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# ADDIS ABABA UNIVERSITY

# COLLEGE OF HEALTH SCIENCES

**Characterization of Connective Tissue Disease Related Interstitial Lung Disease At Selcted Centers in Addis Abeba , Ethiopia A 4 years retrospective study**

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**DEPARTMENT OF INTERNAL MEDICINE**

# Characterization of Connective Tissue Disease Related Interestitial Lung Disease At Selected hospital Addis Abeba , Ethiopia A 4 years retrospective study.

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**A Research Paper submitted to the Department of Internal Medicine, Addis Ababa University in Partial Fulfillment of the Requirements for the Specialty Certificate in Internal Medicine**

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# Abstract

**Background**: CTD-ILD in one of the most frequent systemic manifestation of CTD which is responsible the majority of mortality and morbidity in these group of patient. Indeed characterization of connective tissue diseases related Interstitial lung diseases(CTD-ILD) includes clinical presentation, serological fiding ,Pulmonary function test(PFT) & high-resolution computed tomography (HRCT) findings will help in designing and implementing prevention and management interventions, thereby reducing the severity of illness and the number of deaths that could be associated with the disease. However published evidence are not much available in sub-saharan country including Ethiopia.

**Objective**: To conduct a comprehensive characterization of CTD-related ILD including epidemiology, clinical presentation, radiological finding, PFT, and serological finding who attend the Rheumatology clinic at TASH, Lancet specialized hospital and Rheum specialty clinic from Jan 2020 – Feb 2024

**Methods**: A Multicenter cross-sectional analytical study was conducted by at the rheumatology clinic at TASH, Lancet and Rheum clinic in Addis Ababa, Ethiopia, during the period Jan 1st 2020 - Feb 2024. Data was collected using a structured checklist, and then entered and analyzed using SPSS version 26. Descriptive analysis was employed to identify the management gaps. Tables and figures were used to present the results.

## Result

With a total patient 92 the majority of the patients are female(89.2) and male (10.8%) with a female to male ratio of 1:8 and the mmedianage of onset is 47.33 years. The most common CTD identified are RA (44.6%), SSC (40.9%) , PM/DM (6.5%), MCTD (4.3%), SLE (3.3%) & USCTD (1.1%). The most common clinical presentation is Cough (72.8%), Decreased exercise tolerance (40.5%) and Dyspnea (41.3% ) but 7.6% of the patient are asympromatic . The most identified Common Antibody Found In ILD are are ANA(47.8%), RF (47.8%) , Anti-scl-70 (37.0%) ,ACPA (29.7%) and frequently encountered ANA pattern are speckled (16.3 %), Homogenous (15.2 %) and nuclear (10.9%). The most frequqnt CXR finding is reticilonodular and GGO but 11% of the patient are normal .The most frequent identified HRCT pattern are NSIP (69.6%) and UIP (28.3%). PFT test done for only 7 patients and 4 patients have restrictive pattern and 3 patients have obstructive pattern.

## Conlussion

Our study identified that CTD-ILD are more common in female and patient with RA % SSc. Most RA patient are older and usually have long duration of illness before the diagnosis of ILD. Relatively SSc patient are younger and most of them have Anti-scl-70 and speckled ANA pattern. We do not identified MTX associated pneumonitis.



**KEY WORDS** – CTD connective tissue disease ILD – interestial lung disease

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## Acronyms/Abbreviations

ACCP ..... anti-cyclic citrullinated peptide antibodies

ACR ..... American College of Rheumatology

ARS ..... Anti-aminoacyl tRNA synthetase

ANA .....Anti-nuclear antibodies

ATS ..... American thoracic society

CTD .....connective tissue diseases

CXR ..... Chest X-ray

DAD ..... diffuse alveolar damaged

DIP ..... desquamative interstitial pneumonia

EULAR ..... European League Against Rheumatism

HRCT ..... high-resolution computed tomography

ILD ..... Interstitial lung diseases

LIP ..... Lymphoid inferential pneumonitis

NSIP ..... Non-specific interstitial lung disease

MCTD ..... Mixed connective tissue diseases

MTX ..... methotrexate

OP .....organizing pneumonia

PFT .....pulmonary function tests

PM/DM ..... polymyositis/dermatomyositis

RA ..... Rheumatoid Arthritis

RF .....Rheumatoid factor

SS .....Sjögren's syndrome

SLE ..... systemic lupus erythematosus

SSC …… systemic sclerosis

UIP …… Usual interstitial pneumonia

UCTD……. Undifferentiated connective tissue disease

# CONTENTS

# 1 Introduction

## 1.1 Background

Connective tissue disease related Interestial lung disease (CTD-ILD) is defined as evidence of interestial lung disease(ILD) demonstrated by computed tomography in the setting of an established connective tissue disease (CTD) . pulmonary system is the most commonly involved system (i.e. occur in 1/3 of connective tissue diseases (CTD) patient). It can involve any part of the pulmonary system either separately or in combination. Interstitial lung disease(ILD) accounts for the majority of morbidity and mortality associated with CTD. It can occure in any kindof CTD.

Retrospective research from Nigeria suggests the prevalence of ILD in patients with CTD is around 10%. But its prevalence is different for different CTD Such as IIM 30-50 % but could reach up to70% in antisynthetase positive patients, RA 10% clinically evident (however ,30 - 60 % have radiological evidence on chest CT), SSC 40 -75 % clinically significant and 70 % on HRCT, pSS 10 – 30 %, SLE 3-11%, and MCTD 20 – 85 %.

connective tissue diseases related Interstitial lung diseases (CTD-ILD) is classified similarly to the other ILD from American thoracic society (ATS) classification based on pathologic and radiological into six major groups

1. Nonspecific interstitial pneumonia (NSIP),
2. Usual interstitial pneumonia (UIP),
3. Organizing pneumonia (OP),
4. Desquamative interstitial pneumonia (DIP)
5. Respiratory bronchiolitis- interstitial lung disease (RB-ILD)
6. Acute interstitial pneumonia (AIP)

There is rare cause like lymphoid interstitial pneumonia (LIP), and plueroparenchymal fibroelastosis.

Except for Rheumatoid Arthritis in the other CTD NSIP is the most common ILD whereas in RA UIP is the commonest.

Clinically CTD-ILD is characterized by progressive dyspnea, cough, and decreased exercise tolerance. Diagnosis typically involves a combination of clinical evaluation, pulmonary function test, imaging test, serological finding, and sometimes lung biopsy.

Overall. CTD-ILD represents a challenging clinical entity that requires a multidisciplinary approach for optimal management.

But despite these, there is little research done in Africa and no in Ethiopia so we conduct this research to know the demographic, clinical, radiologic, PFT, and serologic characterization of CTD-ILD who had a follow at TASH.

## 1.2 Statement of the problem

CTD-ILD is a complex and challenging condition that affects the lung and is associated with various connective tissue diseases. In general, the prognosis of CTD-ILD is more favorable than that of IPF. The prognosis of the patient is different based on the type of CTD, age, and type of ILD. In RA mortality increases by 2-10 folds, and P/M/DM mortality increases by 5-7 folds. One research from Portugal estimates the mortality around 20 % with a median of 67.8 months from the diagnosis of CTD and 37.8 months from the diagnosis of ILD. Despite its significant impact on morbidity and mortality in patients with CTD, there is a lack of understanding of this disease including sociodemographic distribution, clinical features, radiological findings, and histopathological, and serological presentation. Especially in our country where resources are limited to investigate and treat the patient, early detection of the problem will save time and money.To the best of my knowledge, there are only a few researches done in Africa but there is no research done in Ethiopia.

# 2. Review literature

## 2.1 Epiolomology

A retrospective cross-sectional study from Lagos State University Teaching Hospital Nigeria shows that the prevalence of ILD in connective tissue disease is 9.7% from 318 patient over a period of 7 years with a median age 0f 38.8 years and female predominance 90.3% . But the frequency is different based on the type of CTD. A multicenter prospective, cross-sectional, observational study from India which was conducted in 100 patient shows the most commonly identified CTD that are associated with ILD are (RA)(26%), (SSC) (21%), (MCTD) (19%), and (SS) (16% ) the majority of the patient is between 40-60 years and 78 % of the population are women .

## 2.2 Clinical presentation

A retrospective study by Zunyi Medical University in China shows that cough, and decrease exercise tolerance are the most common clinical manifestation of CTD-ILD . Other less common symptoms are sputum, hemoptysis, chest tightness, and fatigue. But research from Nigeria and India also adds dyspnea. A cross-sectional study from a South African tertiary hospital shows that 10% of the patient does not have any clinical manifestation and diagnosis is made by incidental finding on imaging done for other purpose. It also identifies older age, smoking, male sex, and disease duration (early in SSc, MCTD, and IIM; advanced in RA, SLE, and pSS . MTX was prescribed for 37.1% of patient before the diagnosis of ILD and 33.9% continued, started or restarted after ILD diagnosis but no case of MTX induced pneumonitis was found. By far the most common respiratory sign is inspiratory bibasilar crackles. The common comorbid condition includes cigarette smoking (> 60% ), previous TB treatment(33.1%), and COPD (22.6%). All SSc patients and more than two-thirds of other patients had GORD .

The presentation of ILD could be before, simultaneous, or after the diagnosis of connective tissue disease. Research from South Africa suggest the Median time for ILD to develop is 2 years but patient with RA are older and take longer time to develop the ILD. A Retrospective, descriptive, and statistical analysis study from CEDOC/NOVA Medical School, Lisboa, Portugal shows that around 57 % of patients develop ILD with in 49.1 months after the diagnosis of CTD, in 8 % of the patient CTD was diagnosed with the median time of 5.1 months after ILD diagnosis and in about 35 % they diagnosed at the same time.

Around 4% of the patient do not have CXR findings of parenchyma disease but the most common finding include reticular, reticulonodular, and nodular.

## 2.3 Serological finding

The most common antibody identified in CTD-ILD is ANA(74.2%) with fine speckled pattern including 86% of RA patient .

A prospective study from Peking Union Medical College Hospital in China suggests that positive serum anti-CCP2, but not RF, may be associated with RA-ILD in RA patients . On the contrary, A cross-sectional study of prevalent ILD and a retrospective cohort study of incident ILD within the Veterans Affairs Rheumatoid Arthritis (VARA) from the USA shows the dual seropositive and individual concentration only associated with increased prevalence not with the incidence of RA-ILD. But this literature shows a strong correlation between RF concentration > 90 iu/ml highly Associated with the increased risk of Incident RA-ILD . Similarly, A Prospective study from NHO Kumamoto Saishunsou National Hospital shows that High titers of rheumatoid factor are associated with increased risks of ILD and AD. High levels of anti-cyclic citrullinated peptide antibodies were associated strongly with AD and less strongly with ILD . 73.3% of R.A patients have both R.F and ACCP.

Autoantibodies are detectable only in 50% of patients with PM/DM but Anti- ARS antibody is the one associated with commonly detected in a patient with ILD (around 70%) .but there are other type of Anti-ARS antibody like anti Pl-7, Anti-Pl-12,Anti-OJ, Anti-ZO ,and anti-tyrosil. These antibodies are rare but they are more highly associated with ILD than anti-JO-1 antibodies . Research from Portugal also supports this Four out of five IIM patients have an anti-jo-1 antibody the rest of one patient has an anti-PL-antibody .

The other Autoantibody is Anti-MDA5-positive and is associated with dermatomyositis-associated, rapidly progressive ILD (only 18% of the total cases reported) but two additional phenotypes were defined, one in which patients only have skin lesions and arthritis/arthralgia with a good prognosis (55%), and the other characterized by severe skin vasculopathy and myositis, with an intermediate prognosis. But it was difficult to differentiate between these groups So they use the anti-MDA5 antibody level, ferritin concentration, and presence of anti-Ro52 antibodies, to identify the patient at risk of rapidly progressing ILD. especially presence of

anti-Ro52 antibodies is associated with poor prognosis. In a retrospective cohort study from Tokyo Women's Medical University, Tokyo, Japan, Serum ferritin can be useful as a predictor of the occurrence of A/SIP and correlates with the prognosis of A/SIP in DM. Intensive treatment using combination therapy with various immunosuppressant agents should be chosen for patients with ILD with DM showing hyperferritinemia, especially levels >1500 ng/ml .

Autoantibody in systemic sclerosis, ANA is found in more than 95% of the patient. At least 12 specific antibodies are identified in patient in SSC patient which is found in 80% of the patient. But only some of them are highly associated with SSCL-ILD like anti-topo I, anti-Th/To, Anti-U11/U12 RNP, anti-eIF2B antibodies, Anti-PM/Scl, and anti-Ku syndromes. The most commonly identified antibody is Anti-topo-I which is found in 20-35 % of SSC patients . In prospective research from Portugal, SSC patient 54% have anti-scl 70, 15.4 % anti centromere antibody, and 7.7% anti-PM/SC antibody [8].

ILD is a feature in up to 48% of MCTD patients Several autoantibodies have been related with the ILD in MCTD, such as anti-Sm125 Anti-Ro52 antibodies and anti-U1 RNP antibodies.

In SLE ILD is very even if we diagnosed it we should have to consider other alternative disease (i.e MCT, SS ) so we need to work up with Anti-Ro/SSA , Anti-La/SSB and Anti-U1RNP. The anti-dnase is not associated with the development of ILD.

## 2.4 HRCT finding

The HRCT finding CTD-ILD is different based on the type of CTD

NSIP is the most commonly identified pattern in most CTD and NSIPs that occur in CTD are more common than idiopathic ILD. So patients with NSIP pattern ILD without extrathoracic manifestation should be investigated for CTD.

UIP pattern is the second most common and the most common pattern RA-ILD . But research from Syrilanka shows the predominance of NSIP despite the usual finding another research from South Africa shows both UIP and NSIP with similar frequency. This study also shows UIP and patient with RA have good PFT result these could be due early mortality of such patient. SSC and other CTD have a worse prognosis.

O.P. pattern could occur in any type of CTD but is more common in PM/DM.LIP is an uncommon pattern in CTD-ILD. Among CTDs, LIP is most closely associated with SS but also with SLE and RA.

A prospective study from Brazil shows that infra and supra-aortic esophageal dilation (i.e > 10 mm) is associated with esophageal dysmotility when compare with Radionuclide esophageal scintigraphy(RES). Another research from Italia shows that increased esophageal diameter (> 11 mm) on chest HRCT is associated with pulmonary and esophageal symptoms, more severe ILD, and lower DLCO .

The PFT results in most of the CTD-ILD have a restrictive pattern, but few patients have mixed and obstructive patterns. A multicenter retrospective cohort – study from the USA shows that the use of PFT alone as a screening test to detect ILD in early systemic sclerosis is inadequate. Another prospective study was done at Northwestern University Feinberg, Chicago, USA that compare the FVC and DLCO result with HRCT finding and Normal" FVC and DLCO in SSc patients, especially those with positive Scl-70 autoantibodies.

## 3. Objective of the study

- ### General objective

  To conduct a comprehensive characterization of CTD-related ILD including clinical presentation, radiological findings, PFT, and serological findings in TASH, Lancet specialized hospital and Rheum specialized clinic in Addis Ababa from Jan 2020 to March 2024.

- ### Specific objective

  To describe clinical manifestations that are frequently seen in CTD-ILD patient attenting rheumatology clinic of at TASH , Lancet specialized hospital and Rheum specialized clinic from Jan 2020 – Feb 2024

  To identify the common serologic result highly associated with CTD-ILD patient attenting rheumatology clinic of TASH , Lancet specialized hospital and Rheum specialized clinic from Jan 2020 – Feb 2024

  To desribe the common HRCT pattern between CTD and to see CXR findings in patient attenting rheumatology clinic at TASH , Lancet specialized hospital and Rheum specialized clinic from Jan 2020 – Feb 2024

  To identify frequent PFT pattern patient attenting rheumatology clinic of TASH , Lancet specialized hospital and Rheum specialized clinic from Jan 2020 – Feb 2024

  To Identify Predictors ILD in CTD-ILD patients attenting rheumatology clinic of TASH , Lancet specialized hospital and Rheum specialized clinic from Jan 2020 – Feb 2024

# 4. Methodology

## 4.1 Study area and period

The study was conducted in TASH , Lancet specialized Specialized Hospital and Rheuma specialized clinic Addis Ababa Ethiopia. Our study will be conducted in TASH which is located in Addis Ababa and giving considerable rheumatology service. TASH and are the largest government hospital in the country. The hospitals offer comprehensive healthcare services for around half a million patients per year through specialty clinics and inpatient service departments.

Lancet Specialized Medical and Surgical Center which is one of the major private owned hospital in addiss abeba. It was established 2020 and currently give more than 85,000 outpatient service from which the Rheumatology service is give with one of the two rheumatologist in the country.

Rheum Rheumatology and internal medicine speciality Cilinic was established in 2023 with well known Rheumatologist was giving maily rheumatology and internal medicine service.

This study was conducted from Jan 2020 to Feb 2024. This period was utilized to finalize the research proposal, collect data, analyze, and produce the last research

## 4.2 Study design

A Multicenter retrospective cross sectional study design was used for this study to address the research objectives considered in this study.

## 4.3 Selection of study population

### 4.3.1 Source population

The source population includes patients with connective tissue disease-related interstitial lung disease at rheumatology unit in TASH, Lancet specialized hospital and Rheum Specilized clinic from 2019 – 2023.

### 4.3.2. Sampling frame

A list of patients with connective tissue disease-related interstitial lung disease in the respective hospital.

### 4.3.3 Study population

The study population was patients with connective tissue disease-related interstitial lung disease in the sampling frame who are enrolled/selected for the study.

### 4.3.4 Study subject

The study subject was the patient with CTD-ILD who enrolled in the study and with full both HRCT and serological findings documented in the chart.

### 4.3.4 Study Unit

The Study unit was the patient electronic record .4.4 Inclusion and Exclusion Criteria

### 4.4.1 Inclusion criteria

- ✓ Patient age > 18 years
- ✓ Patients who had a follow-up at a specified hospital
- ✓ Patient with a confirmed diagnosis of connective tissue disease according to recent EULAR/ACR criteria and other specified for each disease
- ✓ Patient with HRCT, finding suggestive of ILD

### 4.4.2 Exclusion criteria

Patient with other pleuropulmonary manifestations of CTD

Patient with lung cancer

Patient confirmed to have methotrexate associated pneumonitis on subsequent follow up

## 4.5. Sample size and Sampling technique

The study included all CTD-ILD patients who were in follow-up from January 1, 2020 to Feb 2024 at rheumatologic clinic of TASH, Lancet Specialized Hospital and Rheum specialized clinic

## 4.6. Data collection procedure

### 4.6.1. Data collection instrument

Data was collected using a structured questionnaire which was adapted from previously published studies with some modifications to ensure applicability to our current study, validity, and reliability. The questionnaire consists of questions on socio-demographic factors, history of drug intake, clinical

presentation, serological findings, PFT pattern, and CXR & HRCT findings. Data was collected by trained data collector under the supervision of the principal investigator. Data collectors were selected from among the rheumatology unit nursing staff. Data collectors had a two-day training on how to extract the required information from record review (iCare system and patient chart) and complete the structured checklist.

### 4.6.2. Data Collection Method

Data was collected by trained data collectors under the supervision of the Investigator. Data collectors was selected from hospital rheumatology nursing staff. Personnel who assisted in chart retrieval and management recruited among the staff of the respective Hospital working in the patient records storage and retrieval office.

Data collectors have one-day training on how to extract the required information from patients' charts and complete the structured questionnaire.

## 4.7 Study variables

### 4.7.1 Dependent variables

Connective tissue disease-related interstitial lung disease

### 4.7.2 Independent variable

Types of CTD

Sociodemographic of the study (age, sex, marital status, Job …)

Clinical presentation (asymptomatic vs common symptom**)**

Laboratory variable (i.e. serological finding)

Imaging finding

PFT finding

## 4.8. Operational Definitions

**Clinical Manifesatation** is a new respiratory symptom or sign such as dyspnea, cough, fast breathing, sputum, chest pain, rales, hemoptysis that has developed before, at the of diagnosis or after the diagnosis of CTD.

**CTD-ILD** is defined as evidence of ILD demonstrated by CT (i.e., some combination of reticulation, ground-glass opacities, traction bronchiectasis, honeycombing, and/or cysts) in the setting of an established CTD or diagnosed later after the ILD.

**Pulmonary function test** suggestive of ILD are reduced TLC , VC , FEV but normal or increased FEV1/FVC.

**Diagnosis of CTD**

Diagnosis of SLE with 2019 EULAR/ACR classification criteria

Diagnosis of RA with 2010 EULAR/ACR classification criteria

Diagnosis of systemic sclerosis with 2013 EULAR/ACR classification criteria

Diagnosis of polymyosisitis/dermatomositis 2017 ACR/EULAR classification criteria for DM/PM,

Diagnosis of sjogrem syndrome with 2016 EULAR/ACR classification criteria Diagnosis of MCTD and UCTD by clinical manifestation and serologic finding ( i.e Anti-U1RNP)

**GORD** was defined by reflux symptoms and/or barium swallow and/or a dilated oesophagus on HRCT.

## 4.9. Data quality control

The Investigator Examined the appropriateness of the methodologies followed. The questionnaire reviewed for completeness and pre-testing will be undertaken. Data collectors was trained and data has been collected by the trained nurses and supervised by the Investigator. The questionnaires was tested on 5% of the sample (10 charts) in a similar setting, which was not be part of the study. Filled questionnaires was be checked for completeness and consistency of information by the data collector and the Investigator once weekly during data collection. The template have internal consistency checks and any inconsistency or ambiguity was addressed in time.

## 4.10. Data analysis techniques

The data was entered into and analyzed using SPSS version 25. Data cleaning was conducted exclusively by the Investigator. A descriptive summary of the data was presented in Tables and Figures. Frequency distributions was used to organize the data and present the responses obtained. Measures of central tendency and dispersion was calculated and utilized in the study variables as appropriate. In addition to descriptive statistics, Kaplan Meier survival analysis was employed to measure the fraction of AL patients developing pulmonary complications during treatment over time.

## 4.11. Ethical clearance

Proposal approval was obtained before the beginning of data collection from the Research and Publication Committee (RPC) of the Department of internal medicine, College Health Sciences (CHS), TASH, Lance specialized hospital and Rheum specialized clinic . All information was kept confidential and the information collected was used solely for the intended purpose. Personal Identifier Information (PII), including names of patients, was not included in the questionnaire. Codes was used instead and completed questionnaires will be stored safely by the Investigator.

## 4.12. Dissemination of results

The findings of this study will be submitted to the Department of Internal Medicine of College of Health Sciences, Addis Ababa University as a partial fulfillment of specialty certificate in Internal Medicine. The outcome of this study will be presented to other key stakeholders such as annual conferences to reach the wider scientific society. Finally, the manuscript will be submitted to a reputable scientific journal for possible publication.

# 5. Results

## Response Rate

Initially a total of 96 patients (all patients available at TASH and Lancet General Hospital chest and rheumatology clinic follow-up for CTD-ILD) were included in the study. However 4 patients were excluded for 2 patients not fulfilling the inclusion criteria, 1 patient lost to follow-up and 1 patient death. As a result, analysis was made based on the data obtained from 92 patients. The response rate was indicated in the table below (table 1).

Table 1: Response rate

| ITEM | RESPONSE RATE | |
|---|---|---|
| | Number | Percent% |
| Sample size | 96 | 100% |
| Collected | 92 | 95.83% |
| Remaining uncollected | 4 | 4.17% |

Source: own survey

## Socio demographic characteristics of CTD-ILD patients

The mean age of CTD-ILD patients was 47.33, CI (44.48, 50.17). The age of the patients ranges from 21 to 80. From the data presented in table below, majorities (89.1%) of the patients were female and the remaining 10.9% were male. This indicates that the male to female ratio is 1:8. Regarding job status of the patients, majorities (75.0%) of the patients were unemployed, 18.5% worked in governmental office other than school and 3.3% were farmers.. (Table 2)

Table 2: sociodemographic characteristics of patients

| Item | Option | Freq | Valid percent | Cumulative percent |
|---|---|---|---|---|
| Gender | Female | 82 | 89.1 | 89.1 |
| | Male | 10 | 10.9 | 100.0 |
| | Total | 92 | 100.0 | |
| Job status | Not known | 2 | 2.2 | 2.2 |

| | | | | |
|---|---|---|---|---|
| | Another governmental office | 17 | 18.5 | 20.7 |
| | Farmer | 3 | 3.3 | 23.9 |
| | Student | 1 | 1.1 | 25.0 |
| | Unemployed | 69 | 75.0 | 100.0 |
| | Total | 92 | 100.0 | |
| Marital status | Not known | 3 | 3.3 | 3.3 |
| | Divorced | 11 | 12.0 | 15.2 |
| | Married | 60 | 65.2 | 80.4 |
| | Single | 3 | 3.3 | 83.7 |
| | Widow | 15 | 16.3 | 100.0 |
| | Total | 92 | 100.0 | |

Source: own survey

Majority of patients age at onset of CTD symptoms were 50-60 (32.6%), followed by age of 30-40 (31.5%), 14.1% of patients age at onset of CTD was 20-30, and 9.8% of patients age at diagnosis of CTD were 60-70. Similarly majority of patients age at onset of ILD symptoms were 50-60 (33.7%) and 27.2% of the patients age at onset of ILD symptom were 30-40, 14.1% were at age of 40-50, and 10.9% were at age of 20-30. According to the collected data; the most common type of CTD is RA (44.6%), followed by SSC (40.2%), PM/DM (6.5%), MCTD (4.3), and SLE (3.3%). (table 3)

Table 3 Age of onset of CTD and ILD symptoms and type of CTD

| Item | Options | Frequency | Valid Percent | Cumulative Percent |
|---|---|---|---|---|
| Age of onset of CTD symptoms | > 70 | 3 | 3.3 | 3.3 |
| | 20-30 | 13 | 14.1 | 17.4 |
| | 30-40 | 29 | 31.5 | 48.9 |
| | 40-50 | 8 | 8.7 | 57.6 |
| | 50-60 | 30 | 32.6 | 90.2 |

| | | | | |
|---|---|---|---|---|
| | 60-70 | 9 | 9.8 | 100.0 |
| | Total | 92 | 100.0 | |
| Age of onset of ILD symptoms | > 70 | 5 | 5.4 | 5.4 |
| | 10-20 | 1 | 1.1 | 6.5 |
| | 20-30 | 10 | 10.9 | 17.4 |
| | 30-40 | 25 | 27.2 | 44.6 |
| | 40-50 | 13 | 14.1 | 58.7 |
| | 50-60 | 31 | 33.7 | 92.4 |
| | 60-70 | 7 | 7.6 | 100.0 |
| | Total | 92 | 100.0 | |
| Type of CTD | MCTD | 4 | 4.3 | 4.3 |
| | PM/DM | 6 | 6.5 | 10.9 |
| | RA | 41 | 44.6 | 55.4 |
| | SLE | 3 | 3.3 | 58.7 |
| | SSC | 37 | 40.2 | 98.9 |
| | UCTD | 1 | 1.1 | 100.0 |
| | Total | 92 | 100.0 | |

Source: own survey

## Clinical manifestations seen in CTD-ILD

The most common clinical symptoms of CTD-ILD patients were cough (72.8%), Dyspnea (41.3%), fatigue (41.3%), and decreased exercise tolerance (40.2%). 10.9% of CTD-ILD patients experienced sputum and 2.2% experienced chest tightness. On the other hand 7.6% of CTD-ILD patients were Asymptomatic. The most common physical finding of CTD-ILD patients was bilateral inspiratory crackle (70.7%). The other present physical findings were decreased lung sound (14.1%), and wheeze (5.4%). 18.5% of CTD-ILD patients had bilateral leg swelling, or clear chest or unremarkable physical finding. (Table 4)

Table 4 Clinical manifestations seen in CTD-ILD

| Item | Options | Frequency | Percent |
|---|---|---|---|
| Clinical symptom | Cough | 67 | 72.8 |
| | Decreased exercise tolerance | 37 | 40.2 |
| | Dyspnea | 38 | 41.3 |
| | Sputum | 10 | 10.9 |
| | Chest tightness | 2 | 2.2 |
| | Fatigue | 38 | 41.3 |
| | Asymptomatic | 7 | 7.6 |
| | Others (symptoms) | 2 | 2.2 |
| Physical finding | Bilateral inspiratory crackle | 65 | 70.7 |
| | Wheeze | 5 | 5.4 |
| | Decreased lung sound | 13 | 14.1 |
| | Loud P2 | 1 | 1.1 |
| | Others (P/E) | 17 | 18.5 |

Others (symptoms): lower extremity swelling and pleuritic chest pain

Others (P/E): bilateral leg edema, clear chest and unremarkable physical finding

Source: own survey

Majority of CTD patients were diagnosed with ILD with in the first 1-5 years after diagnosis with CTD (40.2%). 22.8% of CTD-ILD patients were diagnosed with ILD with in the first year of diagnosis of CTD, and 20.7% were diagnosed with ILD more than 5 years after diagnosis of CTD. 13.0% of CTD-ILD patient's were diagnosed with ILD at presentation. (Table 5)

Table 5 Diagnosis of ILD from the CTD diagnosis

| Time to Diagnosis of ILD from the CTD diagnosis | Frequency | Valid Percent | Cumulative Percent |
|---|---|---|---|
| > 5 years | 19 | 20.7 | 20.7 |
| 1-5 years | 37 | 40.2 | 60.9 |
| At presentation | 12 | 13.0 | 73.9 |
| before the CTD | 3 | 3.3 | 77.2 |

| | | | |
|---|---|---|---|
| Within 1 year | 21 | 22.8 | 100.0 |
| Total | 92 | 100.0 | |

Source: own survey

The time gap from the onset of CTD to the diagnosis of ILD in RA patient is 1-5 years 14 (34.1 %) , > 5 years 17 (41.5% ) and with in 1 year 4 (9.8%). The most common gap in SSc patient is within 1-5 years 16 (43.2% ) , within 1 year 11 (29.7%) and greater than 5 yaers 5(13.5%). Figure (1)and table (5)

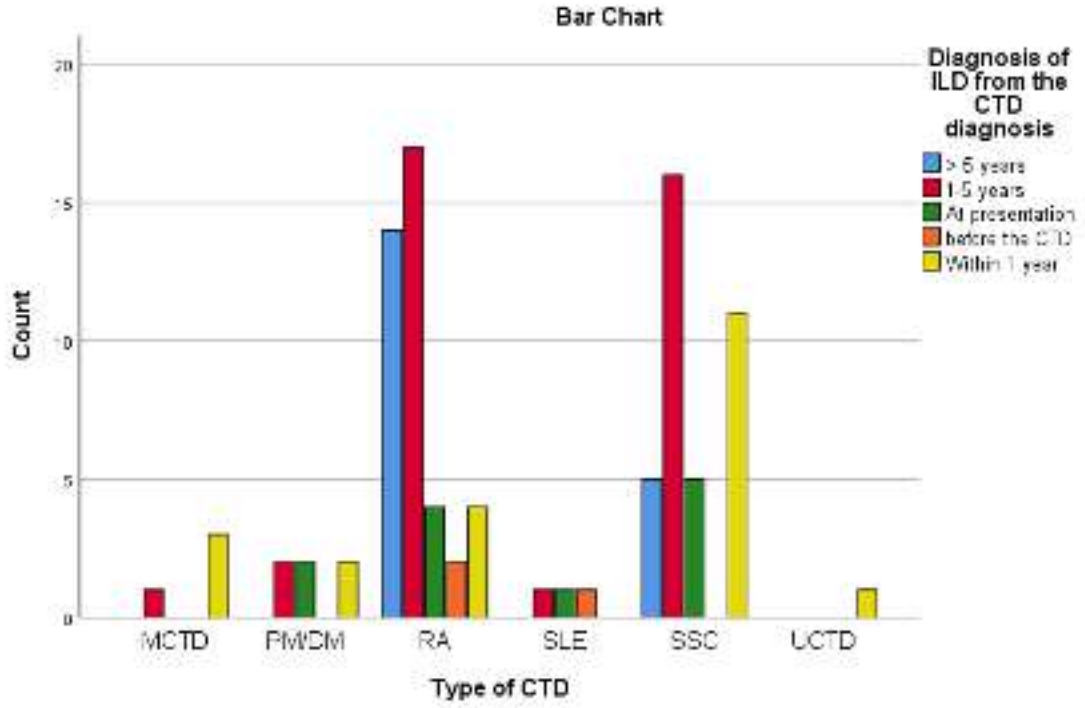


Figure 1: diagnosis of ILD from CTD

Table 5 of type of CTD with time to diagnosis of ILD from CTD

| | | | Diagnosis of ILD from the CTD diagnosis | | | | | |
|---|---|---|---|---|---|---|---|---|
| | | | > 5 years | 1-5 years | At presentation | before the CTD | Within 1 year | |
| Type of CTD | MCTD | Count | 0 | 1 | 0 | 0 | 3 | 4 |
| | | % within Type of CTD | 0.0% | 25.0% | 0.0% | 0.0% | 75.0% | 100.0% |
| | PM/DM | Count | 0 | 2 | 2 | 0 | 2 | 6 |
| | | % within Type of CTD | 0.0% | 33.3% | 33.3% | 0.0% | 33.3% | 100.0% |
| | RA | Count | 14 | 17 | 4 | 2 | 4 | 41 |
| | | % within Type of CTD | 34.1% | 41.5% | 9.8% | 4.9% | 9.8% | 100.0% |
| | SLE | Count | 0 | 1 | 1 | 1 | 0 | 3 |
| | | % within Type of CTD | 0.0% | 33.3% | 33.3% | 33.3% | 0.0% | 100.0% |
| | SSC | Count | 5 | 16 | 5 | 0 | 11 | 37 |
| | | % within Type of CTD | 13.5% | 43.2% | 13.5% | 0.0% | 29.7% | 100.0% |
| | UCTD | Count | 0 | 0 | 0 | 0 | 1 | 1 |
| | | % within Type of CTD | 0.0% | 0.0% | 0.0% | 0.0% | 100.0% | 100.0% |
| Total | | Count | 19 | 37 | 12 | 3 | 21 | 92 |
| | | % within Type of CTD | 20.7% | 40.2% | 13.0% | 3.3% | 22.8% | 100.0% |

In the present study, majority of the patients were non-smokers (88.0%), 7.6% were past smokers, and the remaining 4.3% smoking status were unknown. Regarding Tb history, 8.7% of the CTD-ILD patients had Tb treatment history, while the 91.3% of the patients had no Tb treatment history. Majority of the CTD-ILD patients had comorbid illnesses (77.17%). 21.7% of the patients had GERD. (Table 6, 7)

Table 6 smoking and TB treatment history

| Item | Options | Frequency | Valid Percent | Cumulative Percent |
|---|---|---|---|---|
| Smoking history | Unknown smoking status | 4 | 4.3 | 4.3 |
| | no smoking history | 81 | 88.0 | 92.4 |
| | Past smoker | 7 | 7.6 | 100.0 |
| | Total | 92 | 100.0 | |
| History of Tuberculosis treatment | No | 84 | 91.3 | 91.3 |
| | Yes | 8 | 8.7 | 100.0 |
| | Total | 92 | 100.0 | |

Source: own survey

Table 7 Comorbid illness history

| Co-morbid illness | Frequency | Percent (from the whole) | Valid percent (from pts who had comorbid illness) |
|---|---|---|---|
| GERD | 20 | 21.7 | 28.2 |
| HIV | 1 | 1.01 | 1.4 |
| Others | 54 | 58.7 | 76.1 |
| No co-morbid illness | 21 | 22.8 | |
| Total | 92 | 100.0 | |

Others: HTN,DM,dyslipidemia, dermatomyositis, hypothyroidism, IDA, severe lumbar stenosis, MDD, Osteoporosis, proactinoma, pulmonary HTN, Spinal canal stenosis, and TBpericarditis

Source: own survey

### Common serologic result highly associated with CTD-ILD

The most common serologic tests done and became positive for our patients were RF and ANA (47.8% each). Followed by Anti-sci-70 (37.0%), ACPA (29.3%), and Anti-dsDNA (6.5%) (Table 8)

Table 8 Immunologic characteristics

| Immunologic characteristics | Frequency | Percent |
|---|---|---|
| Rheumatoid factor | 44 | 47.8 |
| ACPA | 27 | 29.3 |
| ANA | 44 | 47.8 |
| Anti-dsDNA | 6 | 6.5 |
| ACA | 0 | 0 |
| Anti-U1-RNP | 3 | 3.3 |
| Anti-Ro/SSA | 1 | 1.1 |
| Anti-La/SSB | 0 | 0 |
| Anti-jo-1 | 5 | 5.4 |
| Other | 8 | 8.7 |
| Anti-MDA-5 | 3 | 3.3 |
| Anti-MI-2 | 2 | 2.2 |
| Anti-scl-70 | 34 | 37.0 |
| Anti-centromere | 11 | 12.0 |
| Anti-RNA polymerase III | 4 | 4.3 |

Source: own survey

ANA titer was done for 30 patients (32.6%) of the total patients. From those 18 (19.6% of the whole patients had ANA 1:320. And the reaming 12 patients had ANA titer of ANA 1:100 or ANA 1:1000 (6.5% each). According to the study, we found that the most common ANA pattern was speckled. It was found in 16.3% of the total patients. Homogeneous ANA pattern was found in 15.2% of the patients and nucleolar was found in 10.9% of the whole patients. (Table 9)

Table 9 ANA Titer and pattern

| Item | Options | Frequency | Percent | Valid Percent | Cumulative Percent |
|---|---|---|---|---|---|
| ANA Titer | Not done | 62 | 67.4 | 67.4 | 67.4 |
| | ANA 1:100 | 6 | 6.5 | 6.5 | 73.9 |
| | ANA 1:1000 | 6 | 6.5 | 6.5 | 80.4 |
| | ANA 1:320 | 18 | 19.6 | 19.6 | 100.0 |
| | Total | 92 | 100.0 | 100.0 | |
| ANA pattern | homogeneous | 14 | 15.2 | 15.2 | 15.2 |
| | Speckled | 15 | 16.3 | 16.3 | 31.5 |
| | Nucleolar | 10 | 10.9 | 10.9 | 42.4 |
| | Total | 39 | 42.4 | 42.4 | |
| | Not done | 53 | 57.6 | 57.6 | |
| | Total | 92 | 100.0 | 100.0 | |

Source: own survey

The most commonly identified ANA pattern in SSc are homogenous 9(24.3%), speckled 9(24.3%), and nucleolar 9 (24.3%).The most fcommon ANA pattern in RA patient is speckled pattern 3(7.3%). Figure 2 and table 10

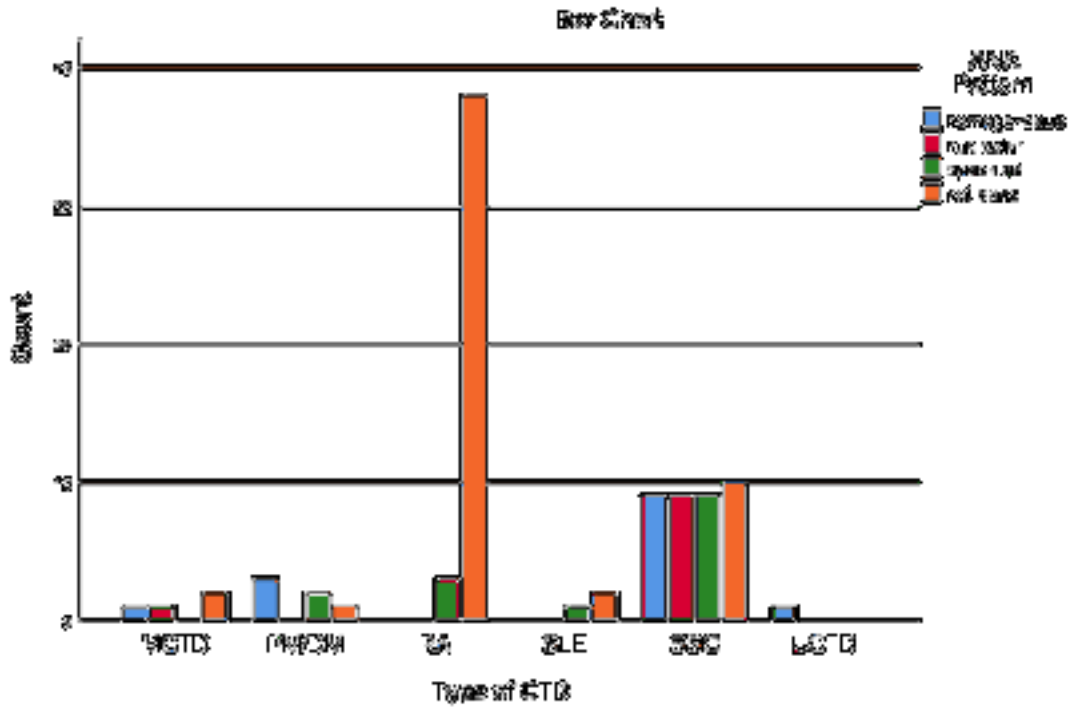

Figure 2 : ANA pattern with type of CTD

Table 10 Cross tabulation of ANA patterns with type of CTDs

| | | | ANA Pattern | | | | |
|---|---|---|---|---|---|---|---|
| Type of CTD | | | homogeneous | nucleolar | speckled | not done | Total |
| | MCTD | Count | 1 | 1 | 0 | 2 | 4 |
| | | % within Type of CTD | 25.0% | 25.0% | 0.0% | 50.0% | 100.0% |
| | PM/DM | Count | 3 | 0 | 2 | 1 | 6 |
| | | % within Type of CTD | 50.0% | 0.0% | 33.3% | 16.7% | 100.0% |
| | RA | Count | 0 | 0 | 3 | 38 | 41 |
| | | % within Type of CTD | 0.0% | 0.0% | 7.3% | 92.7% | 100.0% |
| | SLE | Count | 0 | 0 | 1 | 2 | 3 |
| | | % within Type of CTD | 0.0% | 0.0% | 33.3% | 66.7% | 100.0% |
| | SSC | Count | 9 | 9 | 9 | 10 | 37 |
| | | % within Type of CTD | 24.3% | 24.3% | 24.3% | 27.0% | 100.0% |
| | UCTD | Count | 1 | 0 | 0 | 0 | 1 |
| | | % within Type of CTD | 100.0% | 0.0% | 0.0% | 0.0% | 100.0% |
| Total | | Count | 14 | 10 | 15 | 53 | 92 |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| | | % within Type of CTD | 15.2% | 10.9% | 16.3% | 57.6% | 100.0% |

### Common HRCT pattern between CTD and, CXR findings

The most common HRCT pattern observed was ground glass appearance (76.1%), followed by reticular shadow (50.0%), traction bronchiectasis (37.0%), honey combing (34.8%), and reticulo nodular opacities (19.6%). (Table 10)

Table 11 HRCT pattern

| HRCT pattern | Frequency | Percent |
|---|---|---|
| Ground glass appearance | 70 | 76.1 |
| Reticular shadows | 50 | 50 |
| Traction bronchiectasis | 34 | 37.0 |
| Honeycombing | 32 | 34.8 |
| Reticulonodular opacities | 18 | 19.6 |
| Pleural effusion | 2 | 2.2 |
| Diffuse alveolar opacities | 1 | 1.1 |

Source: own survey

Regarding the Final HRCT conclusion the most common ILD pattern was NSIP (69.6%), followed by UIP (28.3%), and COP (2.2%). CXR was done for 82.6% of the total patients. The most common CTD-ILD CXR findings were reticular opacities, ground glass opacities (38.0%) and bilateral reticulo nodular opacity which was found in 23.9% of patients. 12.0% of the patients had normal CXR. The Pulmonary function test was only done for 7 patients (7.6%). From those 3 of them were obstructive pattern (3.3%) and 4 of them were restrictive pattern (4.3%). (Table 11)

Table 12 final HRCT conclusion, CXR and PFT finding

| Item | Options | Frequency | Valid Percent | Cumulative Percent |
|---|---|---|---|---|
| Final HRCT conclusion | COP | 2 | 2.2 | 2.2 |
| | NSIP | 64 | 69.6 | 71.7 |
| | UIP | 26 | 28.3 | 100.0 |
| | Total | 92 | 100.0 | |
| Chest X-ray finding | Normal | 11 | 12.0 | 12.0 |
| | reticular opacities, ground glass opacities | 35 | 38.0 | 50.0 |
| | bilateral reticulo nodular opacity | 22 | 23.9 | 73.9 |
| | Pneumonia | 1 | 1.1 | 75.0 |
| | old granuloma | 1 | 1.1 | 76.1 |
| | Consolidation | 4 | 4.3 | 80.4 |
| | Cardiomegaly | 1 | 1.1 | 81.5 |
| | old granuloma & reticulonodular pattern | 1 | 1.1 | 82.6 |
| | not done | 16 | 17.4 | 100.0 |
| | Total | 92 | 100.0 | |
| Pulmonary function test finding | Not done | 85 | 92.4 | 92.4 |
| | Obstructive pattern | 3 | 3.3 | 95.7 |
| | Restrictive pattern | 4 | 4.3 | 100.0 |
| | Total | 92 | 100.0 | |

Source: own survey

## Treatment history

Only 12% of the patients had any history of previous treatment before the diagnosis of CTD. Most common previous treatment histories were Amlodipine (5.4%), Metformin (3.3%), and Levothyroxine (2.2%). (Table 12)

Table 13 treatment history before diagnosis of CTD

| Any treatment history before diagnosis of CTD | Frequency | Percent |
|---|---|---|
| Amlodipine | 5 | 5.4 |
| Amitriptyline | 1 | 1.1 |
| Metformin | 3 | 3.3 |
| Bromocriptine | 1 | 1.1 |
| Completed Anti-Tb | 1 | 1.1 |
| Levothyroxine | 2 | 2.2 |
| RVI on HAART | 1 | 1.1 |

Source: own survey

According to the result obtained, 59.8% of the CTD patients were treated with Corticosteroid before diagnosis of ILD, 48.9% of the patients were treated with Methotrexate, 19.6% of the patients were treated with Mycophenolate, and 5.4% of the patients were treated with Azathioprine. (Table 13).

Table 14 type of treatment the patient is getting for diagnosis of CTD

| Treatment type | Frequency | Percent |
|---|---|---|
| Azathioprine | 5 | 5.4 |
| Methotrexate | 45 | 48.9 |
| Leflunomide | 1 | 1.1 |
| Cyclophosphamide | 3 | 3.3 |
| Mycophenolate | 18 | 19.6 |
| Corticosteroid | 55 | 59.8 |
| Others | 50 | 54.3 |

Others: amlodipine, pantoprazole, chloroquine, cyanocobalamine, nefedipine, enalapril, gabapentine, hydroxychloroquinee, folic acid, sulfasalazine, sildenafil

Duration of treatment before the onset of ILD was < 1 year for 42.4% of the patients, and > 1 year for 55.4%. 37 % of the total patients continued the same medication after the diagnosis of ILD. (Table 14).

Table 15 type and duration of treatment

| Item | Options | Frequency | Valid Percent | Cumulative Percent |
|---|---|---|---|---|
| Duration of treatment before the onset of ILD | Not known | 2 | 2.2 | 2.2 |
| | < 1 year | 39 | 42.4 | 44.6 |
| | > 1 year | 51 | 55.4 | 100.0 |
| | Total | 92 | 100.0 | |
| Treatment continued after dx of ILD | No | 58 | 63.0 | 63.0 |
| | Yes | 34 | 37.0 | 100.0 |
| | Total | 92 | 100.0 | |

The collected data on CTD-ILD patients on their treatment for the diagnosis of CTD-ILD revealed that; 79.3% of the patients were treated with Corticosteroid, 42.4% of the patients were treated with Chloroquine, and 30.4% of the patients were treated with Mycophenolate. 6.5% of the patients were treated with Methotrexate.(Table 15).

Table 16 Treatment after diagnosis of ILD

| Treatment after diagnosis of ILD | Frequency | Percent |
|---|---|---|
| Corticosteroid | 73 | 79.3 |
| Mycophenolate | 28 | 30.4 |
| Chloroquine | 39 | 42.4 |
| Methotrexate | 6 | 6.5 |
| Amlodipine | 17 | 18.5 |
| Nifedipine | 9 | 9.8 |
| Intermittent Omeprazole | 1 | 1.1 |
| Azathioprine | 5 | 5.4 |

| | | |
|---|---|---|
| No specific treatment | 2 | 2.2 |
| Intermittent Pantoprazole | 5 | 5.4 |
| Hydroxychloroquine | 1 | 1.1 |
| Sulfasalazine | 1 | 1.1 |
| Prifenidone | 1 | 1.1 |
| Enalapril | 1 | 1.1 |
| Cyclophosphamide | 2 | 2.2 |

**Predictors of CTD-ILD in RA patients**

Using the collected data the presence of association between socio demographic and clinical characteristics of the RA-ILD with presence of RA-ILD was first analyzed by bivariate logistic regression. After examining the statistical significance of independent variables by using the bivariate logistic regression age at onset of ILD symptoms and time to diagnosis of ILD from CTD were found to be statistically significant variables with ($p < 0.25$). Thus, these variables were further analyzed in multivariable logistic regression. Then multivariate logistic regression analysis was done to determine significant variable at $p<0.05$.The table below summarizes the findings of bivariate and multivariable logistic regression.

RA patients within the age of 41-60 were 19.83 times (AOR=19.83, CI (4.78-82.25)) more likely to develop ILD compared to patients with age of < 40. RA patients with the age of > 61 were 2.17 times (AOR=14.64, CI (3.00-71.45)) more likely to develop ILD compared to patients with age of < 40. More than five years for diagnosis of ILD from the CTD diagnosis were 7.67 times (AOR=7.67, CI (1.39-42.15)) more likely to develop ILD compared to RA patients who develop ILD with in first year of CTD diagnosis. (Table 16).

Table 17 Factors associated with RA-CTD

| Variable | No RA-CTD | Presence of RA-CTD | Crude Odds ratio(CI) | Adjusted Odds ratio | P value |
|---|---|---|---|---|---|
| **AGE AT ONSET OF ILD** | | | | | |
| <40 | 32 | 3 | 1 | | |
| 41-60 | 12 | 25 | 22.22(5.65-87.37) | 19.83(4.78-82.25) | **.000** |
| >61 | 7 | 12 | 18.29(4.05-82.48) | 14.64(3.00-71.45) | **.001** |
| **Diagnosis of ILD from the CTD diagnosis** | | | | | |
| > 5 years | 5 | 14 | 11.90(2.67-52.96) | 7.67(1.39-42.15) | **.019** |
| 1-5 years | 20 | 17 | 3.61(1.02-12.82) | 3.18(.73-13.90) | .123 |
| At presentation | 8 | 4 | 2.12(.42-10.75) | 1.58(.24-10.31) | .632 |
| before the CTD | 1 | 2 | 8.50(.61-118.64) | 2.97(.197-44.59) | .432 |
| Within 1 year | 17 | 4 | 1 | | |

ANA pattern is significantly associated with SSC-ILD. Bivariate logistic regression revealed that those SSC patients who had homogeneous ANA pattern were 7.74 times more likely to develop

ILD than those whose ANA pattern was not known. Those SSC patients who had nucleolar ANA pattern were 38.70 times more likely to develop ILD than those whose ANA pattern was not known. Those SSC patients who had speckled ANA pattern were 6.45 times more likely to develop ILD than those whose ANA pattern was not known. (Table 17)

Table 18 bivariate logistic regression analysis of ANA pattern and

| ANA pattern | No ILD-Scc | Presence of ILD-Scc | Crude Odds ratio(CI) |
|---|---|---|---|
| homogeneous | 5 | 9 | 7.74(2.13-28.17) |
| Nucleolar | 1 | 9 | 38.70(4.39-341.52) |
| Speckled | 6 | 9 | 6.45(1.87-22.32) |
| not done | 43 | 10 | 1 |
| Total | 55 | 37 | |

# 7. Discussion

A total of 92 patients, 82 females and 10 males, were included in the study, with a female-to-male ratio of 8:1. The median onset of CTD was 47.2. In our study, most patients were unemployed (75%), government employees (18%), or farmers (3.3%).

Inconsistent with existing literature, our study shows that the most common CTDs Associated with ILD are in decreasing order RA, Ssc, PM/DM, MCTD, SLE & UDCTD, which is consistent with most CTD-ILD series conducted in South Africa, India, and Sri Lanka (4)(6). However, a descriptive study from Nigeria and Portugal shows that SLE and SSC are common CTDs, respectively(7)(10).

The most common symptoms in our study are cough, dyspnea, and fatigue. However 7.6% of the patients were asymptomatic at the time of the imaging study, the frequently identified chest findings are bilateral rale, decreased lung sound, and wheezing (4)(5)(6)(9). In contrast to the study done in South Africa which shows 11% of the patients were asymptomatic, however, our study shows a relatively lower rate of 7.6% of the patients are asymptomatic, these may be due to low screening that we use for our patients, and the lower sample size of the study (7).

The manifestation of CTD-ILD in our study was variable. The majority of patients were diagnosed within 5 years, followed by those diagnosed within one year and within 5 years of CTD diagnosis. However, in 3 (3.3%) patients, ILD was diagnosed before the onset of CTD, all of whom had RA. Relative to other CTD patients, those with RA had a longer time from the onset of CTD to the onset of ILD, at 34%.

The most commonly identified comorbidities are GORD, HTN, and DM. One patient was found to be HIV positive. Most of the patients with GORD symptoms are scleroderma patients who take proton pump inhibitors intermittently(5). In contrast to the study done in South Africa, only 7.6% of the patients had a smoking history, and only 8.7% had a history of TB treatment, which is relatively lower compared to other research (7). These may be due to stigmata associated with smoking in our society or it may the true prevalence of smoking may be low and the lower sample size in our study.

The most commonly identified serologic findings are RF, ANA, Anti-scl-70, and ACPA. All RA patients have RF, but only 65% of the patients have ACPA positive, which is comparable with other literature (7)(12). Inconsistent with other studies, Anti-scl-70 is found in 89% of the patients, followed by anticentromere and anti-RNA polymerase. The most frequently encountered ANA patterns are homogeneous and speckled ANA pattern(23). The rate of ANA positivity (47.8%) in these was lower than in other studies, such as 74% in South Africa and 100% in research from Nigeria. These might be related to financial reasons. The most common ANA patterns are speckled, homogeneous, and nucleolar(23).

From 6 PM/DM patients, Anti-jo 1 was found in 6 patients and Anti-NDA-5 in 3 patients. Anti-Mi2 and anti-TIF were also seen in this group of patients (13).

In our study, PFT was documented for only 7 patients, out of which only 4 had a restrictive pattern, while 3 patients showed an obstructive pattern. The reason is that for most patients, it was done after starting treatment, and for the rest, it was not documented.

In contrast to the study conducted in South Africa, which showed no radiographic abnormality in the parenchyma in only 4% of patients, our study showed 12% (7). However, our result is much lower when compared to a study from India, which shows that 47% of patients have no radiographic abnormality. Inconsistent with other literature, the common radiographic findings are reticulonodular and ground-glass opacities (7)(9)(11).

In consistent with the other study the most common imaging finding in our study is Ground glass appearance, Reticular shadows , Traction bronchiectasis , Honeycombing. The most common HRCT patten is in decreasing order NSIP , UIP and COP. since two study from ayder and BLH done in patient with ILD sugest that the most frequent HRCT pattern is NSIP so we need to work for the CTD in these group of patient (21) (22). Incontrast from the study in south Africa and India which suggest that the most common pattern in in RA is NSIP and equal both NSIP &UIP patterns respectively however our study suggests that the NSIP pattern is more common which

could be due to a smaller sample size and environmental exposure. There are only 2 (2.17%) COP patients in our study both of them are PM/DM the other has an NSIP pattern.

MTX was used for 45 (48.9%) patients before the diagnosis of ILD but only 6 (6.5%) patients continued with it after the diagnosis of ILD but no patient has developed methotrexate-associated pneumonitis (7).
In our study we found that there is strong association between association b/n the ange of the patient and durationof illness with the development of ILD in RA patients which is similar to the other previous study.(24)(25).but for other patient

## 8. Conclusion

The study aim was to characterize the clinical manifestation, serologic, and imaging findings of CTD-ILD. Based on the quantitative and qualitative data that we use most of CTD-ILD patients are female and older with frequent presentation are cough ,dyspnea and exercise intolerance. The most common commornid disease are GORD and HTN.ILD is frequently encountered in RA, SSc,and MCT and with most frequent HRCT pattern of NSIP. Older Age and longer duration of Illness are highly associated with the development of ILD in RA patients. The most frequently identified serologic findings are ANA, RF, Anti-scl-70 and ACPA and frequentely encountered ANA patterns are speckled and homogenous patterns.

## 9. Recommendation

### TO Researcher

We recommend prospective multicenter studies be carried out and prospective disease registries be established to explore the epidemiological, clinical, radiological, and prognostic characteristics of CTD-ILD.

### TO health sector

To have screening HRCT for patients with SSc patients especially those with Ant-scl-70 positive, and also for older RA patients with longer duration of illness(need few prospective trial

### TO physician

To have strong suspicion of CTD-ILD while evaluating patient at clinic with CTD during routine evaluation and to have proper history and evaluation.

**10.Strength of the study**

To the best of my knowledge these is the first study conducted in the ethiopia so it will be a benchmark for future similar study. It is multicenter , include 4 years of patient **,** all patient.

**11. Limitation of the study**

There are three main limitations of study

Since this study involved retrospective data, some of the relevant data could not be retrieved due to the misplacement of reports and records as well as deficiencies in record Keeping. Second even though we have tried to increase the sample size by making the study multicenter and increase the time of investigation to 4 years still we can not have enough sample size. The third is few patients could not afford the investigastion, especially for serological work-up so difficult to complete the investigation.

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# Annex

Addis Ababa University College of Health Science

School of Medicine Department of internal medicine
This checklist is prepared for assessment of **Characterization of connective tissue related interestial lung disease**
in TikurAnbessa specialized Hospital, Yekatit 12
Medical college, and St.Peter Specialized hospitals.
Data collection date:_____
Name of data collector_____

signature_____ Serial NO _____ card NO_____
Address_____

Structured Questioner for Data collection

## Questionnaire

Part-I - Socio-demographic Factors

1. Age
   - ❑ 15-30
   - ❑ 30 - 55
   - ❑ 55-70
   - ❑ > 70
2. Age of onset of the CTD symptom
   - ❑ 10-20
   - ❑ 20-30
   - ❑ 30-40
   - ❑ 50-60
   - ❑ 60-70
   - ❑ > 70
3. Age of onset of ILD symptoms
   - ❑ 10-20
   - ❑ 20-30
   - ❑ 30-40
   - ❑ 40-50
   - ❑ 50-60
   - ❑ >70

4. Sex
   - ❑ MALE
   - ❑ Female
5. Marital statues
   - ❑ Single
   - ❑ Married
   - ❑ Divorced
   - ❑ widow
6. Job
   - ❑ student
   - ❑ Farmer
   - ❑ Teacher
   - ❑ Another governmental office
   - ❑ Unemployed
   - ❑ Factory worker
7. If factory worker please specify----------
8. Type of CTD
   - ❑ RA
   - ❑ PM/DM
   - ❑ SSC
   - ❑ SS
   - ❑ SLE
   - ❑ MCTD
   - ❑ UCTD

part -2 clinical manifestation

9. Clinical symptom
   - ❑ Cough
   - ❑ Decrease exercise tolerance
   - ❑ Dyspnea
   - ❑ Sputum
   - ❑ hemoptysis
   - ❑ chest tightness
   - ❑ fatigue
   - ❑ Asymptomatic
   - ❑ others ----------
10. physical finding
    - ❑ cyanosis
    - ❑ bilateral inspiratory coracle
    - ❑ wheeze

- ❑ decrease lung sound
- ❑ digital clubbing
- ❑ loud P2
- ❑ others------

11. diagnosis of CTD
    - ❑ at presentation
    - ❑ within 1 year
    - ❑ 1-5 years
    - ❑ > 5 years
12. Smocking history
    - ❑ Ever smoker
    - ❑ Past smoker
    - ❑ Current smoker
13. History Tuberculosis treatment
    - ❑ Yes
    - ❑ No

14. Comorbid disease
    - ❑ Asthma
    - ❑ HIV
    - ❑ GORD
    - ❑ COPD
    - ❑ Others
15. Any treatment before the diagnosis of CTD
    - ❑ If please specify the type of medication …….

Part-3 serologic, CXR, HRCT, PFT finding

16. Serological finding
    - ❑ R.F
    - ❑ ACPA
    - ❑ ANA
    - ❑ Anti-dsDNA
    - ❑ Anti-JO-1
    - ❑ Anti scl-70
    - ❑ Anti-centromere
    - ❑ Anti-RNA polymerase III
    - ❑ Anti-U1-RNP
    - ❑ Anti-Ro/SSA
    - ❑ Anti-La/SSB

- ❑ Anti Jo-1
- ❑ Anti-MI-2
- ❑ Anti MDA-5
- ❑ If other please specify------

17. ANA pattern
    - ❑ If done please specify ----------
18. HRCT abnormality
    - ❑ Ground glass appearance
    - ❑ Reticular shadows
    - ❑ Traction bronchiectasis
    - ❑ Honeycombing
    - ❑ Reticulonodular opacities Pleural effusion
    - ❑ Septal bullae Diffuse alveolar opacities

19. Final HRCT conclusion
    - ❑ UIP
    - ❑ NSIP
    - ❑ OP
    - ❑ LIP
    - ❑ Other please specify----------
20. Chest X-ray finding
    - ❑ ----------

21. Pulmonary function test finding
    - ❑ FVC------
    - ❑ FVC1…….
    - ❑ TLC……..
    - ❑ Restrictive pattern
    - ❑ Obstructive pattern
    - ❑ Mixed pattern

Part – 4 Treatment for CTD

22. Type of treatment he is getting
    - ❑ Azathioprine
    - ❑ Methotrexate
    - ❑ Leflunomide

- ❑ Cyclophosphamide
- ❑ Mycophenolate
- ❑ Rituximab
- ❑ corticosteroid
- ❑ If other please specify

23. Duration of treatment before the onset of ILD
    - ❑ < 1 year
    - ❑ > 1 year

Information Sheet

Title of Research : characterization of connective tissue disease related interstitial lung diseasein tertiary hospitals in Addis Ababa –
A retrospective study

Name of Investigator- Dr. Ameha Zewdu kassa

Objective of the study – to assess the clinical manifestation, serologic findind, imaging finding

.

Selection criteria

You are selected randomly among patients who had diagnosed with CTD-ILD at TASH and SPMHC hospital). If you decide to participate n the study you will be asked some Questions based the
attached checklist.

Possible harm

There is no risk you will be exposed to by participating in this study. It will take about 20 minute
of your time for Interview and echocardiography each. You will not be asked to pay for any of
the investigation that will be done for the study purpose.

Confidentiality

Your name and Personal identification will not be asked or included in the interview or study.

Any part of the data collected in this study is confidential and will not be used for purpose other than this study. All information will be coded and data collection tools will be locked and will not be accessed by any individual.

Autonomy

You have the right to decide to participate in this study or not. You can also withdraw from participating at any point of the study. Deciding not participate in the study or withdrawal then after Does not affect your treatment.

Funding of the research

The research grant will be from Addis Ababa University, College of Health Science postgraduate office. The research proposal will be reviewed by research committee of internal medicine department and by institutional review board of AAU, CHS.

Contact address- Dr Ameha Zewdu Phone number +251920343406
Email- Amehazewdu@gmail.com

Informed consent form

Interstitial lung disease is one of the chronic complications of connective tissue disease which causes dyspnea, functional impairment and other complications. It is treatable if detected early by HRCT is a simple and important diagnostic method.

This study assesses the clinical manifastion serology and imaging findin the commonly seen in patient with CTD-ILD.

The information helps to identify patient with clinical manifastion to have proper imaging and early diagnosis .

We kindly ask you to participate in this study by answering the questions listed in the check list, letting as review your medical chart and have an echocardiography.

All the information you give is confidential and you have the right to not participate or withdraw
from the study at any point. We are delighted to answer any of your questions.

I have read (was read to me) and clearly understood the purpose of the research, the procedures,
the risks and benefits, issues of confidentiality, and the right to participate and withdraw from
the study at any time.

I hereby confirm the above statement with my signature.

Name of participant: _____ Signature of participant: _____.

Name of Data collector _____ Signature of Data collector_____