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Role of High Resolution Computed Tomography in the Evaluation of Pulmonary Changes in Connective Tissue Diseases

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***Abstract**: Connective tissue diseases are a heterogeneous group of systemic inflammatory diseases of autoimmune origin that affecta wide range of organs and systems. Many collagen-vascular diseases involve the lungs either directly or as a complication of the treatment. Several components of the respiratory system may be involved, including the airways, vessels, parenchyma, pleura, and respiratory muscles. High-resolution computed tomography (HRCT) is the method of choice for evaluating systemic disease as it is able to detect lung abnormalities, characterize the findings, assess the extent of disease, and help to establish the differential diagnosis. cross sectional study was done in Department of Radiodiagnosis, Regional Institute of Medical Sciences, Imphal to study the HRCT findings in connective tissue diseases for a period of 2 years to assess the spectrum of abnormalities seen on high-resolution computed tomography in patients with connective tissue diseases and To correlate high resolution computed tomography findings in connective tissue diseases with clinical features.A total of 79 patients were included in the study.Performing HRCT thorax on a patient with connective tissue disease will help in early detection and assess the severity of any intrathoracic involvement.Most frequent HRCT abnormality in patients with connective tissue disease encountered was interstitial tissue involvement in the form of Septal thickening presented in 44 % of patients, ground-glass opacification presented in 39 % of patients and bronchiectasis in 20 %. Majority of patients had clinical diagnosis of Rheumatoid arthritis (56%) followed by systemic lupus erythematosus (26%), systemic sclerosis (8%), Dermatomyositis (3.8%), Ankylosing spondylitis (2.5%) and mixed connective tissue disease (1.3%). Dyspnea was the most common symptom followed by cough in patients with HRCT identified interstitial tissue involvement.*

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I. Introduction

Connective tissue diseases also known as the collagen vascular diseases, comprises a number of chronic inflammatory autoimmune disorders. They may involve any tissue in any part of the body; joints, serous membranes and blood vessels are frequently involved and all connective tissue diseases involve lungs and pleura to some extent. Conventionally, the connective tissue diseases comprise rheumatoid arthritis(RA), systemic lupus erythematous(SLE), systemic sclerosis(SS), Sjogren's syndrome, Ankylosing spondylitis, mixed connective tissue disease, dermatomyositis and polymyositis(PMS). CREST syndrome is a subset of systemic sclerosis characterised by cutaneous calcinosis, Raynaud's phenomenon, oesophageal dysfunction, sclerodactyly and telangiectasisias. Mixed connective tissue disease consists of features of SLE,SS and PMS. The term 'overlap syndrome' has been extended to include almost any combination.[1]

Although the lung is particularly vulnerable target organ. The frequency of pleuropulmonary involvement varies widely within the spectrum of disease in each disease.[2] All the elements of respiratory systems are affected either separately or in combination. This includes pleura, small airways, interstitum or the pulmonary vessels.[3]

The prevalence of pulmonary involvement is heterogenous in different types of connective tissue diseases. The variability is also accounted for by discrepancies in the methods and diagnostic criteria used. Although chest xray has traditionally represented the first diagnostic step to investigate pulmonary involvement, has demonstrated low sensitivity and specificity in interstitial lung diseases (ILD),whereas High-resolution computed tomography (HRCT) currently represents the reference technique for a non invasive approach to lung diseases.

HRCT is a non invasive imaging technique in which thin sections are taken at staggered intervals. HRCT is capable of imaging the lung with excellent spatial resolution, providing anatomical detail similar to

that available from gross pathologic specimens and paper-mounted lung slices.[4] HRCT can readily demonstrate the normal and abnormal lung interstitium and morphologic characteristics of both localized and diffuse parenchymal abnormalities.

Since interstitial lung disease (ILD) is the predominant pulmonary manifestation among most of the connective tissue diseases, HRCT is the imaging modality of choice.[5]

HRCT has revolutionised the imaging of ILD, as it enables early detection of disease, characterisation allows a histospecific diagnosis to be made in certain cases and provides insights into disease reversibility and prognosis.

II. Material And Methods

This was a cross sectional study carried out in the Department of Radiodiagnosis, Regional Institute of Medical Sciences, Imphal in collaboration with the Department of medicine, RIMS, Imphal. The study was commenced from September 2016 to August 2018, for a period of two years. A total of seventy nine (79) adult patients with documented connective tissue diseases who have been referredfrom Department of Medicine, were enrolled in the study,who fulfilled the inclusion criteria given below.

Inclusion criteria

Patients referred from Department of medicine with documented connective tissue disease, proven by standard diagnostic criteria whichever applicable.

Exclusion criteria

1. Metallic implants or devices in the chest or back, such pacemaker and Harrington fixation devices
2. Inability to lie on the back with arms raised over the head
3. Patients with pulmonary tuberculosis.
4. Smokers

Study tools

Study was carried out using **64 slice Multidetector CT scanner** manufactured by Philips, Netherland on 9/2007 with model serial number 10311 in the Department of Radiodiagnosis, RIMS, Imphal in collaboration with Department of medicine, RIMS, Imphal.

Procedure

Informed consent were obtained from all the cases before including them in the study (enclosed in annexure). Clinical history of each case including age, sex, marital status, occupation, religion, address, chief complaints with duration, personal history, past history and the details of the general and systemic examinations of the patients were collected from the Department of Medicine. Relevant laboratory diagnostic reports were collected. High resolution computed tomography of the chest will be performed as per HRCT protocol.

During the examination, patients were placed in supine position and were instructed to suspend respiration in full inspiration during scanning. If required prone scanning was taken for dependent densities/subpleural line and expiratory CT to demonstrate air trapping. HRCT chest was taken according to protocol using the following parameters with Reconstruction algorithm in lung and mediastinal windows

Thin section images from the HRCT scans with reconstructed Maximum Intensity Projection (MIP) and Multi Planar Reconstruction (MPR) images were interpreted from the Extended Brilliance Workstation. The images of HRCT wereanalyzed and findings recorded were stored in Digital Versatile Disks (DVD) and at the end of case collection with the help of Consultant Radiologist results were interpreted.

Statistical ananlysis

After thorough scrutinize and checking the data, statistical analysis was performed by using IBM: SPSS Statistics Version 21 and Numerical/continuous variables that follow normality and equality of variances are presented as Mean ± SD (standard deviation) and qualitative/categorical variables are again described as number of cases and percentages.

III. Result And Observation

Age Group (years)	Frequency(n)	(%)
21-30	2	2.5
31-40	18	**22.8**
41-50	17	**21.5**
51-60	18	**22.8**
61-70	15	19.0
71-80	8	10.1

>80	1	1.3
Total	**79**	**100.0**

Table 1: Age distribution of patients studied

In our study population, age of the study subjects ranged from 20-85 years with mean of 58.5 years with maximum number of cases were within the age group of 31 to 60 years comprising 67% of cases. Age of youngest patient was 23 years and age of oldest patient was 81 year.

Table 2: Clinical Diagnosis of patients studied

Clinical Diagnosis	No. of patients	%
Rheumatoid arthritis	**44**	**55.7**
Systemic lupus erythematosus	**21**	**26.6**
Progressive systemic sclerosis	8	10.1
Dermatomyositis	3	3.8
Ankylosing spondylitis	2	2.5
Mixed connective tissue disease	1	1.3
Total	79	100.0

Table 3: Symptoms distribution in relation to diagnosis of patients.

Symptoms	Diagnosis					
	RA (n=44)	SLE (n=21)	PSS (n=8)	DM (n=3)	AS (n=2)	MCTD (n=1)
Cough	**16(36.4%)**	**9(42.9%)**	6(75%)	2(66.7%)	0(0%)	0(0%)
Expectoration	4(9.1%)	3(14.3%)	1(12.5%)	1(33.3%)	0(0%)	0(0%)
Dyspnea	**28(63.6%)**	**9(42.9%)**	6(75%)	2(66.7%)	1(50%)	1(100%)
Chest pain	11(25%)	5(23.8%)	4(50%)	1(33.3%)	0(0%)	0(0%)
Hemoptysis	0(0%)	0(0%)	0(0%)	0(0%)	0(0%)	0(0%)

Table 3 shows presenting symptoms distribution of all cases in relation to patients with specific connective tissue diseases. In rheumatoid arthritis(n=44) patients,most common symptom was dyspnea seen in 28 patients,followed by cough in 16 patients out of which 4 patients presented cough with expectoration. cough and dyspnea were most common symptoms in systemic lupus erythematosus and systemic sclerosis patients followed by chest pain. out of 3 dermatomyosistis patients,2 patients presented with cough with dyspnea. Each patient of ankylosing spondylitis and mixed connective tissue disease presented with dyspnea.

Table 4: High resolution computed tomography findings distribution in relation to diagnosis of patients

High resolution computed tomography findings	Diagnosis					
	RA (n=44)	SLE (n=21)	PSS (n=8)	DM (n=3)	AS (n=2)	MCTD (n=1)
Pleural lesions						
• Pleural thickening	**10(22.7%)**	6(28.6%)	1(12.5%)	0(0%)	0(0%)	0(0%)
• Pleural effusion	2(4.5%)	**6(28.6%)**	0(0%)	0(0%)	0(0%)	0(0%)
• Pneumothorax	0(0%)	0(0%)	0(0%)	0(0%)	0(0%)	0(0%)
Parenchymal lesions						
• Septal thickening	**24(54.5%)**	8(38.1%)	2(25%)	1(33.3%)	0(0%)	1(100%)
• Consolidation	4(9.1%)	5(23.8%)	0(0%)	0(0%)	0(0%)	0(0%)
• Ground glass opacities	**19(43.2%)**	5(23.8%)	**6(75%)**	1(33.3%)	0(0%)	0(0%)
• Mosaic attenuation	11(25%)	1(4.8%)	1(12.5%)	0(0%)	0(0%)	0(0%)
• Honeycombing	11(25%)	2(9.5%)	2(25%)	0(0%)	0(0%)	0(0%)
• Nodules	4(9.1%)	0(0%)	0(0%)	0(0%)	0(0%)	0(0%)
• Abscess	0(0%)	**1(4.8%)**	0(0%)	0(0%)	0(0%)	0(0%)
• Parenchymal bands	11(25%)	7(33.3%)	0(0%)	0(0%)	0(0%)	0(0%)

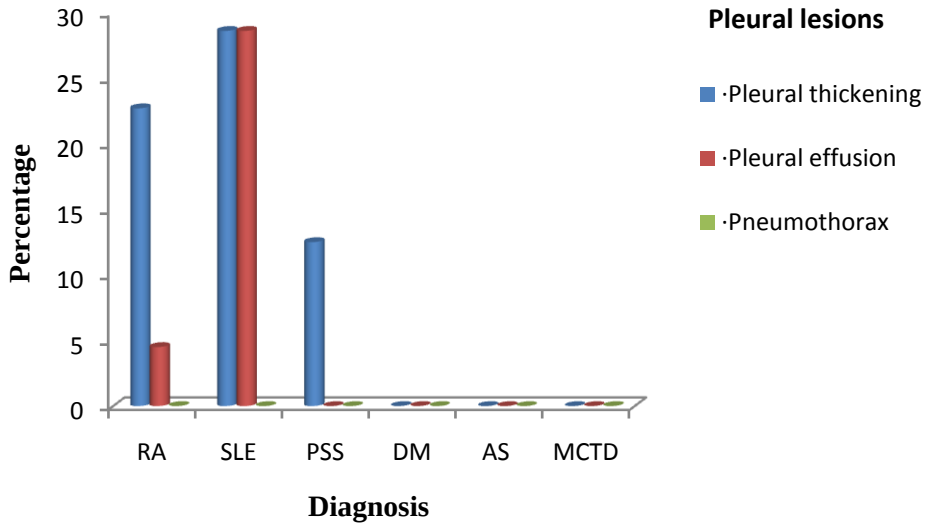


Figure 1: showing HRCT findings of pleural abnormalities in relation to diagnosis

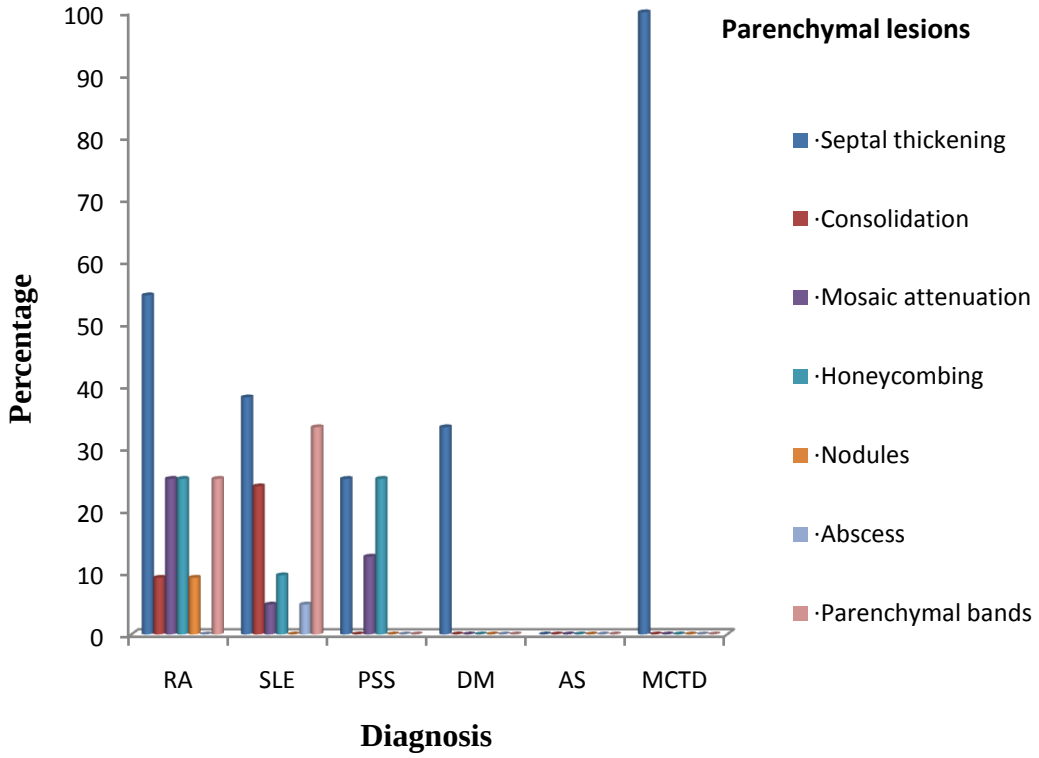


Figure 2: HRCT findings of parenchymal abnormalities in relation to diagnosis

Table 5 : Airway abnormalities distribution in relation to diagnosis of patients

Airway lesions	**Diagnosis**					
	RA (n=44)	**SLE (n=21)**	**PSS (n=8)**	**DM (n=3)**	**AS (n=2)**	**MCTD (n=1)**
Emphysema	6(13.6%)	2(9.5%)	1(12.5%)	0(0%)	0(0%)	0(0%)
Bronchiectasis	**14(31.8%)**	0(0%)	2(25%)	0(0%)	0(0%)	0(0%)
Follicular bronchiolitis	2(4.5%)	0(0%)	0(0%)	0(0%)	0(0%)	0(0%)

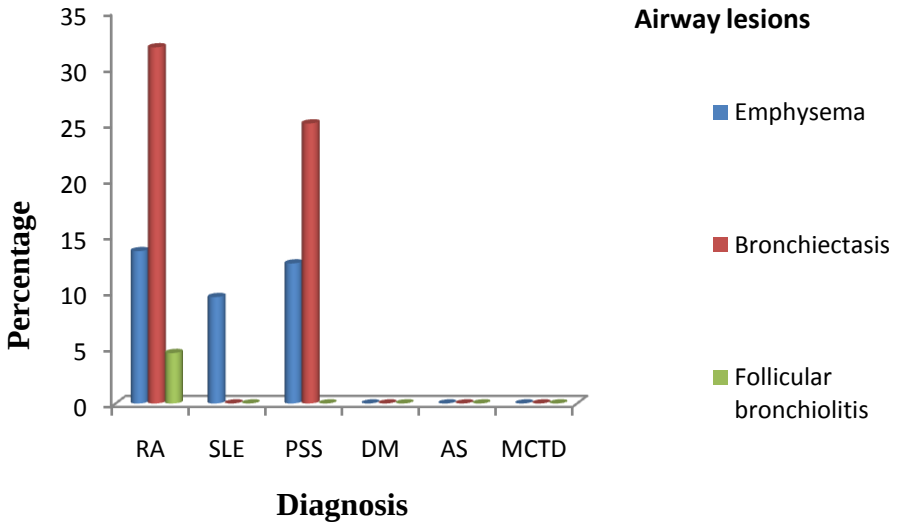


Figure 3: shows HRCT findings of airway abnormalities in relation to diagnosis

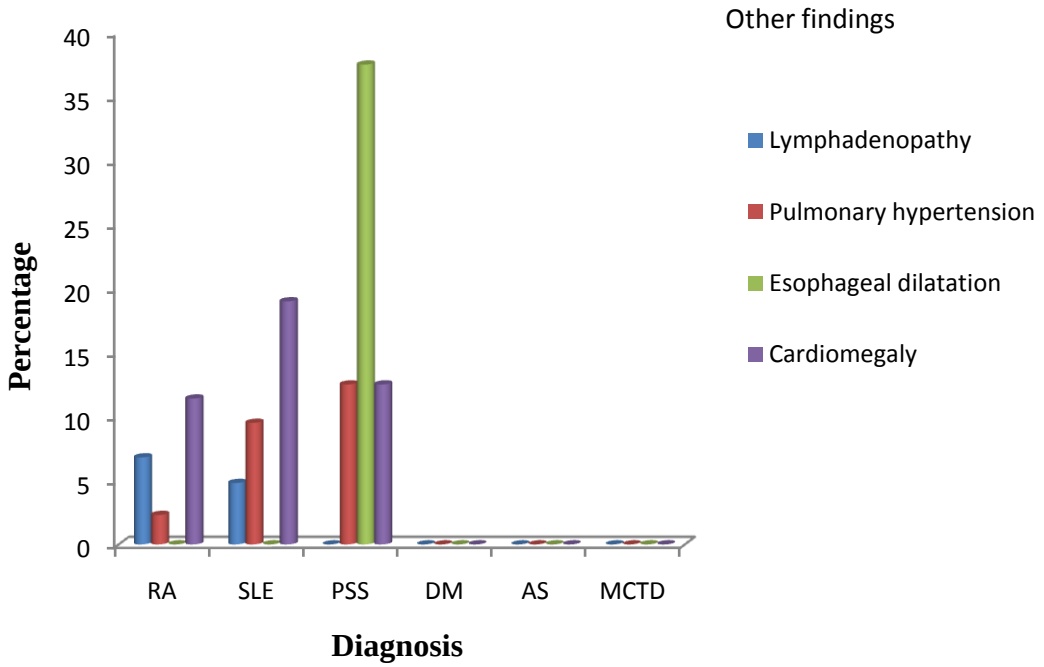


Figure 4: shows HRCT findings of mediastinal abnormalities in relation to diagnosis

Table 6:HRCT findings of interstitial pattern distribution in relation to diagnosis of patients

HRCT- ILD pattern	Diagnosis					
	RA (n=44)	SLE (n=21)	PSS (n=8)	DM (n=3)	AS (n=2)	MCTD (n=1)
Non specific interstitial pneumonia	3(6.8%)	4(19%)	0(0%)	0(0%)	0(0%)	0(0%)
Usual interstitial pneumonia	12(27.3%)	1(4.8%)	1(12.5%)	0(0%)	0(0%)	0(0%)

HRCT pattern of interstitial lung disease was UIP and NSIP. Usual interstitial pneumonia(UIP) seen in 14 patients of which 12 were rheumatoid arthritis patients and one case of each SLE and PSS patients. Non specific interstitial pneumonia seen in 7 patients of which 4 were SLE and 3 RA cases.

IV. Discussion

High-resolution computed tomography (HRCT) is the method of choice for assessment of pulmonary abnormalities in collagen vascular diseases, offering the best correlation with histological findings, disease severity, prognosis, evaluation of disease progression and differential diagnosis. It plays an important role in early detection and characterization of interstitial lung disease associated with collagen-vascular diseases. However, it has some limitations. In many cases, HRCT appearance is nonspecific and may or may not be related to an underlying connective tissue disease. Thus, radiologic findings always interpreted with knowledge of the clinical picture.

In this study, HRCT of the thorax was done in 79 patients, out of which 56 (74%) patients showed a variety of parenchymal, pleural, airway and mediastinal abnormalities. 44 patients had rheumatoid arthritis, 21 systemic lupus erythematosus,8 cases of progressive systemic sclerosis,3 dermatomyositis, 2 ankylosing spondylitis and 1 case of mixed connective tissue disease.

Rheumatoid arthritis (RA) is the most common type of connective tissue diseases, affecting about 1% of people worldwide. pulmonary involvement is one of the common manifestation of rheumatoid arthritis. 18% of the mortality in RA is due to pulmonary causes and approximately 5% of patients with RA present clinical manifestations of pulmonary involvement. In this study, most of the RA patients had many abnormalities detected on HRCT.

Parenchymal abnormalities (which included pulmonary nodules,ground glass opacities, pulmonary consolidation and pulmonary fibrosis) were the most common finding which identified in 80% of cases, this is relatively similar to Afeltra'set al [17]where Parenchymal involvement were 85.1% of patients. In comparison to our findings, a study by Terasaki et al [18]airway diseases were the most common finding in 90% of RA patients. While in Rockall et al[21]study**,** pleural involvement, was the most common thoracic manifestation of RA. These differences may be due to variable ethnicity, disease activity and duration of disease in patients.

In this study, pleural lesions including pleural effusion and pleural thickening, were identified in 27.2% of RA patients , equal to the results of Tanaka et al[19]**,**where pleural involvement was 29% of RA , higher than the results of Zrour et al[9] where pleural involvement was 9.3%.

According to Mori et al [20]HRCT was capable of detecting parenchymal nodules in 10.3 % of RA cases, that is almost similar to our study which identified in 9.1 % of our RA patients.

The HRCT findings of pulmonary fibrosis in RA patients in this study were seen in 54.5%, much higher than Zrour et al[9] .The findings ranging from irregular ground glass opacities or fine linear reticulations to coarse reticulation with end-stage cystic honeycombing with bilateral posterior subpleural lower lobes predominance. This difference can be attributed to the duration and severity of the disease.

A study by Rockall et al [21]bronchiectasis was seen in 30% of cases, the same results were seen in this study with 31.8%. The colonization of these bronchiectases by different microorganisms is the cause of repeated respiratory infections, which is very important to take into account in these patients who receive immunosuppressive treatment for their underlying disease.

Emphysema in RA patients was seen in the current study in 13.6%, equal to the results of Zrour et al [9]**,**less than that recorded in Tanaka et al [19] where it was seen in 24%, of their RA cases.

Regarding SLE about 43% of SLE patients in this study had cough and dyspnea. Dyspnea in SLE may be due to a variety of conditions such as interstitial lung disease, pleural disease, pulmonary hypertension, systolic heart failure, upper airway disease, and obliterative bronchiolitis, shrinking lung syndrome, chronic infections or drugs used to treat lupus.

The most common pulmonary manifestation of SLE is unilateral or bilateral pleural effusion that frequently associated with pericardial effusion. Pulmonary parenchymal abnormalities are also common. Pulmonary hemorrhage is another manifestation, though less common. Pulmonary fibrosisis less common in SLE than in rheumatoid arthritis (RA) or systemic sclerosis .Fibrosis involved predominantly the lung periphery and lower lobes.

In this study pleural abnormality was seen in 29 % of SLE cases where the pleural effusion and pleural thickening seen in 28% each, seen less than results as Fekih et al[22] , where the pleural abnormalities were seen in 50% of SLE patients.

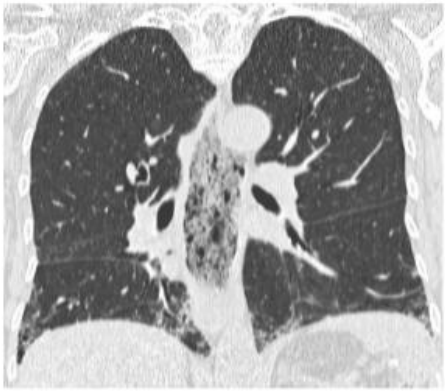
HRCT evidence of pulmonary fibrosis including septal thickening and parenchymal bands were detected in (38% and 33% respectively) relatively similar toKakati et al [23]were septal thickening was seen in 39.4%. Lower levels were seen in a study by Gaude et al [6] where the results recorded were 12.5%. No evidence of bronchiectasis in our SLE patients ,the same results as Gaude et al [6]. Ground-glass opacification in SLE patients was seen in 24% which is nearer to Kakatiet al [23]where it was 26.3%.

Areas of airspace consolidation were seen in 24 % of the SLE cases in this study, while much lower results were seen by Kakati et al[23]as it was only seen in 5.26% of their cases.

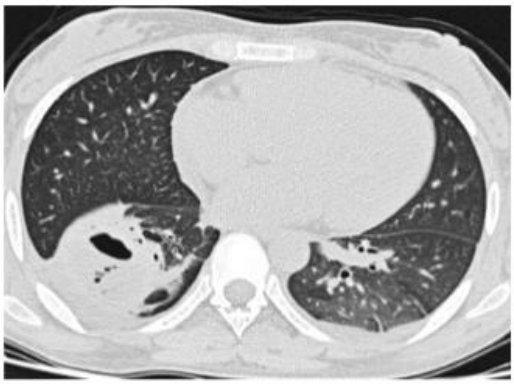
Cardiomegaly was seen in 19 % of cases of SLE, while higher results (50%) were seen in a study by fekih L et al [22] **.**SLE is one of the diseases that affect the heart muscle leading to a clinical syndrome similar to that of congestive cardiomegaly. It may also produce sterile vegetations on the mitral and aortic valves, as well as pericardial effusion.

Pulmonary artery hypertension is uncommon in SLE. It was seen in 8 % in our study, relatively nearer to Fekih et al [22] ,where it was seen in 9.5% of cases. The causal relationship between SLE and PH may be due to multiple small vessel inflammation and/or vasculitis as well as sustained vasoconstriction, in situ thrombosis, and/or thromboembolism and interstitial pulmonary fibrosis.

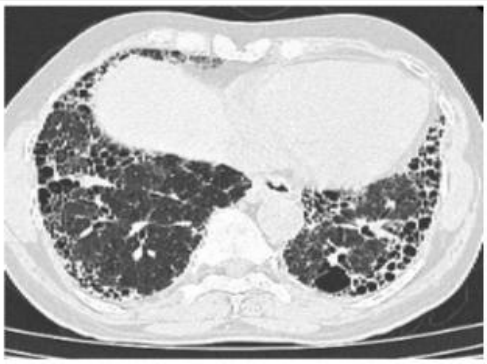
Interstitial lung disease in scleroderma patients manifests as an insidious onset of dyspnea, hypoxia, and fatigue. Later, as the disease progresses, it becomes indistinguishable from idiopathic pulmonary fibrosis. Ground-glass opacification (GGO) was shown in 75% of scleroderma patients in this study, lower results than with Goldin et al [24]who reported ground glass opacification in 91.2% of their cases. On the other hand, lower results were also seen in a study by Shah et al[46]where the GGOs were seen in 66% of cases.



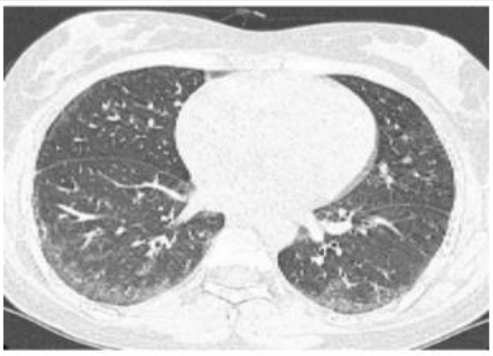
coronal section of HRCT chest in 47 year old **Scleroderma** patient showing subpleural reticular lines peripherally and bibasally with a **dilated esophagus** with food material within



HRCT sections of chest in 23 year old patient of SLE in flare up, showing **Right lower lobe abscess** And mild left pleural effusion



Axial sections of HRCT chest in 62 year old Rheumatoid arthritis showing subpleural honeycombing,predominantly in lower lobes bilaterally characteristic of **Usual interstitial pneumonia (UIP)**



Axial section of HRCT chest in SLE patients showingBilaterally symmetrical fine reticular opacities with relative subpleural sparing consistent with **non specific interstitial pneumonia (NSIP)**

Pulmonary hypertension was seen in 12 % of scleroderma patients in this study, this is nearer to a study by farokh D et al [16]where the pulmonary hypertension was seen in 13.63% cases, less than results of Gaudeet al[6] who reported pulmonary hypertension in 58.3% of their cases.

Pulmonary hypertension is fatal in scleroderma, It can occur alone or in combination with ILD. Dyspnea on exertion is the most common symptom, followed by syncope or right-sided chest pain.

Esophageal dilatation is a very characteristic finding in scleroderma and is helpful in the differential diagnosis from other collagen disease using HRCT. It was seen in 83% of cases in a study by Vonk et al [11] ,Where as in the current study it was seen in 37.5% of cases.

Ankylosing spondylitis (AS) involves the lungs in 1% of patients. Upper lobe and apical lung fibrosis is seen, usually 10 years or more after the onset of the disease. In this study no pleural,airway or parenchymal involvement seen. Usual interstitial pneumonia(UIP) seen in 14 patients of which 12 were rheumatoid arthritis patients and one case of each SLE and PSS patients. Non specific interstitial pneumonia seen in 7 patients of which 4 were SLE and 3 RA cases.

In our study, the most frequent HRCT finding in patients with connective tissue disease encountered was interstitial tissue involvement in the form of Septal thickening presented in 44 % of patients, ground-glass opacification presented in 39 % of patients and bronchiectasis in 20%.

In our study 3 dermatomyositis patients were included, out of which 1 patient shows features of ILD in the form of septal thickening(33%), less than that recorded with Verma SK et al.[29]

V. Conclusion

Most frequent HRCT abnormality in patients with connective tissue disease encountered was interstitial tissue involvement in the form of Septal thickening presented in 44 % of patients, ground-glass opacification presented in 39 % of patients and bronchiectasis in 20 %. Majority of patients had clinical diagnosis of Rheumatoid arthritis (56%) followed by systemic lupus erythematosus (26%), systemic sclerosis (8%), Dermatomyositis (3.8%), Ankylosing spondylitis (2.5%) and mixed connective tissue disease (1.3%). Dyspnea was the most common symptom followed by cough in patients with HRCT identified interstitial tissue involvement.

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