a pleural fluid/serum glucose ratio of greater than 0.5. Good et al.[50] found the mean pleural fluid /serum glucose ratio to be 0.3 or lower. This contrasts with the findings of low glucose levels in the pleural fluids of patients with RA and pleurisy, in whom the glucose concentration is less than 30 mg/dl in 75% of patients[52]. Low glucose concentration, or a low pleural fluid/serum glucose ratio, may also occur in those with malignant effusions, empyema, or tuberculosis[52] . The pH of SLE pleural fluid usually is greater than 7.35. A few patients have a pH of less than 7.3%, which is associated with a low pleural fluid glucose level [50,52].

Classic LE cells have been documented in smears of pleural fluids from patients with SLE [50,53,54]. It has been suggested that the presence of in vivo LE cells in the pleural fluid is highly characteristic with SLE[55]. However, the LE cell test is now largely obsolete and has been replaced by searching for antinuclear antibodies (ANAs) in pleural fluid[11].

The presence of ANA's in the pleural fluid may be a useful diagnostic test for patients with undiagnosed pleural effusions. For instance, Leechawengwong et al.[56] tested pleural fluid from 100 consecutive patients with pleural effusion and found positive ANA in all seven patients with SLE and in one patient with drug induced LE, but not in patients with other diagnosis. Conversely, Small et al.[57] found that a positive ANA in the pleural fluid was not specific for SLE ; it

also was found in patients without SLE but with pleural effusions who tested positive for ANA in the blood. Khare et al.[58] found positive ANA in eight of 74 non–lupus pleural effusions (10.8%), including those associated with malignancy.

Good et al.[50] measured the ANA titer in paired samples of pleural fluid and serum of patients with SLE .In lupus pleuritis , the pleural fluid/serum ANA ratio was greater than 1. In contrast the ratio with less than 1 in patients with SLE who had pleural effusions from other causes, such as congestive heart failure. Moreover, none of 67 patients with pleural effusions of different causes had a positive ANA.

ACUTE LUPUS PNEUMONITIS

Acute lupus pneumonitis is an uncommon clinical manifestation of SLE. Patients with acute lupus pneumonitis usually present with fever, dyspnoea, cough productive of scanty sputum, hemoptysis, tachypnea, and pleuritic chest pain[59] physical finding commonly include basal crepitations, and, when severe central cyanosis may be present.

In Estes and Christians[43] series of 150 patients, 48% had evidence of pulmonary involvement at sometime during the course of their illness, but only 14 (9%) had acute lupus pneumonitis.

Acute lupus pneumonitis carries a poor prognosis. Of 12 patients reported by Matthay et al.,[59] the mortality was 50% during the acute

episode from respiratory failure, opportunistic infection and thromboembolism. All six surviving patients remained relatively well after more than a year follow–up, but three developed residual interstitial infiltrates with abnormal pulmonary function tests, indicating the acute process can progress to chronic interstitial lung disease. Adult respiratory distress syndrome (ARDS) may occur with acute lupus pneumonitis, greatly increases the risk of mortality.

PULMONARY HEMORRHAGE

Pulmonary hemorrhage is a rare, devastating, and frequently fatal manifestation of SLE with mortality rates of 70% to 90%. Frank hemoptysis does not always occur, even with massive intra-alveolar hemorrhage, so the clinical diagnosis is often delayed. For example, in a series of 140 patients with SLE, three developed pulmonary hemorrhage, and in two of these patients the diagnosis was made only at autopsy[60].

The triad of anemia, air space consolidation and hemoptysis should suggest the possibility of diffuse alveolar haemorrhage. Anemia with a dropping hematocrit in the face of worsening radiologic abnormalities is characteristic. Many patients have concomitant lupus nephritis. With cessation of bleeding, radiographic and clinical improvement is rapid. The morality rate has generally been reported to be in excess of 50%[60].

CHRONIC DIFFUSE INTERSTITIAL LUNG DISEASE

Diffuse ILD is a well recognized pulmonary manifestation of systemic rheumatic diseases. Particularly systemic sclerosis, Dermatomyositis, and Rheumatoid arthritis. The initial presentation of diffuse ILD in SLE can be one of the two types. The more common is an insidious onset of a chronic nonproductive cough, dyspnea on exertion, and history of recurrent pleuritic chest pain. Less commonly, ILD may develop in a patient following acute lupus pneumonitis: two studies suggest that between 43% and 50% of patients with acute lupus pneumonitis may go on to develop chronic diffuse ILD.

ILD can occur at any time during the courser of SLE, but most cases develop in those with long-standing disease. Most patients have multisystem involvement and test positive for both ANA and anti–DNA antibodies.

In the study by Eisenberg et al.,[61], the mean age of their 18 patients with SLE and ILD was 45.7 years, with a mean disease duration of 10.3 years. Pulmonary manifestations were present for a mean of 6 years. Initially, 7 patients presented with pulmonary symptoms .All had dyspnoea on exertion, and 3 were dyspnoeic, even at rest.12 complained of cough with scanty sputum ,and a similar number had pleuritic chest pain. All patients had poor diaphragmatic movement, with diminished resonance to percussion over the lung bases. Cyanosis and clubbing was

present in 1 patients, and 12 had basilar rales. All 18 had persistent, diffuse interstitial infiltrates on chest radiography. A pleural reaction was present in 9 patients and plate like atelectasis in 6.

HIGH RESOLUTION CT SCANS IN INTERSTITIAL LUNG DISEASE

High-resolution CT scans (HRCT) of the lungs have been reported to be promising in the diagnosis, assessment of disease activity in the diagnosis, assessment of disease activity in the lung parenchyma, and a providing prognostic information in ILD.

Johkoh et al.,[62] compared HRCT lung scans and pulmonary functions tests in idiopathic pulmonary fibrosis and ILD associated with SLE. The extent of morphologic changes that were observed correlated with severity of impairment of diffusing capacity in both groups. The effectiveness of corticosteroids for treatment was reasonably predicted. Steriod-responsive patients showed a ground glass and alveolar consolidation and no honeycomb lesions on the HRCT scans. On the other hand, patients who failed to respond to therapy had severe honey comb lesions on the HRCT scans.

PULMONARY EMBOLISM

Pleuritic chest pain and dyspnea are relatively common, and most patients with SLE presenting with these symptoms usually have pleurisy

or pneumonitis. However, pulmonary embolism (PE) should always be considered especially if antiphospholipid antibodies are present or there is a previous history of PE. The predictive value of V/Q scans, D-dimer levels, and CT pulmonary angiography has been discussed above and it should be remembered that abnormal perfusion scans may occur in patients with active lung disease in the absence of PE. Nevertheless, if PE is suspected clinically in a patient with a low probability V/Q scan, angiography should be performed.

Peripheral deep venous thrombosis (DVT) is common in patients with SLE and predisposes to PE[12,41,43,63]. Perhaps the most widely recognized risk factor for venous thromboembolism in SLE in the presence of circulating lupus anticoagulants and other antiphospholipid antibodies[64-66]. In European study of 1000 patients, antiphospholipid antibodies including the lupus anticoagulants were significantly associated with thrombosis, fetal losses, thrombocytopenia, and livedo reticularis[45]. Patients who develop DVT and/or PE in the context of antiphospholipid antibodies will usually require lifelong anticoagulation[67].

PULMONARY HYPERTENSION

Clinical presentation

Severe symptomatic pulmonary hypertension (PHT) is a relatively rare manifestations of lung involvement in SLE, but mild subclinical cases are surprisingly common with prevalences 5% and 14%.

Perez and Kramer[71] were the first to report four patients with severe PHT in a group of 43 patients with SLE over a period of 2 years. Other studies, however found rather lower prevalences[72]. Of great interest in a five-year follow-up study of a cohort of lupus patients that showed that the prevalence of PHT rose from 14% to 43% with the mean pulmonary artery pressures rising from 23.4% mm Hg to 27.5mm Hg[73].

The clinical diagnosis of PHT is difficult to make in early and mild cases, and only the severe cases, with right ventricular hypertrophy and/or congestive heart failure, have been reported in the literature. Pulmonary artery pressure at rest and during exercise is significantly higher in unselected patients with SLE as compared to normal subjects, probably secondary to increased pulmonary vascular resistant in lupus patients[74]. A study of the prevalence and the severity of PHT in a group of 36 patients with SLE and healthy controls was undertaken by Simonson et al.[75] using two dimensional and Doppler echocardiographic date to calculate pulmonary artery systole pressure. Five patients (14%) and none of the controls had PHT, as defined by a pulmonary artery pressure of greater than 30 mmHg. This study suggests that PHT is common in SLE, but usually mild in degree. Conceivably, mild cases of PHT in SLE may improve with systemic corticosteroid and/or cytotoxic drug therapy given for other organ involvement, so that mild PHT remains unrecognized.

The symptoms of PHT in SLE are in general similar to those of patients with idiopathic or primary PHT[72]. In most of the reported cases, the symptoms of PHT occurred within a few years of onset of the

multisystem disease, with a mean duration of approximately 2.3 years[72]. The most common complaints are dyspnea on exertion, chest pain, and chronic nonproductive cough. Chronic fatigue, weakness, palpitations, edema, and /or ascites may also occur. Symptoms usually develop insidiously and progress gradually. The physical findings may include a loud second pulmonary heart sound, systolic murmur, and right ventricular lift. Chest radiography findings include cardiomegaly with a prominent pulmonary artery and clear lung fields. Electrocardiography may show changes of right ventricular hypertrophy. Although PFTs may show restrictive abnormalities, these are mild in degree and disproportionate to the severity of the PHT. Pulmonary angiograms in severe cases demonstrate symmetric dilation of the central pulmonary artery trunk, with pruning of the peripheral blood vessels. Cardiac catheterization is the definitive investigation and demonstrates the characteristic elevation of the pulmonary artery pressure and normal wedge pressure with out evidence of intracardiac or extracardiac shunting.

REVERSIBLE HYPOXEMIA

A relatively rare syndrome of acute reversible hypoxemia in acutely ill patients with SLE but without evidence of parenchymal lung involvement may occur[68-70]. The first description was b y Abramson et al.[68].

Among 22 inpatients with acute disease exacerbation, six (27%) had this syndrome. Although some patients had mild pleuropulmonary symptoms, chest radiographs and lung scans were normal. The patients had hypoxemia and hypocapnia with a wide alveolar-arterial (A-a) gradient, which reversed with corticosteroid therapy. The pathogenesis of the syndrome is unclear, but a correlation between hypoxemia and the level of complement split products was noted, and others have suggested a relationship with disease activity[69]. Complement activation may lead to diffuse pulmonary injury with the aggregation of neutrophils in the lungs similar to that seen in cardiopulmonary bypass, hemodialysis with cuprophane membranes, and ARDS.

SHRINKING LUNG SYNDROME

In 1965, Hoffbrand Beck[76] described a group of patients with SLE with breathlessness and reduce chest expansion, but no cyanosis, clubbing, or abnormal auscultatory findings. Many of the patients had a previous history of pleurisy. Chest radiography revealed clear lung fields but with an elevated diaphragm, which moved sluggishly and paradoxically .The vital capacity was extremely reduced.

The authors coined the term shrinking lung syndrome and suggested that the main pathologic lesion is that of alveolar atelectasis secondary to deficiency of the surface tension reducing film that lines the normal alveoli. Gibson patients by determining the transdiaphragmatic

pressure using a double-balloon technique, and they found it to be grossly abnormal. This finding led them to suggest that diaphragmatic dysfunction, rather than parenchymal or pleural disease, accounts for the unexplained dyspnea in these patients. Martens et al.[78] concluded that the restrictive ventilatory defect in these patients results primarily from the weakness of expiratory and inspiratory muscles.

Diaphragmatic dysfunction correlated with the degree of dyspnea but not with overall disease activity, proximal muscle weakness, or serologic markers. Contrary to these reports, however, Laroche et al.[79], using a wide range of tests for determining respiratory muscle strength, found no evidence of isolated weakness of the diaphragm in 12 patients with SLE and this syndrome. The discrepancy between their results and those of previous studies is not entirely clear, but it may result partly from patient selection and differences in the methods that were used to assess diaphragmatic function.

The pathogenesis of the diaphragmatic weakness in patients with SLE is not well understood. Wilcox et al.[80] found no evidence of phrenic nerve neuropathy as the cause of this weakness. Diffuse fibrosis of the diaphragm without evidence of acute inflammatory infiltrates was observed in one patient examined at autopsy[81], supporting an extrapulmonary, restrictive cause for this unusual syndrome.

An electromyographic study of the diaphragm and external intercostal muscles demonstrated that fatigue of the respiratory muscles occurs at lower loads in patients with SLE as compared to those in healthy controls[81].Whether myopathy is an isolated process affecting primarily the diaphragm and other respiratory muscles or is part of a generalized muscle disease in SLE is not entirely clear. When the diagnosis of shrinking lung syndrome is suspected, measurements of transdiaphragmatic pressures and elastic recoil of the respiratory system should be considered.

The clinical course of the syndrome is a chronic, low grade restrictive defect. Follow –up of some patients over a period of several years has shown that the volume restriction is not progressive[77,78]. In symptomatic patients, prednisone therapy (30 to 60 mg daily for several weeks) is clinically beneficial and tends to stabilize the PFT abnormalities[83-85]. Agonist agents and theophylline may also be useful in the treatment of this syndrome[86,87].

AIRWAY OBSTRUCTION

Severe airway obstruction has been reported in a small number of patients with SLE[88,89]. Lung biopsy in one patient showed obliterative bronchiolitis and an acute inflammatory process that affected small bronchi and bronchioles, resulting in necrosis and eventual endobronchial proliferation of epithelial cells and peribronchial infiltration by

lymphocytes. Dense plugs composed of alveolar debris and fibrin strands within the bronchioles caused partial or complete obstruction. Bronchiolitis obliterans with organizing pneumonia has been described in SLE[90].

Evidence of airway obstruction has been described in several controlled studies of PFT in patients with SLE[91-94]. Some series did not take into consideration the effect of cigarette smoking, but in those that did it was evident that airway obstruction occurred even in nonsmoking patients with SLE. The frequency of airway obstruction is variable, primarily because of differences in the criteria that are used to define the abnormality and in the selection of patients.

In the only controlled study of lifelong nonsmoking patients with SLE, Andonopoulos et al.[27] observed a high prevalence (24%) of isolated small airway disease in patients with SLE.

The clinical significance of this observation remains unclear, however, because a similarly high frequency (17%) of small airway disease was found in their healthy, non smoking age-and sex –matched controls.

Very occasionally the upper airways have been affected in lupus. Case reports have described hypopharyngeal ulceration, laryngeal inflammation, vocal cord paralysis, epiglottitis and subglottic stenosis.

MATERIALS AND METHODS

Data for the study were collected from patients diagnosed to have SLE and attending regular follow up at the Department of Rheumatology, and at the Institute of Internal Medicine, Madras Medical College and Research Institute, Chennai. The above patients were investigated for Pulmonary abnormalities at the Department of Rheumatology and the Institute of Internal Medicine. Serological investigations were done at the Immunology Department. Pulmonary Function testing was done at Institute of Internal Medicine. High resolution Computed tomography was carried out in the Barnard Institute of Radiation and Oncology (BIRO), Madras Medical College.

STUDY PERIOD

The study was conducted during the period Feb 2005 to Feb 2006. Thirty SLE patients were enrolled for the study after satisfying inclusion and exclusion criteria. After enrollment, the patients were evaluated for the presence of pulmonary abnormalities.

STUDY DESIGN

To evaluate the pulmonary profile in patients with SLE, prospective study design was chosen. The cases were selected based on inclusion and exclusion criteria.

CASE IDENTIFICATION AND VALIDATION

Patients who were diagnosed to have SLE and were attending the Department of Rheumatology and the Institute of Internal Medicine for regular follow up during the period Feb 2005–Feb 2006 were examined and the possibility of inclusion in our study and evaluated.

Patients were diagnosed as having SLE based on the American College of Rheumatology (ACR) criteria.

1. Malar Rash
2. Discoid Rash
3. Photosensitivity
4. Oral ulcers
5. Arthritis
6. Serositis
7. Renal Disorder
8. Neurologic Disorder
9. Hematologic Disorder
10. Immunologic Disorder
11. Antinuclear Antibodies(ANA)

If four of these criteria are present at any time during the course of disease, a diagnosis of Systemic Lupus can be made.

INCLUSION CRITERIA

A patient with SLE diagnosed on the basis of the American College of Rheumatology (ACR) criteria.

EXCLUSION CRITERIA

The following patients were excluded from the study.

1. Smokers
2. COPD
3. Pulmonary Tuberculosis(PT)
4. Bronchial asthma
5. Chronic Lung disease
6. Patients with exposure to dusts

The patients were questioned about the duration of the disease and enquired whether they had symptoms of respiratory disease or not. They were then divided into symptomatic patients.

Among the symptomatic patients, a questionnaire were prepared to extract details about respiratory complaints .The duration of symptoms namely cough, breathlessness, chest pain, hemoptysis were noted .

The patients were asked whether they developed the symptoms before or after the diagnosis of SLE. If pulmonary symptoms were present before the diagnosis of SLE, then the cases were excluded. Also if

patients had chest pain, breathlessness of cardiac origin, they were excluded from the study.

Patients with history of smoking, chronic obstructive pulmonary Disease (COPD), Previous history of Pulmonary Tuberculosis, Bronchial Asthma and Chronic lung disease were excluded. Also patients with occupational exposure to dusts were excluded.

Patients with history of smoking, chronic obstructive pulmonary Disease (COPD), Previous history of Pulmonary Tuberculosis, Bronchial Asthma and Chronic lung disease were excluded. Also patients with occupational exposure to dusts were excluded.

EVALUATION OF CASES

Patients who were included in the study were admitted in the Medical/ Rheumatology wards and through physical examinations was carried out to disclose respiratory findings. After clinical exam, the patients underwent laboratory investigation like complete hemogram, renal parameters, etc.

Preliminary imaging was done with chest skiagram, Serological testing included anti nuclear antibody (ANA), double Stranded DNA(ds DNA) anti Sm antibody, for all patients.

Then the patients were subjected to subsequent radiological imaging with High Resolution CT and Pulmonary Function Testing.

TECHNIQUE OF HIGH RESOLUTION TOMOGRAPHY

CT is based on the principle that the internal structure of an object can be reconstructed from multiple projections of it. The CT image is a two– dimensional representation of a three-dimensional cross – selectional slice, the third dimension being the section or slice thickness. The CT image is composed of multiple picture elements known as pixels.

A pixel is a unit area, ie, each square on the image matrix, it reflects the attention of a unit volume of tissue or voxel, that corresponds to the area of the pixel multiplied by the scan collimation. The x-ray attention of the structures within a given voxel are averaged to produce a image. This volume averaging results in loss of spatial resolution, the thicker the slice, the lower the ability of CT to resolve small structure. Slice thickness can be varied to provide optimal assessment. For instance, in the evaluation of fine parenchymal detail such as interlobular septa, thin sections (1-2mm) are superior to thicker sections (7-10mm). More over, as section thickness increase noise increases and gainer images result[31] .

A conventional CT scan of the chest consists of a series of individual cross-sectional slices obtained during suspended respiration. After each slice is obtained, the patient is allowed to breath while the table is moved to the next scanning position. This method of obtaining a series of individual cross–sectional images is known as incremental CT scanning.

Spiral (Helical) CT is a major technical advance that allows continuous scanning while the patient is continuously moved through the gantry. The continuous nature of the data acquisition allows true volumetric scanning and the production of multiple over lapping images that result in increased spatial resolution in the longitudinal axis.

In the majority of the cases, the CT scan data are reconstructed by using a standard or soft tissue algorithm that smooth the image and reduces visible image noise. This reconstruction algorithm is preferred in the assessment of abnormalities of the mediastinum and chest wall. It reduces image soothing and increases spatial resolution, thereby allowing better visualization of small abnormalities. The combination of thin section CT (1-2mm) and a high spatial frequency reconstruction algorithm provides for the optimal assessment of interstitial and air space lung disease and is referred to High Resolution CT (HRCT).

The main indications for the use of HRCT (1-2mm, high –spatial frequency reconstruction algorithm) include:

1. Diagnosis of Bronchiectasis

2. Detection of Parenchymal Lung Disease. Patients with symptoms or pulmonary function abnormalities suggestive of parenchymal lung disease but normal or questionable radiographic findings can be assessed.

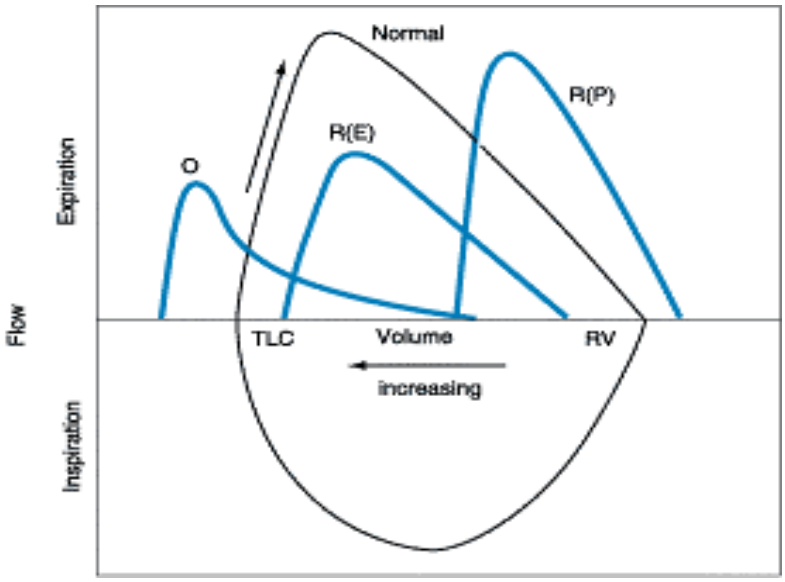
3. Differential Diagnosis of Diffuse lung disease HRCT can be used to assess patients in whom the combination of clinical and radiographic findings does not provide a confident diagnosis and further radiographic assessment is considered warranted. This indication in particular include patients with chronic interstitial and air space disease and immune comprised patients with acute parenchymal abnormalities, in such patients the different diagnosis can be narrowed or a specific diagnosis often made on HRCT even when the radiographic findings are non specific.

PULMONARY FUNCTION TESTS

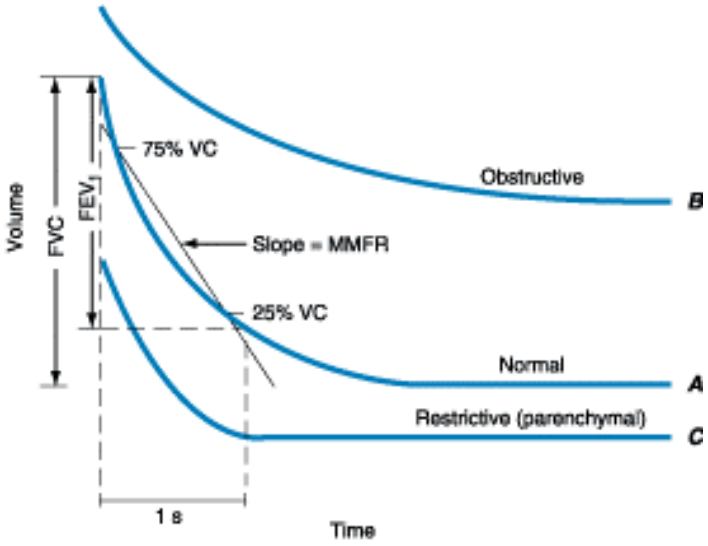
The clinical significance of pulmonary function test has been established exemplifying the statement of sterling “the physiology of today is the medicine of tomorrow”. The pulmonary function tests (PFTs).

1. Give an objective evidence of lung function that has been deranged by the disease process involving the bronchial tree and the lung, the pulmonary vasculature and the chest bellows.

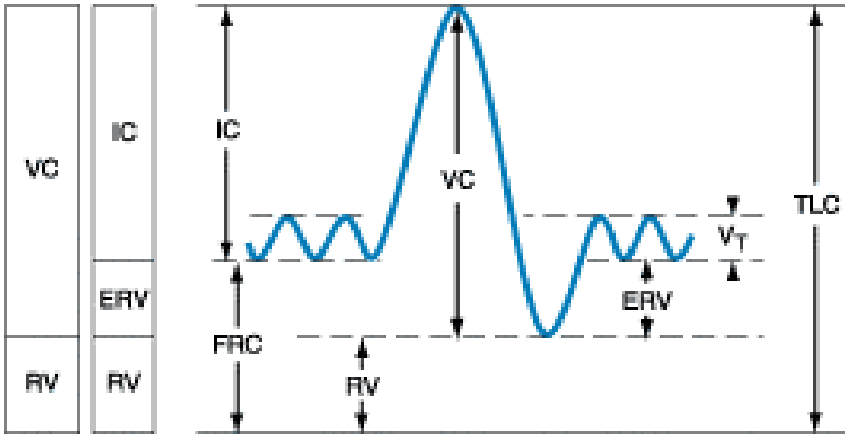
2. Help to execute a respiratory cause of breathlessness.



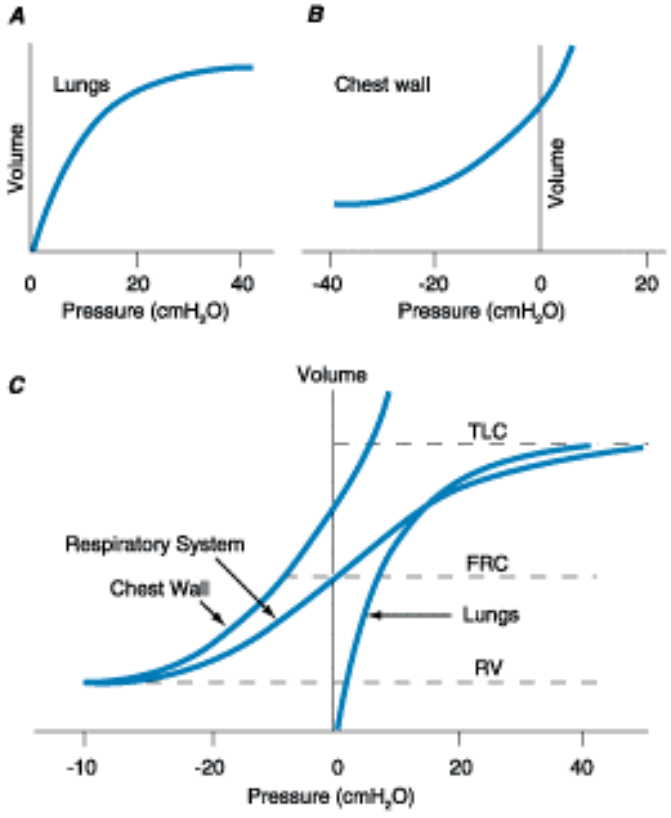
Flow-volume curves in different conditions: O, obstructive disease; R(E) Extra parenchymal restrictive disease with limitation in both inspiration and expiration. Forced expiration is plotted in all conditions; forced inspiration is shown only for the normal curve, TLC, Total lung capacity; RV; Residual volume.



Spirograpic tracings of forced expiration, comparing a normal tracing (A) and tracings in the obstructive (B) and Parenchymal restrictive (C) disease. Calculation of FVC, FEV_1 and $FEF_{25-75\%}$ are shown only for the normal tracing. Since there is no measure of absolute starting volume with the spirometry, the curves are artificially positioned to show the relative starting volume in different conditions.



Lung volumes, shown by block diagrams (left)and spirograpic tracing (right). TLC : Total lung capacity, VC : Vital capacity, RV : Residual volume IC: Inspiratory capacity, ERV : Expiratory reserve volume, FRC: Functional residual capacity, V_T : Tidal volume



A. Pressure-volume curve of the lungs, B. Pressure-volume curve of the chest wall, C. Pressure-volume curve of the respiratory system, showing superimposed component curves of the lungs and the chest wall. RV: Residual volume, FRC : Functional residual capacity, TLC: Total lung capacity

3. Help in the assessment of the course of a disease overtime such as COPD.

4. Help in differentiating the types of respiratory failure and

5. Detect airway responsiveness.

THE SPIROMETER

Volume changes of the lung are usually measured at the mouth, preferably by means of a spirometer or else in pneumotachograph and integrator. The types of spirometer are

1. Closed system and

2. Open system, which uses a differential pressure transducer.

The spirometer should be capable of recording the full vital capacity as a function of time. The minimal driving pressure, ie the minimum pressure at the mouth that causes volume deflection, should be 0.03kPa.

THE TECHNIQUE

The technician is required to calibrate the spirometer to a given standard, daily, before subjecting any patient to a spirometric test. Each patient’s anthropometric data in terms of race, sex, age, height and weight is entered in the computer. The machine is corrected for ambient temperature and pressure.

The patient is then connected to the spirometer tubing using a mouthpiece and all leaks around the mouthpiece are seen to be occluded. Nasal leaks are prevented by occluding the nose with nasal clips. The patient is then asked to breath normally in the spirometer circuit for a couple of breaths and then take a maximum inspiration and a maximum forceful expiration and continue till he cannot exhale any further and then again take an inspiration and stop. The computer then analyses these flows and volume in flow-volume and time-volume formats to give results, comparing them with the normal predicative values.

STATIC LUNG VOLUMES AND CAPACITIES

Pulmonary gas transport depends on the degree and speed with which the pulmonary gas volume can change[23].

Static lung volumes are measured by methods in which the velocity of the gas plays no part[27].

- The Total Lung Capacity (TLC) is the volume of gas contained in the lungs after maximum inspiration.

- Residual Volume (RV) is the volume of gas remaining in the lungs at the end of maximum expiration.

- The Vital Capacity (VC) is the volume of gas that is exhaled from lungs in going from TLC to RV.

- Functional Residual Capacity (FRC) is the volume of gas in the lungs at the end of normal expiration.

DYNAMIC LUNG VOLUMES

The measurements taken during fast breathing movements were described as dynamic volume changes.

The forced expiratory volume in one second (FEV1), is the gas volume expired during the first second of a maximal forced expiration beginning at the end of complete inspiration.

The maximal voluntary ventilation (MVV) is the maximum volume of gas which can be expired per minute, the subject breathing at a frequency of 30 breaths per minute.

PATTERNS OF ABNORMAL VENTILATORY CAPACITY

In obstructive lung disease, the FEV1, is marked decreased, VC is decreased or normal, the ratio FEV1/FVC is decreased (<70%).

In restrictive lung disease, FEV1 and VC are decreased and the Ratio FEV1/FVC is normal or increased.

Lung volumes and measurements made during forced expiration are interpreted by comparing the values measured with the values expected given the Age, Height, Sex and Race of the patient. Regression curves have been constructed on the basis of data obtained from large number of normal.

Non-smoking individuals without evidence of lung disease. Predicted values for a given patient can then be obtained by using the patient's age and height in the appropriate regression equation. Different equations are used depending on the patient's age and gender because there is some variability among normal individuals, values between 80 and 120% of predicted value have traditionally been considered normal. Increasingly, calculated percentiles are used in determining normality. Specifically, values of individual measurements falling below the fifth percentile are considered to be below normal. The normal values of ratio FEV1/FVC is approximately 0.75 to 0.80, although this value does fall somewhat with advanced age.

RESULTS

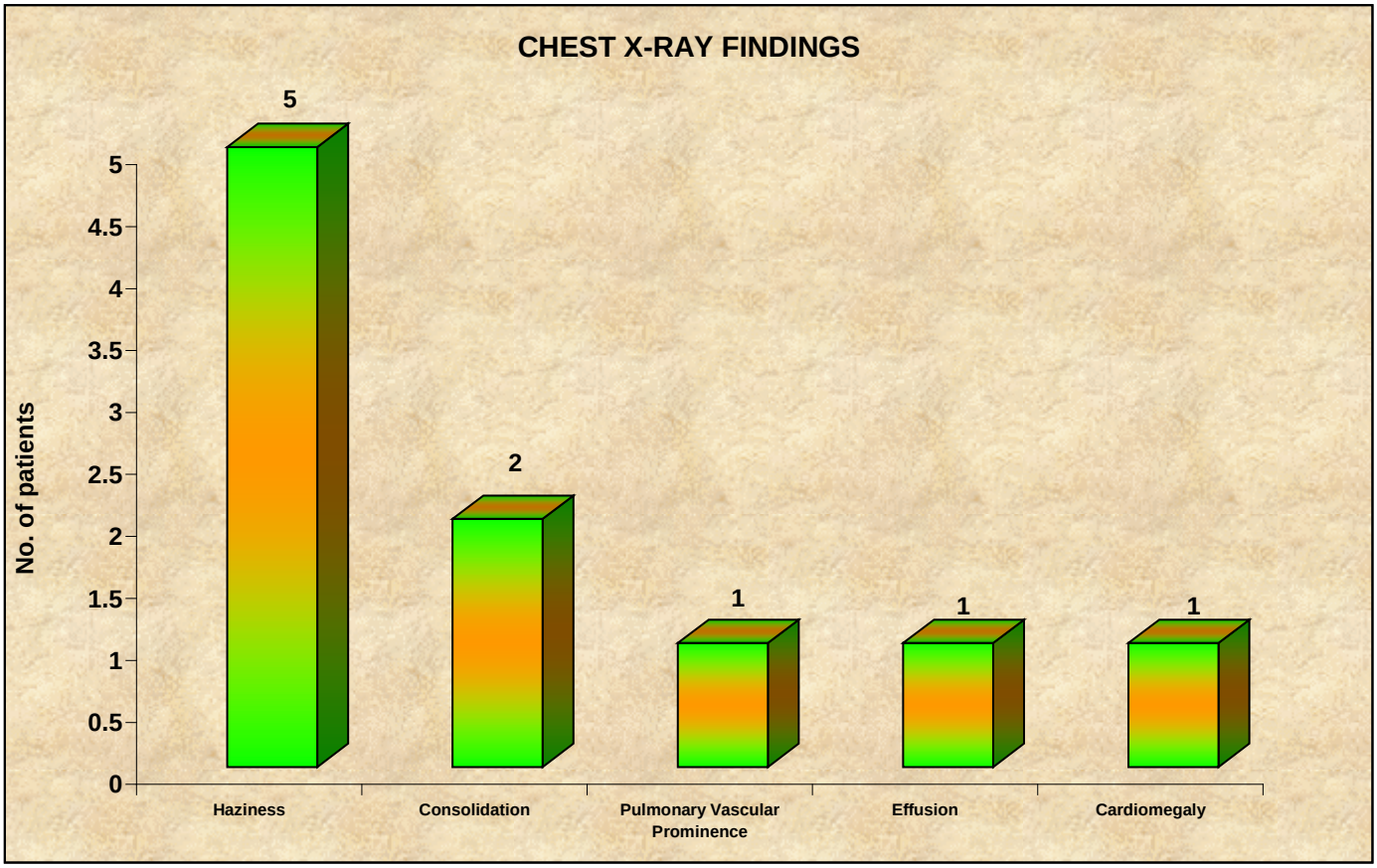
CLINICAL FINDINGS

Among the thirty patients who were enrolled for the study, 27 were females and 3 were males (Female: Male ratio 9:1). The mean age was 26 years, the youngest patient being 12 years and oldest patient being 53 years. Patients had the disease for an average period of 3 years. The duration of respiratory symptoms varied from 1 month to 1 year, the average duration being 6 month.

Out of the thirty Patients, 20 were symptomatic (66%). The predominant symptoms was breathlessness, which was present in 18 patients (60%). Cough was the presenting complaint in 8 patients (30%). The other symptoms were fever, pleuritic chest pain, and generalized weakness. Clinical examination revealed abnormal findings in only 13 patients (43%).

Two patients, who were admitted with fever and cough had high pitched bronchial breath sounds bilaterally, suggesting the impression of pneumonitis (6%). Two patients had diminished intensity of breath sounds (6%).

Nine patients had fine respiratory basal crepitations (30%). In the remaining 17 patients, clinical examination was normal.

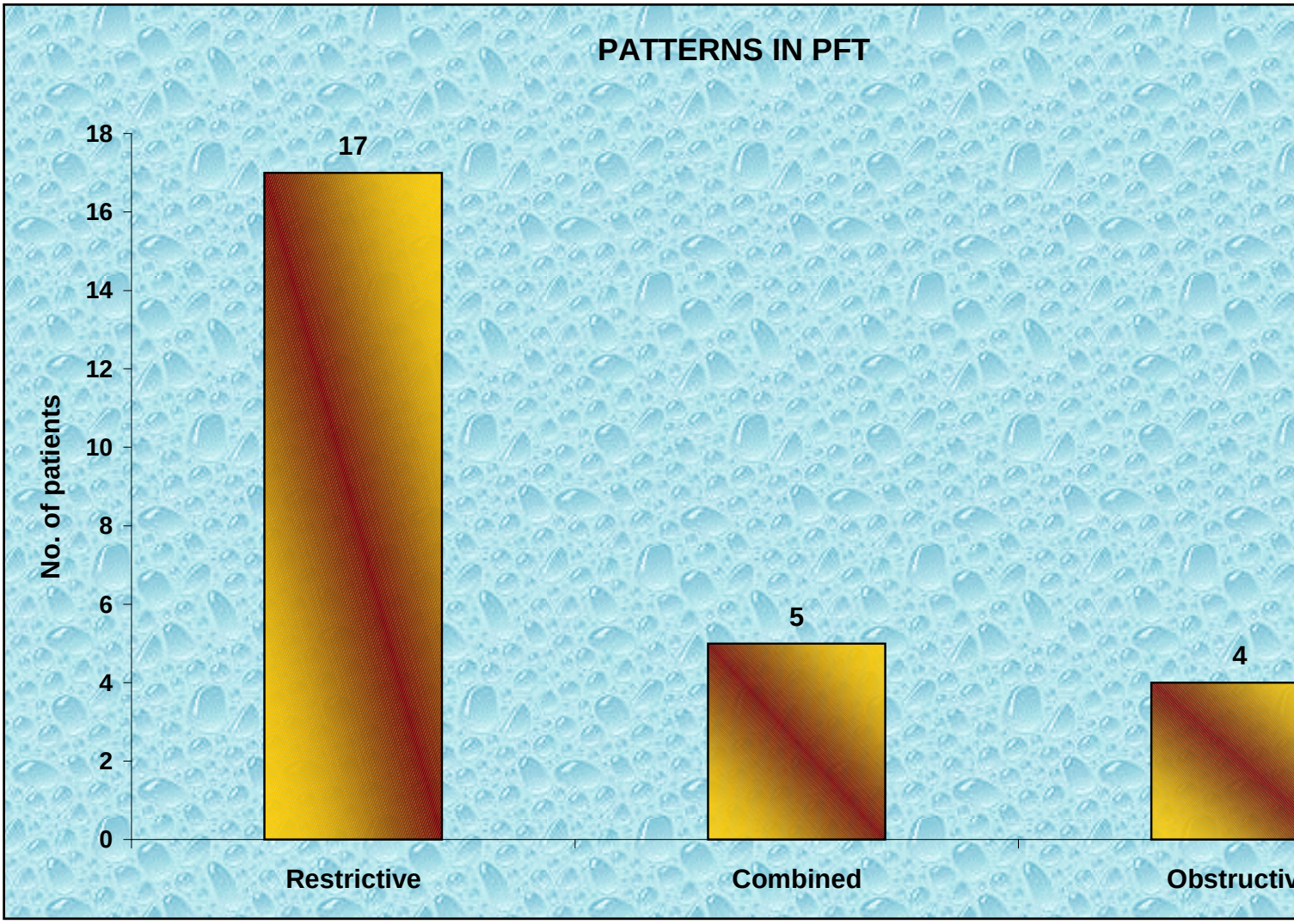


RADIOLOGIC IMAGING

Chest Skiagram showed abnormal findings in 10 patients (33%). The commonest radiological pattern was bilateral haziness in both lower zones, which was present in 5 patients (16%). The haziness was homogenous, involved the lower zones. Consolidation pattern was seen in 2 patients (6%). One patient had bilateral patchy opacities occupying both mid and lower zones. The other patient had a patchy opacity in the (R) lower zone. Both the patients had clinical features suggestive of pneumonitis.

Cardiomegaly was present in one patient (3%), who also had prominence of pulmonary markings, raising the suspicion of pulmonary hypertension.

Evidence of pleural effusion in the form of bilateral opacities of both lower zones with obliteration of costophrenic and cardiophrenic angle was seen in one patient (3%).



PULMONARY FUNCTION TEST REPORTS

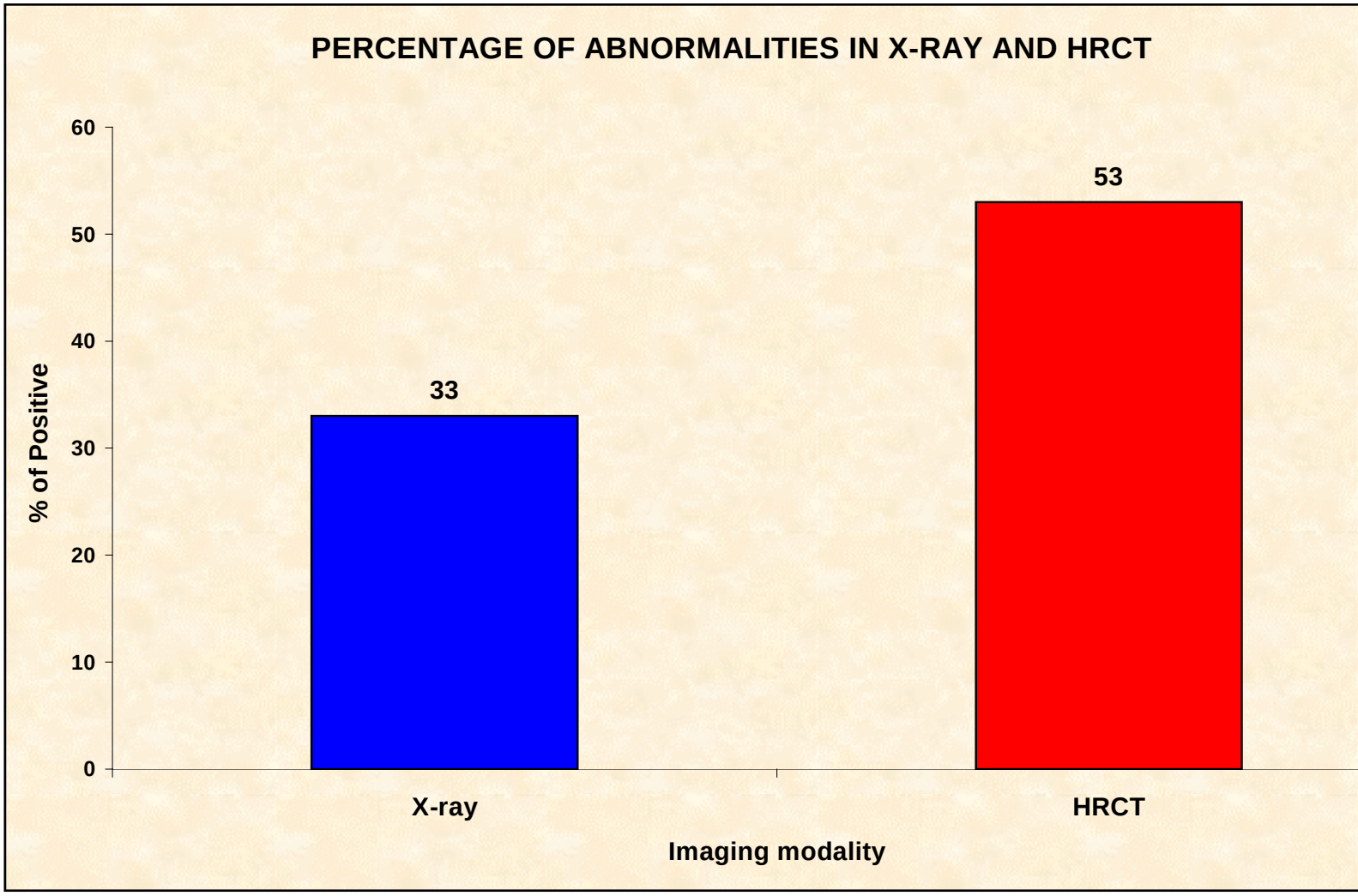
Among the 30 patients who underwent pulmonary function testing, 26 patients showed abnormal pattern (86%). The pattern of abnormality was restrictive type in 17 patients (56%). The pattern was mildly restrictive in 4 (23%), moderately restrictive in 4 (23%), and severe in 9 patients (52%). The patients had reduction in forced expiratory volume in one second (FEV1), and Forced Vital Capacity (FVC) with normal or

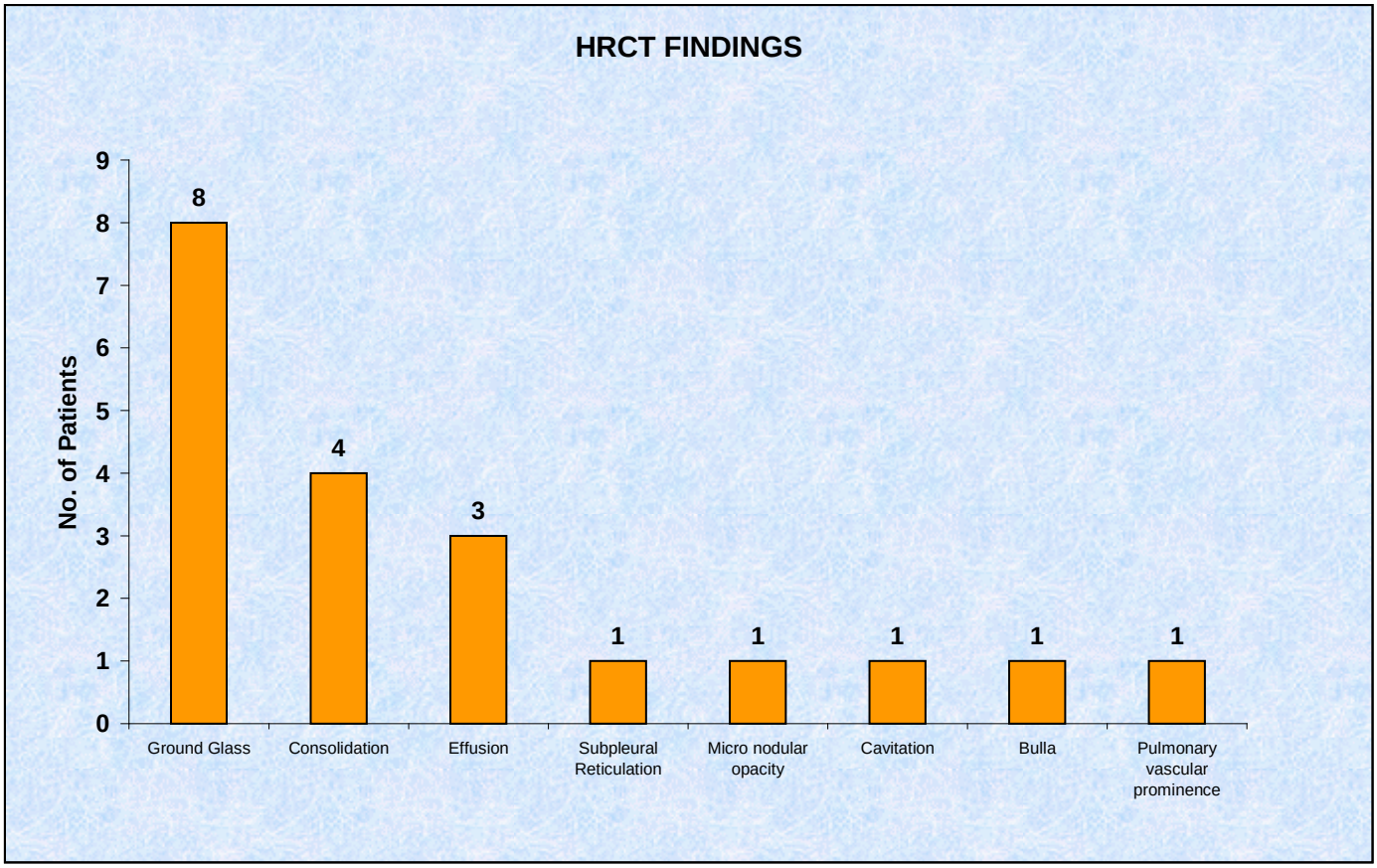
elevated FEV1/FVC. A decrease in Residual Volume and Total Lung Capacity (TLC) was also evident.

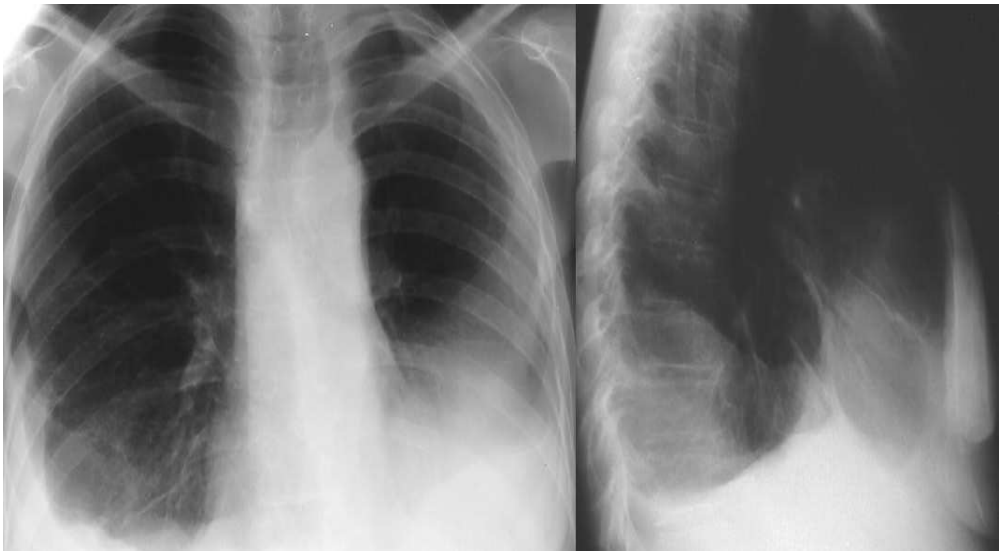
The staging of the restrictive pattern was made mainly on basis of these lung volumes, which were expressed in percentage of predicted normal after calibration with the units in terms of litres per minute. The volumes are normal if they were more than or equal to 80% of predicted normal, mild if 60-79%, moderate if 40-59%, and severe if less than 40%.

Four patients (12%) had patterns suggesting air flow limitation, with reduced FEV, IFVC and normal or increased TLC, and elevated Residual Volume (RV).

Five patients (16%) demonstrated combined restrictive obstructive impairment, showing decreased forced vital capacity and expiratory flow rate. The total lung capacity was normal or low.

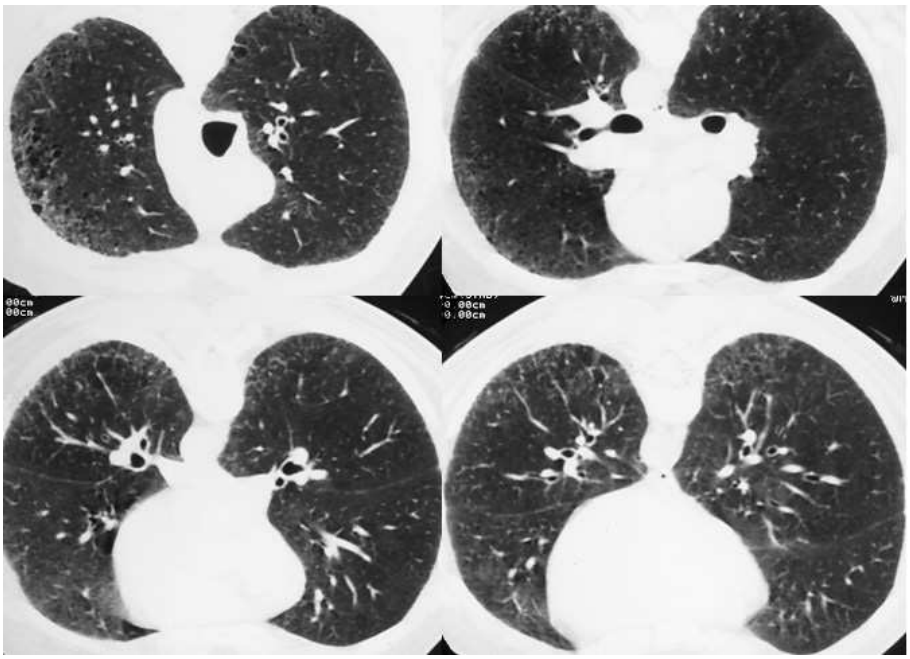

PERCENTAGE OF ABNORMALITIES IN X-RAY AND HRCT
60
50
40
30
20
10
0
% of Positive
33
53
X-ray
HRCT
Imaging modality


HRCT FINDINGS
No. of Patients
0
1
2
3
4
5
6
7
8
9
8
4
3
1
1
1
1
1
Ground Glass
Consolidation
Effusion
Subpleural Reticulation
Micro nodular opacity
Cavitation
Bulla
Pulmonary vascular prominence

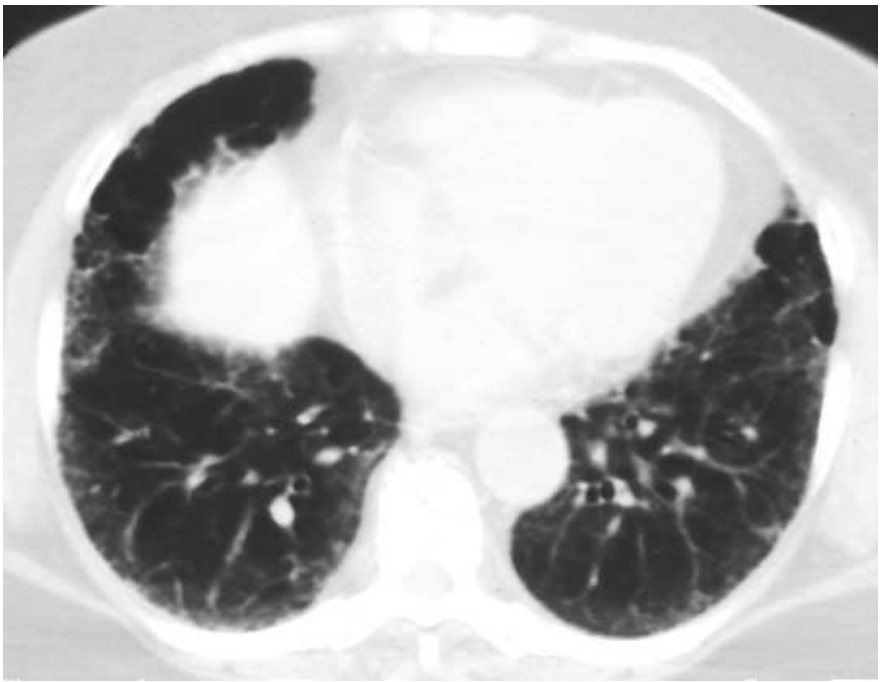


Fluid collection in the anterior ,posterior and lateral costophrenic recess , bilateral hemithroax .

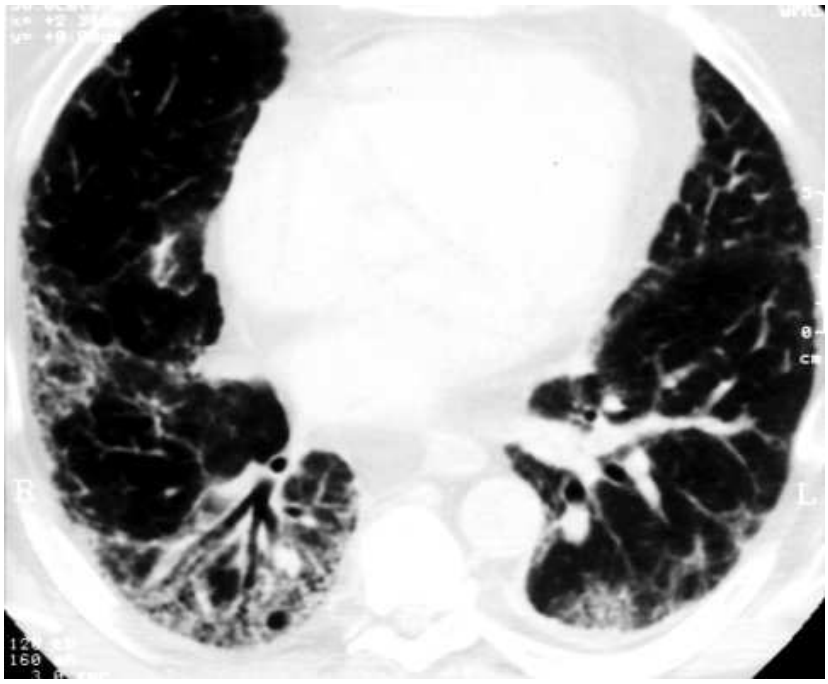
Left sided pleural effusion with chronic pleural thickening



Subpleural and interlobular septal thickening along with few subpleural cystic changes in bilateral lung fields along posterior costal aspects (prone)

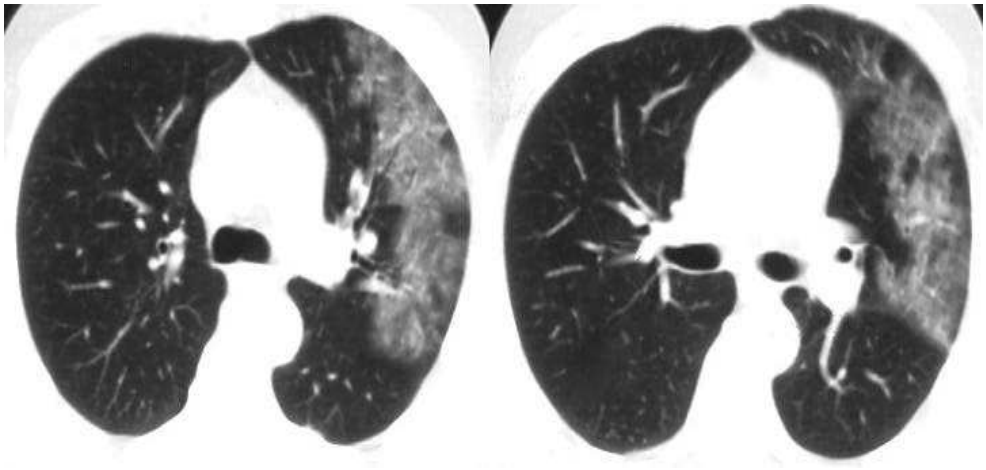


Subpleural / interlobular septal thickening imparting irregular interphase along the pleural aspect.

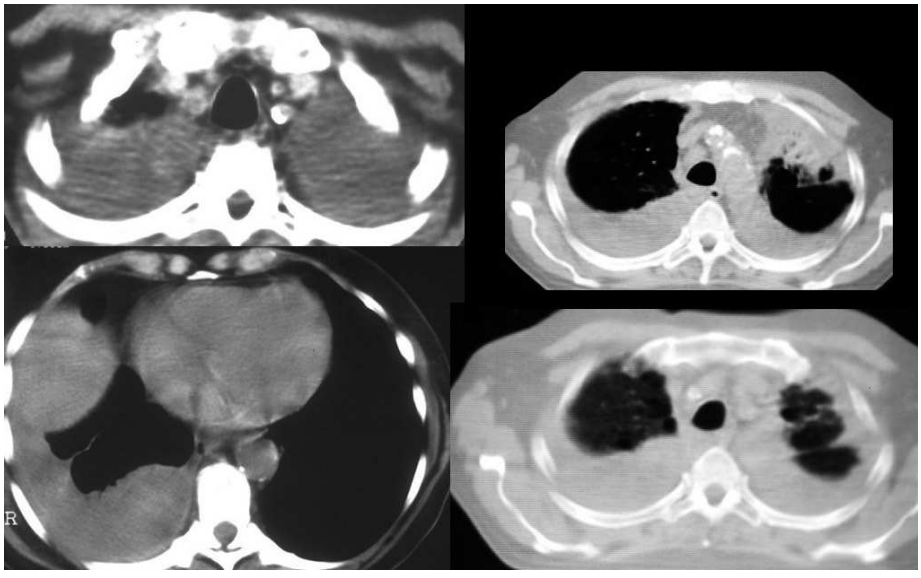


Subpleural interstitial abnormality in the form of subpleural and interlobular septal thickening admist segmental ground glass opacity.

End stage lung disease characterized by honeycombing and traction bronchiectasis in anterior and lateral basal segment of the left lower lobe.



Geographical pattern of air space opacities involving anterior and posterior segments of right upper lobe.the disease process is being limited posteriorly by the major fissure



Bilateral fluid collection in the pleural space with loculation on the right side.

HIGH RESOLUTION CT

- HRCT revealed abnormal findings in 16 patients (53%). It showed abnormalities even in patients who were asymptomatic and clinically normal.

- The commonest finding was that of bilateral ground glass homogenous shadows which were present in 8 patients (26%) the pattern was distributed mostly in the lower zones, the posterobasal segments being commonly affected. These radiologic abnormalities are seen in patients in the early stages of interstitial lung disease (ILD).

- Four patients (12%) had consolidation changes with patchy homogenous opacities and air bronchogram. The distribution was bilateral in one patient and unilateral I in the other three patients. There was evidence of pleural effusion in the patient who had bilateral basal pneumonitis, and another patient had pleural thickening adjacent to the consolidation The changes were noted in the lower zones, the commonest segment being posterior basal.

- Three patients (9%) had bilateral pleural effusion among which 2 patients had mild haziness in the chest x-ray.

- One patient (3%) had bilateral sub pleural reticulation, one of the early findings in ILD.

- There were diffuse micronodular opacities present bilaterally and scattered around the hilum in one patient (3%).

- Findings indicative of pulmonary hypertension, namely prominent pulmonary vasculature, with cardiomegaly was seen in one patient (3%).

- A bullous lesion was seen occupying the posterior basal segment of the left lower lobe in a patient who was symptomatically normal (3%).

- And finally, a cavitary lesion with pleural thickening in the left lower lobe was demonstrated in a patient (3%).

DISCUSSION

On analysing the results from the study, it is evident that 66% of the patients had respiratory abnormalities.

Out of the 20 patients who had respiratory abnormality, the commonest one was that suggestive of early interstitial lung disease (ILD). This was evident from the ground glass shadows on HRCT, present in 8 patients (26%).

Patients with features suggestive of early ILD presented with cough which was unproductive in nature and breathlessness. The symptoms had evolved about an average of 6 months since the diagnosis of SLE. In these patients, there was obvious clinical findings in only 30% .The diagnosis in the rest of the patients was made by HRCT.

Two patients presented with clinical picture of pneumonitis, which was unresponsive to antibiotics. Sputum examination did not reveal any micro organism. The patients were treated with antibodies for a long period of time without any improvement. Then, when the patients were referred to this hospital, the possibility of lupus pneumonitis was strongly considered and glucocorticoids were administered. The response were good and the general condition of the patients improved and the radiological findings also resolved. Thus, lupus pneumonitis should be considered in patients with SLE who present with pneumonitis unresponsive to antibiotics.

Pulmonary hypertension was the diagnosis in a patient who presented with progressive breathlessness. Imaging revealed prominence of pulmonary vasculature and cardiomegaly. The diagnosis was confirmed by echocardiogram.

The duration of the disease strongly plays a role in the development of respiratory abnormalities. Patients who had longer duration of SLE presented with more pulmonary pathology than those in whom the disease was diagnosed recently.

Clinically examination revealed abnormality in 13 patients. In 9 patients, the clinical suspicion of ILD was made after excluding infection. In 2 patients, there was evidence of consolidation and in the other 2, there were findings suggestive of pleural effusion.

Chest x-ray was normal in 10 patients (33%) and the commonest pattern being haziness involving both lower zones in 5 patients (15%). The other findings were pneumonitis in 2 patients (6%), prominence of pulmonary vessels in 1 (3%), pleural effusion in 1(3%), and cardiomegaly in 1(3%).

Pulmonary function tests showed that 26 patients (86%) had abnormal patterns. Restrictive pattern was seen in 17 patients (56%), air flow limitation in 4(12%) and combined pattern in 5 (16%).

HRCT proved to be useful tool in identifying subtle anatomic changes in 16 patients (53%) had abnormal findings, the common pattern being ground glass pattern bilaterally in 8 patients (26%) the other pattern were consolidation in 4(12%), and bilateral pleural effusion in 1 (3%), subpleural reticulation in 1 (3%), cardiomegaly in 1 (3%), prominent pulmonary vessels in 1(3%) and micronodular changes in 1 (3%). Bullous lesion was evident in a patient who was asymptomatic and another patient had cavitary lesion without any previous pulmonary disease.

In the study by Bankier et al..[30] out of the 48 patients, chest radiographs were abnormal in 3 patients (6%) and HRCT was abnormal in 17(38%). The duration of SLE in this group of patients ranged from 8-52 months.

Fenlon et al.,[31] showed in his study on 34 patients with SLE that chest x-ray was abnormal in 8 patients(24%), PFT in 14 (41%) and HRCT in 24(70%).

Ooi GC, Ngan H.Peh WCG et al.,[32] found that the prevalence of respiratory abnormality is highest in patients who have long standing SLE and chronic respiratory symptoms. All patients had abnormal PFT and HRCT, the most common pattern in HRCT being ground glass appearance in 8 out of 10 patients and pleural thickening in eight.

In our study x-ray was abnormal in 10 patients (33%) PFT in 26 patients (86%), and HRCT in 16 patients (53%). 33% of patients who were clinically normal showed abnormality in HRCT.

Thus, with a sensitivity of 53% HRCT emerges as an invaluable non-invasive investigation in detecting pulmonary changes in SLE patients.

CONCLUSION

- Respiratory abnormalities were present in 66% of patients with SLE.
- The longer the duration of the disease, the more the likelihood of pulmonary pathology.
- The commonest respiratory abnormality was found to be of early ILD, with ground glass pattern in HRCT.
- HRCT evidence of ILD was frequently present despite absence of symptoms and normal chest radiograph.
- Most patients had abnormalities in their PFT but did not demonstrate anatomically abnormality. Reduction in lung volumes was the most common finding, suggestive of restrictive patten of ILD.
- HRCT was more sensitive in detecting anatomical abnormalities than any other non –invasive investigatory modality.

SUMMARY

A Prospective study of respiratory abnormalities in systemic lupus erythematosus was done to correlate the clinical features with plain radiographs, pulmonary function test and HRCT. Thiry, SLE patients were questioned about their symptoms of respiratory disease or not. After clinical examination, patient underwent lab investigations and imaging modalities. On analyzing the results from the study two-thirds of the patients had respiratory abnormalities. It was found that longer the duration of the disease, more likelihood of developing pulmonary pathology. HRCT is more sensitive in detecting the anatomical abnormalities than any other non–invasive investigating modality.

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ABBREVIATIONS

ACR	-	American College of Rheumatology
ANA	-	Anti Nuclear Antibody
ARDS	-	Adult Respiratory Distress Syndrome
BAL	-	Broncho Alveolar Lavage
CD	-	Cluster Differentiation
COPD	-	Chronic Obstructive Pulmonary Disease
DLCO	-	Diffusing Capacity of Carbonmonoxide
DVT	-	Deep vein thrombosis
FRC	-	Functional Residual Capacity
FEV	-	Forced Expiratory Volume
FVC	-	Forced Vital Capacity
HRCT	-	High Resolution Computed Tomography
ILD	-	Interstitial Lung Disease
Ig	-	Immunoglobulin
LE	-	Lupus Erythematosus
MVV	-	Maximum voluntary ventilation
PFT	-	Pulmonary Function Test
PHT	-	Pulmonary Hypertension
PE	-	Pulmonary embolism
RV	-	Residual Volume
RA	-	Rheumatoid Arthritis
SLE	-	Systemic Lupus Erythematosus
TV	-	Tidal Volume
TLC	-	Total Lung Capacity
V/Q	-	Ventilation /Perfusion

PROFORMA

DATE:

NAME: AGE: SEX:

OCCUPATION:

ADDRESS:

FIRST VISIT ON:

NO OF YEARS AFTER DIAGNOSIS OS SLE:

Presenting problems at the first visit:

PAST ILLNESS:

H/o. Diabetes

H/o. Hypertension

H/o. Ischemic Heart Disease

H/o. Pulmonary Tuberculosis

H/o. COPD

PERSONAL HISTORY:

H/o. Smoking:

FAMILY HISTORY:

LABORATORY INVESTIGATIONS DONE AT THE TIME OF DIAGNOSIS:

DETAILS OF TREATMENT:

NATURAL HISTORY OF DISEASE SINCE DIAGNOSIS :

PATIENTS IS AT PRESENT ON DRUGS:

EXAMINATION ON:

Presenting Problems Now:

H/o. Breathlessness:

H/o. Cough:

H/o. Chest Pain

H/o. Hemoptysis

General Examinations:

PR: BP:

CVS:

RS:

ABDOMEN:

CNS:

INVESTIGATIONS

CHEST X RAY:

PULMONARY FUNCTION TEST:

HIGH RESOLUTION COMPUTED TOMOGRAPHY OF CHEST:

MISCELLANEOUS INVESTIGATIONS:

FINAL DIAGNOSIS:

MASTER CHART

Sn	Name and IP No.	Age	Sex	Duration Since diagonosis Of SLE	Duration of RS symptoms	Cough	Dyspnea	Clinic Exam	CXR	PFT						Interpretation	HRCT
										FEV1 %	FVC %	FEV1/ FVC%	RV %	IC %	TLC %		
1	Venilla 780925	25	F	5 years	6 months	-	+	Normal	Normal	62	54	104	26	87	46	Normal	Bullous lesion poster basal seg.Left LL
2	Subbulakshmi 782933	22	F	1 year	-	-	-	Normal	Normal	76	92	78	147	135	107	Mild air flow limitation gastrapping 0.43L	Normal
3	Sanhara 782657	12	F	1 year	-	-	-	Normal	Consolidation R powerzone	74	78	94	40	110	65	Mild restriction vol loss 0.88L	Pneumonic changes postero basal segment R lower lobe
4	Shanthi 781020	14	M	2 years	2 months	+	+	Reduced breath sound both axillae	B/L pleural effusion	65	60	104	84	91	92	Normal	B/L pleural effusion
5	Ramya 781084	18	F	2 years	-	-	-	Normal	Normal	67	66	100	48	94	61	Moderate restrictive pattern	Patchy consolidation & pleuralthickening posterior segment let LL
6	Saroja 780177	21	F	3 years	1 month	-	+	Reduced breath sounds both bases	Haziness both lower zones	84	66	108	21	78	54	Moderate restrictive pattern vol.loss 1.09L	B/L Pleural Effusion
7	Kanmani 779908	14	F	2 years	-	-	-	Normal	Normal	47	44	104	22	59	38	Severe restriction vol. Loss 1.82L	B/L ground glass shadow posterobasal segments
8	Logaranjini 779275	14	F	2 years	-	-	-	Normal	Normal	77	71	108	30	91	61	Mild restriction vol.loss IL	Normal
9	Thenmozhi 777618	18	F	2 years	1 month	+	+	B/L Bronchial Breathing Fine creps	B/L Consolidation air Bronchogram	90	81	102	44	103	72	Mild restrictive pattern	B/L Basal pneumonitic pleural effusion

10	Jansirani 777361	20	F	4 years	1 Year	-	+	Creps both bases	Haziness both lower zones cardiomegaly	30	23	130	8	18	19	Combined pattern vol.loss 2.19L	B/L ground glasss shadow
11	suganthamani	21	F	2 years	1 month	-	+	normal	B/L lower zone haziness cardiomegaly	39	32	111	9	30	26	Severe restrictive vol loss 2.11L	Pericardial effusion
12	Nagammal 775789	23	F	3 years	1 month	+	+	normal	Haziness right lower zone	35	36	96	50	74	94	Combined pattern	Pneumonitic lateral base segment
13	Indrakumari 775321	21	F	1 year	6 weeks	-	+	Normal	Prominent Pulmonary vessels	93	79	109	29	54	65	Mild restrictive pattern vol.loss 1.11L	Ground glass shadows prominent pulmonary vessels
14	Uthra 774467	27	F	2 years	1 year	-	+	Normal	Normal	67	63	100	36	81	54	Combined pattern mild airflow limitation	Normal
15	Baby 774153	47	F	3 years	1 year	-	+	B/L creps	Normal	54	43	116	7	59	32	Severe restrictive vol. loss	Normal
16	Saroja	24	M	2 years	-	-	-	Fine creps R infra axillary region	Normal	19	88	23	593	97	206	Moderate restriction vol.loss IL	Normal
17	Radhika 771661	25	F	5 years	4 months	+	+	Normal	Normal	57	50	105	27	51	43	Severe restrictive pattern vol. loss l.93L	Normal
18	Dhanalaxmi 772340	23	F	2 years	1 month	+	-	Normal	Haziness both lower zones	64	53	114	11	68	42	Severe restrictive pattern vol loss 1.78L	B/L ground glass shadow
19	Logaranjani	24	F	3 years	-	-	-	Normal	Normal	65	49	132	16	69	40	Combined pattern	Cavitary lesion L lower lobe
20	Subatha 770745	28	F	months	1 month	+	_	Coarse creps both bases	Normal	73	77	84	50	94	64	Moderate restriction vol.loss 1.09L	Normal
21	Njamma 770621	29	F	6 years	1 year	-	+	Normal	Normal	64	66	96	19	93	51	Combined pattern air flow limitation vol.loss 1.45 L	B/L ground glass shadows subpleural reticulation

22	Gulab John 770352	53	F	5 years	1 year	-	+	Normal	Castophrenic angle obliteration L side	50	34	132	5	51	23	Severe restrictive pattern vol. Loss 2.4L	Diffuse micronodular opacities B/L ground glass shadows B/L
23	Shankari 768945	27	F	3 years	-	-	-	Normal	Normal	69	98	101	210	124	126	Air flow limitation	Normal
24	Amuda 767513	18	M	1 year	1 month	-	+	Creps both bases	Normal	75	74	101	60	82	88	Normal	Normal
25	Alamelu 767486	52	F	5 years	1 year	+	+	Fine creps	Normal	75	40	196	40	29	61	Severe restrictive pattern	B/L ground glass shadow
26	Poornima 766778	22	F	2 years	-	-	-	Normal	Normal	77	70	107	34	70	60	Normal	Normal
27	Rekha 765400	23	F	3 years	6 months	-	+	Normal	Normal	54	73	68	143	70	92	Mild air flow limitation	Normal
28	Valarmathi 763174	20	F	3 years	-	-	-	Normal	Normal	76	74	101	47	110	67	Mild restrictive pattern vol.loss 1.11L	Normal
29	Radhika 762908	34	F	3 years	1 year	-	+	B/L creps	Normal	54	43	116	7	59	32	Severe restrictive pattern vol.loss 2.18	Severe restrictive pattern
30	Sumathi 762880	41	F	2 years	-	-	-	Normal	Normal	74	23	288	6	51	17	Severe restrictive vol.loss 2.79 L	B/L ground glass shadow postero basal segments.