



**PREVALENCE AND CHARACTERISTICS OF INTERSTITIAL LUNG
DISEASE IN ST. PAUL'S HOSPITAL MILLENNIUM MEDICAL
COLLEGE CHEST CLINIC.**

INVESTIGATOR: Dr. KIBROM GEBRU (MD, INTERNAL MEDICINE RESIDENT)

ADVISORS: Dr. ABEL MUREJA (INTERNIST)

Mrs. SISAY TANI (MSC, BIOSTATISTICIAN)

A RESEARCH THESIS SUBMITTED TO DEPARTMENT OF INTERNAL MEDICINE,
SPHMMC, IN PARTIAL FULFILLMENT OF THE REQUIREMENT FOR SPECIALTY
CERTIFICATE IN INTERNAL MEDICINE.

OCTOBER, 2022

Addis Ababa, Ethiopia

Table of Contents

ACKNOWLEDGMENT	4
LIST OF TABLES	5
LIST OF FIGURES	5
ACRONYMS AND ABBREVIATIONS	6
ABSTRACT	8
1. INTRODUCTION.....	9
1.1 BACKGROUND.....	9
1.2. STATEMENT OF THE PROBLEM	10
1.3 SIGNIFICANCE OF THE STUDY	11
2. LITERATURE REVIEW	12
3. OBJECTIVE OF THE STUDY	15
3.1. GENERAL OBJECTIVE	15
3.2. SPECIFIC OBJECTIVES.....	15
4. METHODS AND MATERIALS	16
4.1. STUDY AREA AND PERIOD	16
4.2. STUDY DESIGN.....	16
4.3. POPULATION.....	16
4.3.1 SOURCE POPULATION	16
4.3.2.STUDY POPULATIONS.....	16
4.3.3.ELIGIBILITY CRITERIA	16
4.4STUDYPERIOD.....	16
4.5. STUDY VARIABLES	17
4.5.1.DEPENDENT VARIABLE.....	17
4.5.2.INDEPENDENT VARIABLE	17
4.6. DATA COLLECTION PROCEDURES	17
4.7.DATA COLLECTION INSTRUMENTS AND METHODS	17
4.7. DATA QUALITY CONTROL.....	17
4.8.OPERETIONAL DEFINATIONS.....	18
4.9. DATA PROCESSING AND ANALYSIS	18
4.10.ETHICAL CONSIDERATION	18
4.11. PLAN FOR DISSEMINATION OF THE STUDY	18
5. RESULT	19

6.	DISCUSSION	23
7.	LIMITATION OF THE STUDY.....	24
8.	CONCLUSSION.....	25
9.	RECOMMENDATIONS.....	25
	REFERENCES.....	26
	APPENDIX I DATA COLLECTION FORMAT.....	30
	APPENDIX II: ASSURANCE OF PRINCIPAL INVESTIGATOR.....	32

ACKNOWLEDGEMENT

First of all, I would like to thank to almighty God for giving me patience and courage to make this thesis. Next, I would like to pass my gratitude to my advisers Dr. Abel Mureja (Internist) and Mrs.Sisay Tani (MSc, Biostatical) for guidance and support they have given for completion of this thesis. I would like to thank SPHMMC staffs working in medical record department, staffs working in chest clinic & all who participate in this thesis. Finally, I Would like to thank SPHMMC, department of INTERNAL MEDICINE for giving me this opportunity to make this research.

LIST OF TABLES

Table 1: Pattern of patients who visited chest clinic of St. Paul's Hospital Millennium Medical College, Addis Ababa, Ethiopia from January 2019 to November 2021

Table 2: Sociodemographic characteristics of ILD patients who visited chest clinic of St Paul's Hospital Millennium Medical College, Addis Ababa, Ethiopia from January 2019 to November 2021

Table 3: Clinical patterns of patients diagnosed with ILD who visited chest clinic of SPHMMC Addis Ababa, Ethiopia, from January 2019 to November 2021

Table 4: Associated factors of among ILD patients who visited chest clinic of SPHMMC Addis Ababa, Ethiopia, from January 2019 to November 2021

Table 5: Pearson correlation between age of the patients and diagnosis of ILD

Table 6: Analysis of associated factors of ILD patients with significance level and adjusted odd ratio

LIST OF FIGURES

FIGURE 1: Gender variation in interstitial lung disease subtypes

ACRONYMS

ACSH----Ayder comprehensive specialized hospital

AIP----Acute Interstitial Pneumonia

ATS/ERS---- American Thoracic Society/European Respiratory Society

BAL----Broncho Alveolar Lavage

BOOP---- Bronchiolitis Obliterans Organizing pneumonia

CFA----cryptogenic fibrosing alveolitis

COP-----Cryptogenic Organizing Pneumonia

CT---- Computerized Tomography

CTD-ILD---Connective Tissue Disease Associated Interstitial Lung Disease

CTDs----Connective Tissue Diseases

DIP----Diffuse Interstitial Pneumonia

DPLD-----Diffuse Parenchymal Lung Disease

EAA---Extrinsic Allergic Alveolitis

HBsAg---Hepatitis B Virus Surface Antigen

HCV Ab---Hepatitis C Virus Antibody

HRCT----high resolution computed tomography

HP---Hypersensitivity Pneumonitis

IIPs-----Idiopathic Interstitial Pneumonias

ILD-----Interstitial Lung Disease

IPF-----Idiopathic Pulmonary Fibrosis

LAM -----Lymphangioleiomyomatosis

LIP----Lymphocytic Interstitial Pneumonia

NSAIDs----Non-Steroidal Anti-Inflammatory Drugs

NSIP---Non-Specific Interstitial Pneumonitis

PAP -----Pulmonary Alveolar Proteinosis

PLCH ---Pulmonary Langerhans cell histiocytosis

RB-ILD--- Respiratory Bronchiolitis-Interstitial Lung Disease

RA-associated ILD-----Rheumatoid arthritis associated ILD

SPHMMC---St Paul hospital millennium medical collage

UIP---Usual Interstitial Pneumonitis

USA---United States of America

WHO----World Health Organization

ABSTRACT

Background

Interstitial lung disease (ILD) or Diffuse parenchymal lung disease refers to a heterogeneous collection disorder affecting the lung mainly the space between the alveolar epithelium and capillary endothelium. Although some of ILD causes are known (connective tissue disorder, environmental exposure), most of patients cause of ILD is unknown. Determining the risk factors that are associated with the development of ILD might have an important role in understanding the pathogenetic mechanism of ILD, early diagnosis, adequate treatment and prevention. Knowing local prevalence and associated factors will help to design preventive measures for those who are at high risk.

OBJECTIVE

To determine the prevalence and Characteristics of ILD in patients visiting SPHMMC chest clinic from January 1, 2019-December 30,2021.

METHOD

Facility based retrospective analytical cross-sectional study was done among 311patients' charts who have **chest HRCT** visited SPHMMC Chest clinic from January 1,2019-December 30,2021 to determine prevalence & characteristics ILD. The data was collected using data collection format which is prepared to meet the study objectives. Analysis was made on SPSS 24 software. Descriptive statistics, frequency and proportions were utilized for Socio-Demographic variables. The results were summarized using tables, graphs & texts.

RESULT

The prevalence of ILD was **7.9%(n=29)**. The three most common diagnosis from top to bottom in the chest clinic were Bronchiectasis (n=75, 19.6%), COPD (n=73, 19.1%), post TB fibrosis (n=35, 9.2%). ILD is the 4th most common diagnosis among studied patients in chest clinic in the studied period. Both NSIP & Sarcoidosis are the most common types of ILD with equal frequency each account 34.5% (n=10), followed by IPF(n=5,17.2%). The median age of patient with ILD was 55 years & female patients account for 69%.

CONCLUSION

ILD was the 4th most common diagnosis in the clinic following Bronchiectasis, COPD and post TB fibrosis. This study is alarming for the need for further larger population & facility-based studies in the topic & the need for proper diagnosis, management & prevention of ILD & need for creating awareness on importance of early treatment seeking behavior & prevention in the community.

1. INTRODUCTION

1.1 BACKGROUND

Interstitial lung disease (ILD) refers to a heterogeneous collection of more than one hundred distinct lung disorders that tend to be grouped together because they share clinical, radiographic, and pathologic features (1). Some develop in the setting of other conditions, such as connective tissue disease; others are idiopathic (2).

The term *interstitial lung disease* (ILD), in general, implies the clinical manifestation of inflammatory-fibrotic infiltration of the alveolar walls (septa) resulting in profound effects on the capillary endothelium and the alveolar epithelial lining cells (2). While remodeling of the interstitial space, the region between the epithelium and endothelium, tends to be the dominant site of involvement for most of the ILDs. (3)

Commonly, ILD presents with dyspnea on exertion, diffuse bilateral infiltrates on chest imaging, and restriction with diffusion impairment on physiologic testing. When tissue is obtained, the lung parenchyma may contain any combination of abnormalities, including inflammation, fibrosis, and granulomas (1).

It is often helpful in the case of any individual patient to incorporate a combination of historical, clinical, radiographic, and pathologic features. Distinguishing those patients who have a known cause for their ILD (e.g., connective tissue disease, occupational or environmental exposure, or drug toxicity) from those who do not (e.g., IPF, sarcoidosis) is an important first step, (1).

Clinical features, such as acuity of onset, may help to classify disease as well. For example, the subacute time course of a patient with organizing pneumonia will be quite different than the insidious onset of dyspnea in IPF. The radiographic pattern of IPF will be characterized by bibasilar traction bronchiectasis and honeycombing, while sarcoidosis may demonstrate upper lobe-predominant nodular opacities with retraction and volume loss. (1)

The cause of ILD is not known for most of the cases (i.e. Idiopathic). Some studies found association with history of bacterial and viral infection, genetic background, geographic location, radiation, occupational exposure to chemicals, smoking, gender, age of a patient and drugs (4-14). From global incidence of ILD 2.5-3% of cases are drug induced. There are over 450 drugs recognizing as being implicated in interstitial lung disease.(9)In cancer patients, drug associated ILD is most commonly observed during mitomycin, paclitaxel, docetaxel, or

gemcitabine therapy. Nonspecific interstitial pneumonia is seen in association with a variety of drugs, the most common being methotrexate, amiodarone and carmustine a number of drugs may result in hypersensitivity pneumonitis, including methotrexate, cyclophosphamide and anti-depressants such as fluoxetine and amitriptyline. Bronchiolitis Obliterans Organizing pneumonia (BOOP)-like reaction, has been reported most frequently in association with methotrexate, cyclophosphamide, gold, nitrofurantoin, amiodarone, bleomycin and busulphan (10).

The idiopathic interstitial pneumonias include the entities of idiopathic pulmonary fibrosis (IPF), nonspecific interstitial pneumonia (NSIP), cryptogenic organizing pneumonia (COP), acute interstitial pneumonia (AIP), respiratory bronchiolitis-associated interstitial lung disease (RB-ILD), desquamative interstitial pneumonia (DIP), and lymphocytic interstitial pneumonia (LIP). For the purposes of this document, the following terms are viewed as synonymous: idiopathic and cryptogenic as well as pneumonia and pneumonitis. (15)

The prevalence of ILD studied in some population based and studies done on the registries. The most important registry study was undertaken in Bernalillo County, New Mexico, USA, using data from a dedicated ILD registry and employing broad case-identification procedures and systematic chart review. (16). A few published reports suggest international differences in the prevalence of IPF.

1.2 STATEMENT OF THE PROBLEM

Evidence from recent analyses of populations suggests that the incidence and prevalence rates of ILD are on the increase, particularly when the broad definition of ILD is used. (20) Nonstandard disease classifications have created difficulties in determining the rates of prevalence and incidence of ILD. (20) Internationally, as coding for the disease has varied, it has proved quite difficult to apply the new classification to the many population registers. (20)

On European lung white book, it was reported that from prospective registries of data reported by respiratory physicians, for example in Flanders (Belgium), Germany, Italy, Spain and Greece the most frequent ILDs are IPF and sarcoidosis, which together comprise about 50%. The data also show some interesting differences between countries, such as lower proportions of IPF in Flanders, of sarcoidosis in Spain, of ILD associated with CTD in Germany, and of extrinsic allergic alveolitis (hypersensitivity pneumonitis) (EAA) in the Italian, Spanish and Greek registries. The highest mortality rates due to ILD, of more than 2.5 per 100 000 people,

are recorded in the UK, Ireland, Scandinavia, the Netherlands and Spain. (20) Other study from Belgium confirms that IIP is predominantly a disease of elderly man, with a mean age of 62 years and a female to male ratio of 0.7. Patients who present with the diagnosis of sarcoidosis tend to be younger in comparison with the other ILD, and ILD due to CTD is a female disease with a female to male ratio of 1.1. The survival rates between the different forms of ILD in this study were different, with a mean survival after 5 years of 91.6% in Sarcoidosis, 84.1 in Hypersensitivity pneumonitis, 69.7% in CTD, 35.4% in IPF, 85.5% in other IIP and 69.5% in undefined forms of lung fibrosis. (21) The recent Global Burden of Disease Study reported that interstitial lung diseases showed an increment of 86% regarding global years of life lost in 2013, compared to 1990. (22)

There is less data on the prevalence of ILD and associated factors in Africa and our country Ethiopia. This might be due to need for HRCT, invasive modalities like lung biopsy and bronchoalveolar lavage and underreporting of cases. In the cross-sectional study done on 2018 in Mekelle, ETHIOPIA, AYDER REFERRAL chest clinic hospital Prevalence of Interstitial Lung Disease is found to be 8.4%. Interstitial Lung Disease is the third common diagnosis in chest clinic. Idiopathic Interstitial Pneumonias are the leading types (22).

1.3. SIGNIFICANCE OF THE STUDY

There is a little data on our study topic in our continent AFRICA and our country Ethiopia. Ethiopia is one of the growing countries and there is expansion of construction and manufacturing industries which increase the community risk of interstitial lung disease. This study will provide understanding on the burden of the problem and will help governmental and non-governmental organizations as input to plan larger population and facility- based studies & improving the health facilities' capacity for diagnosis and management of ILD.

2. LITRETURE REVIEW

It is not possible to precisely estimate the incidence and prevalence rates of ILD. Despite the guidelines for diagnosis with clearly described criteria, ILD remains a diagnosis of exclusion requiring extensive investigation, which is seldom possible (23). In addition, much of the available data are taken from registries or hospital clinics and therefore suffer from selection biases, making them unrepresentative of the general population (24).

The most important registry study in the world was undertaken in Bernalillo County, New Mexico, USA, using data from a dedicated ILD registry and employing broad case-identification procedures and systematic chart review (16). Very little data from population-based registries are available from other countries. The few published reports suggest international differences in the prevalence of IPF. It is estimated to be 4.1 per 100 000 in the Japanese Hokkaido registry (17), 7–12 per 100 000 in the Czech Republic (18) and 16–18 per 100 000 in the Finnish registry (19), compared with 20.2 per 100 000 in men and 13.2 per 100 000 in women in Bernalillo County (16). It is unclear whether these variations reflect the disease prevalence or differences in registry methodology or completeness of case ascertainment. (20)

Several European studies have reported on the frequency and distribution of ILD. Studies show that the most frequent ILD are IPF and sarcoidosis, which together comprise about 50% of cases. The data also show considerable variability between countries, such a lower proportion of IPF in Belgium, of sarcoidosis in Spain, of ILD associated with CTD in Germany, and a higher incidence of HP in Germany. A Danish cohort study reported an incidence of ILD and IPF were 4.1 per 100,000 persons per year and 1.3 per 100,000 persons per year, respectively (25). In a Spanish ILD registry including cases from 23 pulmonary medicine centers, the estimated incidence of ILD was 7.6 per 100,000 persons per year (26). Finally, in Greece, the ILD incidence rate was estimated to be 4.63 per 100,000 persons per year (27)

ILD have been more closely associated with occupational exposures than any other respiratory disease. Classic examples of occupational diseases are the pneumoconiosis caused by asbestos (asbestosis), silica (silicosis), and coal dust (coal worker's pneumoconiosis). In 2000 in Europe, it was estimated that a total of 7,200 cases of pneumoconiosis were related to occupational exposures to asbestos, silica, and coal dust (28). In data from European Registries, occupational ILD accounts for 4% to 18% of prevalent and 13% to 19% of incident cases of ILD.

Occupational ILD accounted for a greater proportion of ILD in the European disease registries than connective tissue disease, drugs or radiation, and vasculitis combined. (6)

On review of literatures done by Kamel Marzouk and his colleagues, Epstein – Barr virus was associated with lymphocytic interstitial pneumonia and Langerhans cell histiocytosis. (11) Indeed, there are data to associate other viral infections with ILD; for example, there are data from Egypt (12), Italy (13) and Iran (14) which showed increased prevalence of hepatitis C infection in a patient with IPF and which can be a predisposing factor for the development of a more severe form of IPF.

Few studies have evaluated the rates of ILD in Asia. An epidemiological study done in 31 Turkish centers showed an overall incidence of ILDs of 25.8 cases per 100,000 persons. Overall, in 24% of ILD cases a specific etiology could be identified, 39% were granulomatous diseases, 24% were idiopathic, and 4% were unclassified. Sarcoidosis (37%) was the most common disease, whereas cases with IPF constituted 20% of patients (29) In India, chronic hypersensitivity pneumonitis (CHP), pulmonary fibrosis associated to CTD, sarcoidosis and IPF are the most common entities (30). A more recent ILD-India registry, reported (14%) of IPF and (14%) of CTD-ILD, among 1,084 patients with ILD (29). In Pakistan chart review from single center shows clear predominance in female (69%), mean age was 49-year-old. IPF was the most common disease subtype (37.5%) followed by HP (12.3%), CTD-ILD (9.1%) and sarcoidosis (4.3%) (31). Two studies examine the epidemiology of ILD in China (32) the mean age at time of diagnosis was 57.9 years and 55.5% of patients were male. The most common ILD was IPF (20.3%), followed by CTD-ILD (18.3%) & Interstitial pneumonia with autoimmune features (IPAF) (17.9%). A single-center study of 330 ILD cases from Saudi Arabia found that the most frequent disease was CTD-ILD (35%), followed by IPF (23%) and sarcoidosis (20%) (33).

In a study done in Japan it was demonstrated that exposure to metal dust was significantly associated with an increased risk of IPF and 20.0–39.9 pack-years of smoking was significantly associated with an increased risk of IPF. (4) In a 9-year Nationwide population-based study done in Daegu, Republic of Korea on Risk factors for interstitial lung disease; Smoking, hepatitis C, history of tuberculosis, history of pneumonia, chronic obstructive pulmonary disease, male sex, and older age were significantly associated with interstitial lung disease development. (5)

Less data is available about the prevalence of ILD in Latin America. However, a Mexican study that abstracted cases from the National Database of Mortality showed that fibrotic ILD represents the 0.4% of all registered deaths (34).

Longitudinal cohort study in Australia showed the mean age of participant was 68.3 years with 54.7% male. the most common diagnosis was IPF (34%) followed by CTD-ILD (17.7%), HP (9.4%) & sarcoidosis (6.2%) (35).

There are few studies done in Africa related with prevalence of ILD. In retrospective review of case notes of patients in respiratory clinic of university of Nigeria in 2018 among 900 patients ILD constituted 2.3% (21) of patients and IPF (14.3%), NISP (38.1%), sarcoidosis (47.6%) patient with IPF and NISP had mean age of 66.5 years and were mostly male (63.6%) (36).

In our country Ethiopia, there was one Retrospective cross-sectional study done among patients visiting chest clinic in Ayder comprehensive specialized hospital, Mekelle, Ethiopia. Prevalence of Interstitial Lung Disease is found to be 8.4%. Interstitial Lung Disease is the third common diagnosis in chest clinic. Idiopathic Interstitial Pneumonias are the leading types (NSIP (44%), IPF (30%), LIP (4%), COP (2%), RA-associated ILD (6%). Median age of ILD patient was 55 years. Female patients were predominant. (22)

In a study done on cotton textile mill workers in Ethiopia, the prevalence of byssinosis was 43.2% among blowers and 37.5% in carders and there was a significant increase in the prevalence of byssinosis with duration of exposure to cotton dust which was similar with studies from Sudan and Egypt. (8)

3. OBJECTIVE OF THE STUDY

3.1. GENERAL OBJECTIVE

To determine the prevalence and characteristics of ILD In patient visiting SPHMMC, Chest clinic from January 1,2019 -December 30,2021

3.2 SPECIFIC OBJECTIVES

1. To determine the prevalence of ILD in patient visiting SPHMMC, chest clinic from January 1,2019-December 30,2021
2. To assess the Characteristics of ILD in SPHMMC, chest clinic from January 1,2019-December 30,2021

4. METHODS AND MATERIALS

4.1 STUDY AREA

This study was conducted in St. Paul's hospital millennium medical college, one of the largest specialized referral hospitals in the capital Addis Ababa, Ethiopia. It's the fastest expanding medical college after it started working as medical college in 2007. Its center of excellence serving as renal center providing dialysis and also the first hospital in the country with kidney transplantation center. It has huge residency and sub specializations center in different field contributing to fill the gap of health worker shortage in health facility of the country as well as the neighboring countries. Among the residency programs Internal medicine is one the field with different subunits like, Pulmonology, Hematology, Cardiology, Endocrinology, Neurology, Nephrology, Gastroenterology.

Chest unit gives both inpatient and outpatient service for the patients. Currently It has 1 pulmonologist ,2 residents and 3 nurses. It gives two times per week outpatient service & 50-60 patients would be seen in each visit. About 8-10 patients' bed will be occupied by the chest patients.

4.2 STUDY DESIGN

- ✓ Facility-based Retrospective analytical Cross sectional study design.

4.3 POPULATION

4.3.1. SOURCE POPULATION

- ✓ All individuals visiting SPHMMC Chest clinic

4.3.2. STUDY POPULATION

- ✓ **ALL individuals** visiting chest clinic in SPHMMC in study period and fulfill inclusion criteria

4.3.3 ELIGIBILITY CRITERIA

Inclusion criteria

- ✓ Individuals visited SPHMMC chest clinic on the specified time period who have **chest HRCT**

Exclusion criteria

- ✓ Incomplete chart

4.4 Study period: June1-30,2022

4.5. STUDY VARIABLES

4.5.1 Dependent variable

- Status of Interstitial lung disease

4.5.2 Independent variable

- Age
- Sex
- Cigarette Smoking history
- Occupation
- Presence of known CTD or vasculitis
- History of medication use associated with ILD
- Modality of Diagnosis
- Residency place (urban vs. rural)
- Viral markers (HCV Ab, HBsAg)
- History of pneumonia treatment
- History of Tuberculosis treatment

4.6 Data collection instrument and methods

Data was collected on the month of June 2022 G.C. Quantitative data was collected using a questionnaire prepared in English language, prepared based on review of similar literature (22) which is done in ACSH on prevalence of ILD and associated factor in 2018. The data was collected by Two General Practitioners after Appropriate brief explanation given on how to fill questioner, inclusion and exclusion criteria & patient confidentiality. Entering and checking secondary data was done by principal investigator.

4.7 DATA QUALITY CONTROL

The data was carefully collected based on the inclusion criteria by appropriately designed data collection instrument. The collected data was reviewed and checked for completeness & entered on daily basis by the investigator. To ensure quality data all charts selected for this study are patients' chart who have **chest HRCT** which help us not to miss patients who have underling interstitial lung disease despite having other concomitant chest condition that patients have follow up in chest clinic.

4.8 OPERATIONAL DEFINITIONS

- **ILD:** Inflammatory-fibrotic infiltration of the lung parenchyma evidenced by high-resolution computed tomography (HRCT).
- **HRCT:** A CT technique in which thin-slice chest images are obtained and post-processed in a high spatial-frequency reconstruction algorithm.
- **Bronchoalveolar Lavage:** Is a diagnostic method of the lower respiratory system in which a bronchoscope is passed through the mouth or nose into an appropriate airway in the lungs, with a measured amount of fluid introduced and then collected for examination.
- **Lung biopsy:** Is a procedure for obtaining a small sample of lung tissue for examination.

4.9 DATA PROSSESING AND ANALYSIS

Data collected through a structured checklist and entered into epi data and exported into and analyzed using SPSS Version 24 statistical package software. Descriptive statistics as percentages, mean, median, IQR and standard deviation were calculated to summarize the data. The results were summarized using tables, graphs & texts.

4.10 ETHICAL CONSIDERATIONS

Ethical clearance was obtained from the Ethical Review Board of St. Paul hospital Millennium medical college (SPHMMC). The officials at different level in the study area were communicated through letters from SPHMMC, department of Internal Medicine. Each patient's information was collected using a structured checklist. Data collected in this study was de-identified and stored in a password-secured computer.

4.11. PLAN FOR DISSEMINATION

The findings of this study will be disseminated to SPHMMC department of internal medicine in partial fulfillment the requirement for a specialty certificate in Internal medicine. It will also be submitted to chest unit & chief clinical director bureau. Attempts will be made to publish the information in peer-reviewed journals and make presentations in scientific conferences.

5. RESULT

A total of 311 patients who were seen from January1,2019-December 30,2021 fulfilled the inclusion criteria. The most common diagnoses of the patients were Bronchiectasis (n=75, 19.6%) (out of this post TB Bronchiectasis 40%, n= 30) followed by COPD (n=73, 19.1%) and post-TB fibrosis (n=35, 9.2%). ILD was the 4th most common diagnosis.

Table 7: Pattern of patients who visited chest clinic of St. Paul's Hospital Millennium Medical College, Addis Ababa, Ethiopia from January 2019 to November 2021.

Variables		Frequency(n)	Percent (%)
Diagnosis related with chest condition, n=382**	Bronchiectasis	45	11.8
	Post-TB bronchiectasis	30	7.8
	COPD	73	19.1
	Post TB fibrosis	35	9.2
	ILD	29	7.6
	Post-COVID fibrosis	22	5.7
	Disseminated TB	19	5.0
	PTE	18	4.7
	PAH	17	4.4
	Aspergillosis	17	4.4
	SPN	12	3.1
	Asthma	10	2.6
	Lung cancer	5	1.3
	Pulmonary TB	4	1.0
	Pneumonia	4	1.0
	Others*	16	4.2
Sex	Male	148	47.6
	Female	163	52.4
Residential status	Urban	198	63.7
	Rural	113	36.3
Prior history of treatment for pneumonia	Yes	245	78.8
	No	66	21.2
Prior history of treatment for tuberculosis	Yes	144	46.3
	No	167	53.7
Smoking history	Yes	63	20.3
	No	248	79.7

TB – Tuberculosis, COPD – Chronic Obstructive Pulmonary Disease, ILD – Interstitial Lung Disease, SPN – Solitary Pulmonary Nodule, PAH – Pulmonary Arterial Hypertension.

** Chest empyema, small airway disease, restrictive lung disease, PCD, bronchial cyst, hypoplastic lung, pneumothorax*

*** some patients have more than one diagnosis.*

A total of 29 patients were found to have ILD. Among patients who were diagnosed with ILD males accounted for 31 % (n=9) with male to female ratio of 1:2.2. The median age of the

patients was 55 years (Interquartile range, IQR= 17.5). Fifteen (51.7%) of patients resided in urban area. Among patients for whom occupational status was documented (n=9) majority were housewives. Two patients were farmers and one patient was working in a tobacco factory (Table 8).

Table 8: Sociodemographic characteristics of ILD patients who visited chest clinic of St Paul's Hospital Millennium Medical College, Addis Ababa, Ethiopia from January 2019 to November 2021

Characteristics		Male, n=9 Frequency (percent)	Female, n=20 Frequency (percent)	Total Frequency (percent)
Age	21-30	1	1 (5%)	2 (6.9%)
	31-40	1	0	1 (3.4%)
	41-50	1 (11%)	5 (25%)	6 (20.6%)
	51-60	1 (11%)	9 (45%)	10 (34.5%)
	61-70	3 (33.5%)	3 (15%)	6 (20.7%)
	≥71	2 (22.5%)	2 (10%)	4 (13.9%)
Residential status	Urban	6 (60%)	9 (47.3%)	15 (51.7%)
	Rural	4 (40%)	10 (52.6%)	14 (48.3%)
Occupational status	Farmer	0	2 (10.5%)	2 (6.9%)
	Tobacco factory worker	1 (10%)	0	1 (3.5%)
	Housewife	0	5 (26.3%)	5 (17.2%)
	Retired	1 (10%)	0	1 (3.5%)
	Not documented	8 (80%)	12 (63.2%)	20 (70.0%)

Six types of ILDs were identified among patients diagnosed to have the disease. The leading types of ILD were NSIP (n=10, 34.5%), sarcoidosis (n=10, 34.5%), and IPF (UIP) (n=5, 17.2%). The other types of ILD were LIP (n=2, 6.9%), Chronic hypersensitivity pneumonitis (n=1, 3.4 %), and RA-ILD (n=1, 3.4 %). The gender variation of these ILD subtypes is presented in **figure 3**. The duration of illness of ILD patients ranged from 1 year to 20 years with a median duration of 3 years (IQR=3). Computed Tomography (CT) scan and chest X-ray was used for diagnosis in all patients whereas bronchoalveolar lavage, Pulmonary function test (spirometry), and Lung Biopsy were used to diagnose ILD in 13 (44.8%), 16 (55.2%) and 2 (6.9%) respectively. The number of ward admission related to ILD of these patients ranged from having no admission (n=17, 58.6%) to being admitted five times (n=1, 3.4%). Similarly, the number of Emergency Room (ER) visit due to ILD ranged from having no visit (n=10, 34.5%) to visiting the ER five times visit (n=1, 3.4%) (Table 3).

Table 9: Clinical patterns of patients diagnosed with ILD who visited chest clinic of SPHMMC Addis Ababa, Ethiopia, from January 2019 to November 2021.

Variables		Frequency (n)	Percent (%)
Types of ILD	NSIP	10	34.5
	LIP	2	6.9
	UIP	5	17.2
	Sarcoidosis	10	34.5
	Chronic hypersensitivity pneumonitis	1	3.4
	RA-ILD	1	3.4
Method of diagnosis	CT scan	29	100
	Chest X-ray	29	100
	Bronchoalveolar lavage	13	44.8
	Pulmonary function test (spirometry)	16	55.2
	Lung biopsy	2	6.9
Number of ward admissions related with ILD	None	17	58.6
	Once	1	3.4
	Twice	9	31.0
	Three times	1	3.4
	Five times	1	3.4
Number of Emergency room visits due to exacerbation	None	10	34.5
	Once	8	27.6
	Twice	5	17.2
	Three times	3	10.3
	Four times	2	6.9
	Five times	1	3.4

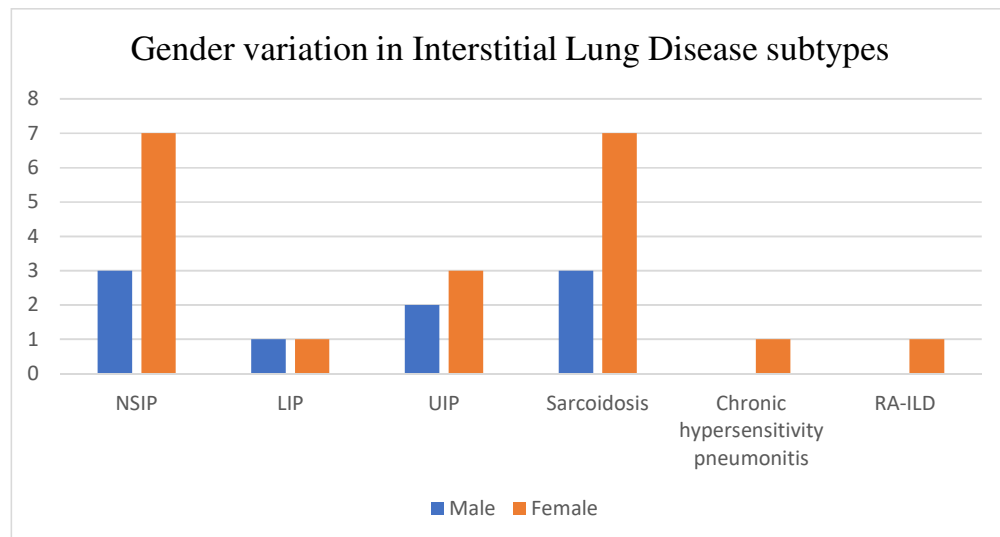


Figure 1: Gender variation in interstitial lung disease subtypes

Several factors were shown to occur in patients with ILD. All 29 patients reported to have been treated for pneumonia prior to diagnosis with ILD whereas 12 patients (41.4%) were documented to have previous history of treatment for Tuberculosis. 6 patients (20.7%) had a history of smoking. 3 patients (10.3%) had a family history of similar illness. 25 of the patients (82.6%) had their HIV infection status determined out of which 2 patients (8.0%) were found to be positive. Out of 21 patients who were screened for Hepatitis B and C infection with HBsAg and HCV antibody, 6 (28.6%) and 1 (4.8%) were found to be positive for Hepatitis B and Hepatitis C infection respectively. None of the patients had prior radiotherapy or used any medication that is considered a risk for ILD.

Table 10: Associated factors of among ILD patients who visited chest clinic of SPHMMC Addis Ababa, Ethiopia, from January 2019 to November 2021

Factors		Frequency (percent)	Percent (%)
Prior treatment for pneumonia		29	100
Prior history of treatment for Tuberculosis		12	41.4
Smoking		6	20.7
Family history		3	10.3
Hepatitis B infection, n=21		6	28.6
Hepatitis C infection, n=21		1	4.8
HIV infection, n=25		2	8.0
Prior history of radiotherapy		0	
Prior history of medication use		0	
Comorbidities	Type II DM*	8	27.6
	Hypertension	8	27.6
	Heart Failure	4	13.8
	Dyslipidemia	1	3.4
	RA	2	6.9
	Gouty Arthritis	1	3.4
	CKD**	1	3.4
	BPH***	1	3.4
	Ovarian Cancer	1	3.4
	MNG****	1	3.4

*Diabetes Mellitus **chronic kidney disease ***Benign Prostatic Hyperplasia

****Multinodular Goiter

6. DISCUSSION

The prevalence of ILD in this study 7.9% which is comparable with studies done in ACSH, Ethiopia (8.4%) (22). It is higher than study done in Nigeria (2.3%) (36). This difference might be due to difference in study method, variation in study population & the number of studied patients in this study are much lower. We couldn't compare with other studies because the epidemiological studies done to find the prevalence of ILD were population-based studies.

The predominant types of ILD in this study are IIPs. NSIP is the predominant from IIPs which is similar with studies done in ACSH (22), studies done in Nigeria (36). But it's different from studies done in India, Europe, Italy (29,25-27,13) in which IPF was the predominate IIPs. The difference could be due to variation in study population, study methodology, difference in genetics and geographical distribution of the disease. Sarcoidosis has equal frequency with NSIP in this study which is different from study done from ACSH, Mekelle, Ethiopia (22) & study done in Nigeria (36). The difference might be due to difference in study population and Methodology.

ILD associated with occupational and smoking exposures are less in this study which is different from studies done in Japan where smoking is strongly associated with development of ILD (4), studies in Europe where their high association of occupational and smoking exposure related with ILD (6). This might be due difference exposure variability between study populations, Limited number of ILD patients in our study have documentation on occupation and exposure. RA- related ILD are less in our study compared with studies done ACSH (22), Ethiopia and other studies done in French, Saudi Arabian, Mexican studies. (37,16,38) Which might be due to under diagnosis due of subclinical ILD masked by co-existent peripheral symptoms of & patient may not necessarily referred to pulmonologist and there may be difference in study population.

The median age of patient with ILD in our study 55 years which is similar with study done ACSH, Mekelle (22) and it is in between the finding in Pakistan study (mean age 49 years) (31), Greece (median age 58.9) (27), Nigeria (median age 66.4 years). (36) This can be explained with difference in the commonest type ILD diagnosis because it is expected age variation in distribution of ILDs. It could also be due to the difference in the nature of the studies because most of them were population-based studies. About 89.7% of ILD patients are more than 40 year of age which is consistent with findings from ACSH (22) and Indian study (30). Despite most of patients diagnosed with ILD are more than age 40 years in this study

similar with finding from study done in ACSH & comparable overall prevalence of ILD among studied patients in both studies(7.9% vs. 8.4%), relatively less number of ILD patients were identified in this study among patients age between 31-40 years(1(3.4%) vs 7(14%)) and in those $\geq$ 71 year of age (4(13.9%) vs 10(20%)). This difference might be due to relatively small number of studied patients in this study (311 vs 595) which lead to findings of overall small number of ILD patients and difference in frequency in the age distribution among patients in this two studies. Difference in study methodology and variation in the studied population also might contribute for this difference. The small number of patients identified in this study also contribute to high frequency (%) patients in each age group classification we use to study despite having few numbers of patients in some of age groups.

Female predominance was seen our study which is consistent with study done in ACSH (22), and study from India (30), Pakistan (31) but it's not consistence with findings from study in Nigeria (36). This can be due to difference in predominant diseases, where male predominance was seen in studies with IPF as a predominant ILD. but in this study females were predominating in all type of ILD identified. This might be due to small number of patients studied & identified ILD patients.

When we compare the residential status of our patients with ILD the number of patients living in urban area is little higher than those living Rural area. This might be due to higher risk of occupational and smoke exposure in Urban areas. This finding is also similar with study done in ACSH, Mekelle, Ethiopia. (22)

7. LIMITATION OF THE STUDY

- I. Small numbers of ILD patients were identified from the studied number of patients' charts, so the data was not fit to do multivariate logistic regression which help us to check association between associated factors and ILD. so It need large multicenter study should be done in this topic.
- II. It is retrospective chart review which makes difficult to get adequate information from patients chart only.
- III. The study was done only in Tertiary care referral Hospital (SPHMMC) which cannot be representative general population

8. CONCLUSION

Interstitial lung disease is the 4th most common diagnosis in the clinic following Bronchiectasis, COPD and post TB fibrosis. NSIP & Sarcoidosis are most common types of ILD having equal frequency followed by IPF. Despite small number patient studied and limited study area, this is alarming for the need for wide population & facility-based studies for the future to determine burden of the problem and responsible bodies should work on prevention, proper diagnosis and management of ILD.

9. RECOMMENDATIONS

Organizations

- Since Ethiopia is one of growing country and there are growing industrial and mining factories and increasing environmental and occupational exposure, Governmental & non-Governmental organization should work together to strengthen health facilities for proper prevention, diagnosis and management of ILD & need for creating awareness on the need for early treatment seeking behavior & prevention of the disease.

Researchers

- There are limited studies done on the topic in our country and continent. Wide population, facility-based studies & further prospective studies should be conducted in the future to understand the burden of the disease in the population and to help policy makers & institutions to develop better policy and strategy which help for proper, diagnosis & management of the disease and strengthen health facilities.

REFERENCES

1. Alfred P. Fishman JAE, Jay A. Fishman, Michael A. Grippi, Robert M. Senior, Allan I. Pack. Fishman's pulmonary diseases and disorders. 5th ed ed. New York: McGraw-Hill companies; 2015.
2. Robert J. Mason VCB, Thomas R. Martin, Talmadge E. King, Jr, Dean E. Schraufnagel, John E. Murray, Jay A. Nadel. Murray & Nadel's textbook of respiratory medicine. 6th ed. Philadelphia: Saunders Elsevier 2016.
3. Dennis L. Kasper ASF, Stephen L. Hauser, Dan L. Longo, J. Larry Jameson, Joseph Loscalzo. Harrison's principles of Internal Medicine. 20th ed ed. New York McGraw-Hill Education; 2018
4. YOSHIHIRO MIYAKE SS, TETSUJI YOKOYAMA. Occupational and Environmental Factors and Idiopathic Pulmonary Fibrosis in Japan. Ann occup Hyg. 2005; 49:259–65
5. al. Ce. Risk factors for interstitial lung disease: a 9-year Nationwide population-based study. BMC Pulmonary Medicine. 2018; 18:96.
6. C.S. Glazer LSN. Occupational interstitial lung disease. Clin Chest Med. 2004; 25:467–78
7. Kathy B. Baumgartner JMS, David B. Coultas, volume 152, issue 4, August 2000, . Occupational and environmental risk factors for Idiopathic Pulmonary Fibrosis: A Multicenter Case-Control Study. American Journal of Epidemiology. August 2000;152(4):307-15
8. Woldeyohannes B, Mgeni, Theriault. Respiratory problems among cotton textile millworkers in Ethiopia. British Journal of Industrial Medicine 1991; 48:110-5
9. Martin Schwaiblmair WB, Thomas Haeckel, Bruno Märkl, Wolfgang Foergand Thomas Berghaus. Drug Induced Interstitial Lung Disease. The Open Respiratory Medicine Journal. 2012; 6:63-74.
10. NL Muller DW, H Jiang and A Gemma. Diagnosis and management of drug-associated interstitial lung disease. British Journal of Cancer. 2004;91: S24 – S30.

11. Kamel Marzouk L, Samer Saleh, Om P Sharma. Epstein – Barr virus induced interstitial lung disease. *Curr Opin Pulm Med*. Sep 2005;11(5):456-60
12. Abd El Monaem Rabea M, Rasha Daabis, Perihan El Sayed, Sally Samir. Prevalence of chronic hepatitis C virus (HCV) infection in patients with idiopathic pulmonary fibrosis. *Egyptian Journal of Chest Diseases and Tuberculosis* 2015; 64:907–13.
13. Riccardo Meliconi P. Incidence of hepatitis C virus infection in Italian patients with idiopathic pulmonary fibrosis. *Thorax*. 1996; 51:317-9
14. Rasoul Aliannejad MG. Hepatitis C and pulmonary fibrosis. *Hepat Mon*. 2011;11(2):71-3.
15. An Official American Thoracic Society/European Respiratory Society Statement: Update of the International Multidisciplinary Classification of the Idiopathic Interstitial Pneumonias. *Am J Respir Crit Care Med* 188:733–748, 2013
16. Coultas DB, Zumwalt RE, Black WC, Sobonya RE. The epidemiology of interstitial lung diseases. *Am J Respir Crit Care Med* 1994; 150:967–972
17. Munakata M, Asakawa M, Hamma Y, Kawakami Y Nihon Kyobu Shikkan Gakkai Zasshi. Present status of idiopathic interstitial pneumonia--from epidemiology to etiology, 1994 Dec; 32 Suppl ():187-92
18. Kolek V Acta Univ Palacki Olomuc Fac Med. Epidemiology of cryptogenic fibrosing alveolitis in Moravia and Silesia. 1994; 137():49-50.
19. Hodgson U, Laitinen T, Tukiainen P Thorax. Nationwide prevalence of sporadic and familial idiopathic pulmonary fibrosis: evidence of founder effect among multiplex families in Finland, 2002 Apr; 57(4):338-42
20. *G Raghu,1, * F Nyberg,2,3 and G Morgan. The epidemiology of interstitial lung disease and its association with lung cancer.*
21. *Chernecky C, Sarna L Crit Care Nurs Clin North Am. Review Pulmonary toxicities of cancer therapy. 2000 Sep; 12(3):281-95*
22. Habtamu Mesele Gebray. The PREVALENCE AND CHARACTERISTICS OF INTERSTITIAL LUNG DISEASES AMONG PATIENTS WHO VISITED

AYDER COMPREHENSIVE SPECIALIZED HOSPITAL CHEST CLINIC,
MEKELLE, ETHIOPIA,

23. Hunninghake GW, Zimmerman MB, Schwartz DA, King TE Jr, Lynch J, Hegele R, Waldron J, Colby T, Müller N, Lynch D, Galvin J, Gross B, Hogg J, Toews G, Helmers R, Cooper JA Jr, Baughman R, Strange C, Millard M *Am J Respir Crit Care Med*. **Utility of a lung biopsy for the diagnosis of idiopathic pulmonary fibrosis**, 2001 Jul 15; 164(2):193-6
24. Mapel DW, Hunt WC, Utton R, Baumgartner KB, Samet JM, Coultas DB *Thorax*. **Idiopathic pulmonary fibrosis: survival in population based and hospital-based cohorts**, 1998 Jun; 53(6):469-76
25. Hyldgaard C. A cohort study of Danish patients with interstitial lung diseases: Burden, severity, treatment and survival. *Dan Med J*. 2015; 62(4): B5069
26. Xaubet A, Ancochea J, Morell F, et al. Report on the incidence of interstitial lung diseases in Spain. *Sarcoidosis Vasc Diffuse Lung Dis*. 2004; 21(1): 64–70
27. Karakatsanis A, Papakosta D, Rapti A, et al. Epidemiology of interstitial lung diseases in Greece. *Respir Med*. 2009; 103(8): 1122–1129. DOI: 10.1016/j.rmed.2009.03.001
28. ERS. Occupational lung diseases In: ERS European Lung White-book. Chapter 24. ERS; 2015. <http://www.erswhitebook.org/chapters/occupational-lung-diseases/>. Access date: September 15, 2016
29. Collins B, Singh S, Joshi J, et al. ILD-India registry: Idiopathic pulmonary fibrosis (IPF) and connective tissue disease (CTD) associated interstitial lung disease (CTD-ILD). *Euro Resp J*. 2016; 48(Suppl 60): PA812 DOI: 10.1183/13993003.congress-2016.PA812
30. Jindal SK and Gupta D. Incidence and recognition of interstitial pulmonary fibrosis in developing countries. *Curr Opin Pulm Med*. 1997; 3(5): 378–383. DOI: 10.1097/00063198-199709000-0001
31. Jafri S, Ahmed, Saifullah N, Musheer M. Epidemiology and clinical-radiological features of Interstitial lung diseases. *Pak j med Sci*. (2020)36: 365-70.doi:10.21037/pjms.36.3.1046

32. Guo B, Wang L, Xia S, Mao M, Qian W, PengX, et al. The interstitial lung disease spectrum under a uniform diagnostic algorithm: a retrospective study of 1,945 individuals. *J Thorac Dis.* (2020) 12: 3688-96.doi:10.21037/jtd-19-4021
33. Ahamad EH. Interstitial lung diseases in Saudi Arabia: A single-center study. *Ann Thorac Med.* 2013; 8(1): 33–37. DOI: 10.4103/1817-1737.105717
34. Martínez-Briceño D, García-Sancho C, Fernández-Plata R, et al. Tendencia de la mortalidad por enfermedades intersticiales en México, período 2000–2010. *Neumol Cir Torax.* 2014; 73(3): 179–184
35. Moore I, robe J, Rhodes J, LIN Q, Webster S, Jo H, et al. Australasian interstitial lung disease registry (AILDR): Objective. Design and rationale of bi-national Prospective database *Pulm ME.* (2020) 20: 257.doi:10.1186/s12890-020-01297-2
36. N. I Nwosu, V. Uduma, P. Nlewei, K. N. Ukuwaja, C. Chukwuka; Medicine, University of Nigeria Teaching Hospital, outuku Ozalji, Nigeria, Department of Medicine.
37. Duchemann B, Annesi-Maesano I, de Naurois CJ, et al. Prevalence and incidence of interstitial lung diseases in a multi-ethnic county of Greater Paris. *Euro Respir J* 2017; 50:1-13
38. Opez-Campos JLL, iguez-Becerra ER. Incidence of interstitial lung diseases in the south of Spain 1998–2000: the RENIA Study. *European Journal of Epidemiology* 2004; 19:155–61.

APPENDIX I. Data collection format

SPHMMC, department of internal medicine

The Purpose of This study is to evaluate prevalence & characteristics of ILD in patients visiting SPHMMC, chest clinic

I kindly request your willingness to perform these reviews. The information gathered will be used confidentially

General Information

- Code-----
- Date-----
- MRN -----

Socio-demographic data and diagnosis

1. Age -----
2. Sex = Male ☐ Female ☐
3. History of Smoking Yes ☐ No ☐
4. History of TB treatment Yes ☐ No ☐
5. History of Pneumonia treatment Yes ☐ No ☐
6. Occupation -----
7. Residency Urban ☐ Rural ☐
8. Viral Markers
 - 8.1. HBsAg = Positive ☐ Negative ☐ Unknown ☐
 - 8.2. HCV Ab = Positive ☐ Negative ☐ Unknown ☐
9. Diagnosis _____
10. Diagnosed with ILD YES ☐ NO ☐, If yes, Date of Diagnosis-----
11. If yes to no 10, Type of ILD, IPF ☐ NISP ☐ LIP ☐ CTD-ILD ☐ Other ☐
12. Duration of illness-----years

13.Modality of Diagnosis

- Chest CT scan
- Bronchoalveolar Lavage
- Lung Biopsy
- Chest X-ray
- Pulmonary function test (Spirometer)

14.Family history of similar illness YES ☐ NO ☐

15.HIV/AIDS POSITIVE ☐ NEGATIVE ☐

16.Previous history of irradiation YES ☐ NO ☐

17. Previous medication uses (Bleomycin, cyclophosphamide, Amiodarone, NSAID, Methotrexate, Amphotericin B,... Etc.) NO ☐ YES ☐ IF YES, SPECIFY
.....

18. IF yes to number 17, Duration of use..... Currently use medication ☐ stopped ☐
if stopped when

19. Number of ward admissions related with ILD

20. Number of EMOPD visit due to exacerbation

21. Comorbidity.....

APPENDIX II. ASSURANCE OF INVESTGATOR

I, the undersigned resident, agree to accept all responsibilities for the scientific and ethical conduct of the research project. This is my original work, in partial fulfilment of the requirement for certificate of specialty in internal medicine. I also declare that it has never been presented in this or any higher institution and all the resources and materials used in the research work have duly acknowledged.

Name of the investigator: Dr. KIBROM GEBRU (MD, RESIDENT)

Signature: _____

Date: _____

Approval of the Major Advisors

Clinical Advisor: Dr. ABEL MUREJA

Signature: _____

Date: _____

Public health Advisor: Mrs. SISAY TANI

Signature -----

Date