

**Evaluating the Utility of Chest High Resolution Computed
Tomography in Early Detection of Fibrosing Interstitial Lung
Diseases**



SUPERIOR UNIVERSITY

**Thesis Submitted to
The Superior University Lahore
In Partial Fulfillment of the
Requirement for the Degree of
Master of Science in Allied Health Sciences**

By

HADIQA SHAUKAT

SU91-MSAHW-S23-016

Session: 2023-2025

Faculty of Allied Health Sciences

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FAHS

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No part of this thesis has been submitted anywhere else for any other degree. This thesis is submitted to the Faculty of Allied Health Sciences, The Superior University, Lahore in partial fulfillment of the requirements for the degree of Master of Philosophy in the field of “**Medical Imaging Technology**” in Faculty of Allied Health Sciences at The Superior University, Lahore.

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DEDICATION

Firstly, I dedicate this research work to Allah Almighty who is our creator and make me capable for doing this project. Secondly, I dedicate my work to my father Hakeem Muhammad Shaukat Ali (late) who has always been my back bone my strength and taught me to never let down. He is my strength my hero, he never failed to give me financial and moral support and always taught me that the best kind of knowledge to have is that which is learned for its own sake. I also dedicate my work to my mother Balkeas Akhtar who taught me that even the largest task can be accomplished if it is done one step at a time. And last but not least I dedicate my work to those patients who gave me their personal medical record to fulfil my research work without their help this work can't be reach to an end.

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LIST OF ABBREVIATIONS

ILD: Interstitial Lung Disease

IPF: Idiopathic Pulmonary Fibrosis

HRCT: High-Resolution Computed Tomography

NSIP: Nonspecific Interstitial Pneumonia

HP: Hypersensitivity Pneumonitis

UIP: Usual Interstitial Pneumonia

DIP: Desquamative Interstitial Pneumonia

PFTs: Pulmonary Function Tests

RB-ILD: Respiratory Bronchiolitis-Associated Interstitial Lung Disease

CTD-ILD: Connective Tissue Disease-related Interstitial Lung Disease

MDT: Multidisciplinary Team

ABSTRACT

Background: Interstitial lung diseases (ILDs) represent a diverse group of pulmonary disorders. High-resolution computed tomography (HRCT) is a cornerstone in their diagnosis and management.

Objective: This study aimed to evaluate the association between HRCT patterns and diagnoses in patients with suspected ILD at a tertiary care center.

Methods: This cross-sectional study with a prospective component included 128 adult patients (17-85 years) with clinical suspicion of ILD undergoing HRCT at Arif Memorial Teaching Hospital, Lahore, over a 4-month period. Non-probability convenient sampling was used. HRCT scans were reviewed by experienced radiologists, and clinical data (demographics, symptoms, exposures) were collected. Associations between HRCT patterns (UIP, NSIP, HP, organizing pneumonia, DIP) and final diagnoses were analyzed. Short-term and long-term outcomes were also assessed.

Results: The mean age of participants was 47.9 ± 14.2 years, with a slight male predominance (54.7%). Common presenting symptoms included dyspnea (94.5%) and chronic cough (91.4%). Occupational dust was the most frequently reported exposure (18.8%). Strong associations were observed between specific HRCT patterns and diagnoses: UIP with IPF (77.8%), NSIP with NSIP (75.9%), HP with HP (70.5%), organizing pneumonia pattern with organizing pneumonia (75%), and DIP pattern with DIP (66.7%). Short-term outcomes showed symptom improvement in 81.0% and PFT stabilization in 79.5% of patients. Long-term follow-up revealed an 86.7% survival rate, with 18.0% experiencing disease progression and 23.4% requiring advanced therapies.

Conclusion: This study reinforces the crucial role of HRCT in suggesting specific ILD diagnoses based on characteristic patterns.

Keywords: Interstitial lung diseases, High resolution computed tomography, pneumonia, cough.

Chapter 1

INTRODUCTION

Fibrosing interstitial lung diseases (ILDs) refer to a broad group of lung disorders where fibrosis, or scarring, occurs in the lung tissue (specifically in the lung interstitium, which is the tissue surrounding the air sacs). This scarring affects the lung's ability to function properly, leading to progressively worsening lung performance (1, 2). Over time, as the scarring thickens and stiffens the lungs, gas exchange (the process by which oxygen enters the bloodstream and carbon dioxide is removed) is compromised. This results in respiratory insufficiency, which can cause symptoms such as difficulty breathing (dyspnea), decreased physical activity, and lower quality of life (3). Ultimately, if untreated or not managed effectively, these diseases reduce life expectancy due to the chronic decline in lung function (2).

The fibrotic process in ILDs often arises due to repeated injury to lung cells and the surrounding tissue matrix (a structural network of proteins and fibres that support the lung cells). These injuries can result from a variety of factors such as physical trauma, exposure to harmful chemicals, thermal burns, low oxygen levels (hypoxia), or immune reactions where the body's immune system mistakenly attacks healthy lung tissue. Over time, this damage leads to the excessive deposition of fibrous tissue, resulting in permanent scarring (2).

Fibrosing Interstitial Lung Diseases (ILDs) encompass a group of chronic, progressive lung disorders characterized by fibrosis (scarring) of lung tissue (3). Key examples include idiopathic pulmonary fibrosis (IPF), chronic hypersensitivity pneumonitis, and non-specific interstitial pneumonia (NSIP). These conditions are often not diagnosed early due to less specific symptoms which include shortness of breath and dry cough, these symptoms are similar to other respiratory diseases (4).

This abstract will refer to one of the leading concepts of fibrosing ILDs as the 'repeatedly alveolar injury' where many small injuries of the alveoles (small air sacs in the lungs) over time result in fibrosis (4, 5). This theory helps explain the occurrence of several specific ILDs, including:

Idiopathic Pulmonary Fibrosis (IPF): This is the most common fibrosing ILD there is. IP is a recognized antecedent of chronic and progressive fibrosing ILD and carries a poor prognosis with median survival of 3 to 5 years after diagnosis. This is especially important because IPF is generally a poorly prognosticate illness if treated conservatively.

Connective Tissue Disease-associated ILD (CTD-ILD): ILD that develops due to subjects suffering from autoimmune diseases such as RA or SSc. Occupational asthma is caused by constant breathing in of allergens that cause inflammation and fibrosis within the lung tissue.

Fibrotic Hypersensitivity Pneumonitis (HP): Pulmonary inflammation and fibrosis due to long term environmental exposures including mold or bird proteins and the resultant immune response (6). Sometimes, it has a better prognosis than IPF, however, correct differential diagnosis of the disease at the early stage and distinguishing it from other types of ILD is critically important for adequate treatment.

Fibrosing ILDs include several other rarer entities that also lead to similar pathological fibrosis in the lungs (7). Including Idiopathic Nonspecific Interstitial Pneumonia (NSIP) is an ILD in which the cause of lung fibrosis is not clear, and the fibrosis pattern is not as characterized as in other forms of ILD. NSIP may progress but patients with such conditions may have better prognosis if diagnosed early.

Langerhans Cell Histiocytosis is a rare and rare disease in which there is dysfunction and formation of histiocytes, most commonly Langerhans cells in different organs of the body, including lungs. In the lungs Langerhans cell histiocytosis can lead to cystic and fibrotic changes and smoking is a known association (8). Although traditionally a disease of smokers Langerhans cell histiocytosis can present in non-smokers, especially in children. Sarcoidosis is an autoimmune pathology that manifests with granulomatous inflammation in multiple organs, commonly the lungs. Although sarcoidosis can spontaneously remit in some patients, others can develop fibrotic pulmonary sarcoidosis, resulting in fibrosis of lungs. Here, we found that the extent of pulmonary involvement in patients with sarcoidosis can range from mild to severe disease and severe fibrosis with impaired respiratory function (8, 9).

Morbidity from asbestosis and silicosis are typical occupational pneumoconias resulting from inhalation of asbestos particles or silica dust respectively. These

conditions, together with the signs of chronic inflammation and fibrosis of the lungs, can culminate in progressively more severe scarring, increasingly poor lung function and, ultimately respiratory failure if they are not diagnosed and managed properly. Workers in industries such as construction, mining, and manufacturing are particularly at risk of developing these conditions due to long-term exposure to harmful particles. Together, these rare fibrosing ILDs highlight the broad spectrum of diseases that can result in lung fibrosis, each with distinct etiologies and clinical courses. However, what unifies them is the necessity of early detection to prevent disease progression and initiate timely intervention (10).

Reliable national figures regarding the prevalence of fibrosing Interstitial Lung Diseases (ILDs) within Pakistan remain limited. However, existing research points towards a pattern of both underdiagnosis and frequent misdiagnosis of ILDs. Notably, pulmonary fibrosis, especially Idiopathic Pulmonary Fibrosis (IPF), is gaining recognition as a significant health issue. Reports in expert healthcare setups indicate a rise in ILD cases, reflecting increased awareness and advancements in diagnostic tools (11). A study conducted at a major medical center in Karachi found that IPF accounts for a significant portion—approximately 25-30%—of diagnosed ILD cases. A major concern is that most patients present with the disease at advanced stages (12). Regional research suggests that ILDs, including IPF, contribute to a substantial 15-20% of respiratory-related hospital admissions. A significant trend observed in fibrosing interstitial lung diseases (ILDs) is the rapid progression of the disease, often attributed to delays in diagnosis. Fibrosing ILDs, which is primarily characterized by scarring of the lung tissue, consist a heterogeneous group of disorders with different etiologies and factors that may contribute. Early diagnosis and timely intervention are essential to slow disease progression and improve patient prognosis(12).

The role of diagnostic imaging is essential in ILDs diagnosis, particularly when clinical symptoms and pulmonary function tests have nonspecific findings. Though chest radiographs have traditionally been the first and foremost imaging modality used in ILD, they are known not to be sensitive in picking up fibrosing ILDs at an early stage. Notably, chest X-rays often miss subtle pulmonary abnormalities, including ground-glass opacities and reticular patterns, characteristic of early fibrosis (13).

HRCT (High-Resolution Computed Tomography) stands as the best way to confirm an ILD diagnosis. This cutting-edge imaging method produces sharp clear pictures of lung tissue helping doctors spot early signs of scarring that regular CT scans or chest X-rays might overlook. HRCT shines at picking up fine web-like patterns, honeycomb-like structures, and hazy areas giving crucial info for diagnosis. What's more, it plays a key role in telling apart scarring ILDs from non-scarring types, which is vital to choose the right treatment plan (13).

A big challenge in dealing with scarring ILDs is getting a quick diagnosis. Sometimes, these conditions turn into a scarring type marked by ongoing, self-feeding tissue buildup. This causes rapid loss of lung function worse quality of life, and early death. Getting the diagnosis right is key, as treatments—from steroids and immune suppressants to new anti-scarring drugs—depend on the exact ILD type. But making a diagnosis is tricky because symptoms scan results, and tissue samples can look alike for different types often needing a team of experts to classify them. (14).

This is different from patients diagnosed at a later time when they present with advanced fibrosis more, with few interventional possibilities. By this time, lung function has become permanently lost and irreversible and is associated with greater morbidity and mortality. Treating late-stage ILDs mechanically is more difficult because fibrosis is more extensive, and the treatment is more invasive, like lung transplantation in some cases. It aggravates the acuity of other heart diseases such as acute exacerbations, pulmonary hypertension, and failure of the right heart (16).

Chest high-resolution computed tomography (HRCT) has become an essential tool for the initial evaluation and diagnosis of patients with fibrosing interstitial lung diseases (ILDs). HRCT has largely replaced older imaging methods, such as standard chest X-rays (plain radiography) and fluoroscopy, which have limitations in visualising fine details of the lung tissue. While traditional chest radiographs can provide basic information, they often miss early or subtle abnormalities in the lung parenchyma (the functional tissue of the lungs involved in gas exchange) that are essential for diagnosing fibrosing ILDs (17).

HRCT is an advanced imaging modality specifically designed to capture detailed, cross-sectional images of the lung parenchyma. Unlike standard CT scans, HRCT

utilises thin-slice imaging (1-2 mm slices) to produce high-definition images of the lungs, allowing for the precise visualisation of even minor changes in lung architecture. HRCT works by applying a lesser amount of radiation and computing thin sections of the lung tissue; this increases the scans' resolution without a greatly higher dose of radiation. This imaging technique shows greater precision in defining irregular patterns of interstitial disease, including fibrosis, distortion of hear structure and the initial signs of fibrosis, such as the presence of ground glass opacities, honeycombing (18).

HRCT is useful in showing fibrosis in part of the lung in ILDs that may otherwise be invisible using other imaging techniques. Thus, the fine reticulations and ground-glass opacities in disease like IPF and NSIP that manifest with minimal and/or early fibrotic changes render HRCT an essential modality in the current diagnostic armamentarium 18. In addition, HRCT is useful in distinguishing fibrosing ILDs from other pulmonary disorders including COPD or asthma which although may have similar manifestations, have different management approaches (18).

HRCT, in contrast, provides much better picture quality that can provide cross-sectional images of the lungs. This affords a much more detailed and better resolution of the lungs than conventional radiography allowing for the early stage or minimal lung pathologies to be visualized. HRCT can visualise particular features in the lung parenchyma where thin slices of the chest are taken besides imaging methods that are improved so that patterns and changes of fibrosis that are mandatory for the diagnosis of different categories of ILD can be detected. Employing fine cross-sections of the thorax coupled with refined visualization methods, High-Resolution Computed Tomography (HRCT) enables the identification of distinct fibrotic configurations and other pulmonary alterations. These are indispensable in differentiating various forms of Interstitial Lung Diseases (ILDs) (19). Within the array of patterns discernible through HRCT, two hold particular clinical significance: Usual Interstitial Pneumonia (UIP) and Nonspecific Interstitial Pneumonia (NSIP) (20). These patterns not only help in the early detection of ILDs but also offer crucial insights into the underlying disease, its prognosis, and potential therapeutic strategies:

The Usual Interstitial Pneumonia (UIP) pattern is most frequently associated with Idiopathic Pulmonary Fibrosis (IPF), a typically progressive and potentially fatal form

of fibrosing ILD (20). HRCT findings in UIP are characterised by several distinct features:

Honeycombing: There is presence of small grouped cystic structures commonly sighted at the peripheral and basal part of the lung. They are usually multiple and when grouped they seem to be piled up like a series of beehives (21). Honeycombing is a characteristic feature of end stage lung fibrosis and depicts permanent derangement of the lung structure. Variable in distribution, it also has a high specificity for UIP when present and when combined with other archetypal features.

Reticular Opacities: These are thin, net-like lines that represent fibrotic tissue in the Lung interstitium.” Those with the features of reticular opacities are another characteristic of the UIP pattern and are usually localized in the lower lobes of the lungs. In UIP, these opacities are often associated with traction bronchiectasis, where the fibrotic tissue pulls on and distorts the bronchi, further impairing lung function.

Subpleural and Basal Distribution: UIP often manifests with fibrosis concentrated in the areas close to the pleura (the lining of the lung) and the lower lung regions, which is a key distinguishing feature on HRCT. The basal-predominant and subpleural distribution is important for differentiating UIP from other ILD patterns (20).

Identifying the UIP pattern on HRCT is critical because it has profound implications for prognosis and management. UIP, particularly when associated with IPF, is known to have a worse prognosis compared to other ILD subtypes. IPF typically follows a progressive course, with a median survival time of 3 to 5 years after diagnosis, making early detection and accurate diagnosis vital for initiating appropriate treatment . HRCT helps avoid unnecessary invasive procedures like lung biopsies in cases where the imaging findings are definitive for UIP (19, 20).

The second subtype, the Nonspecific Interstitial Pneumonia (NSIP) pattern is related to a much wider spectrum of diseases such as connective tissue disease associated ILD, drug induced lung disease and Hypersensitivity pneumonitis to name but a few. The NSIP pattern almost always appears dissimilar to UIP and it often has a relatively favourable prognosis (20).

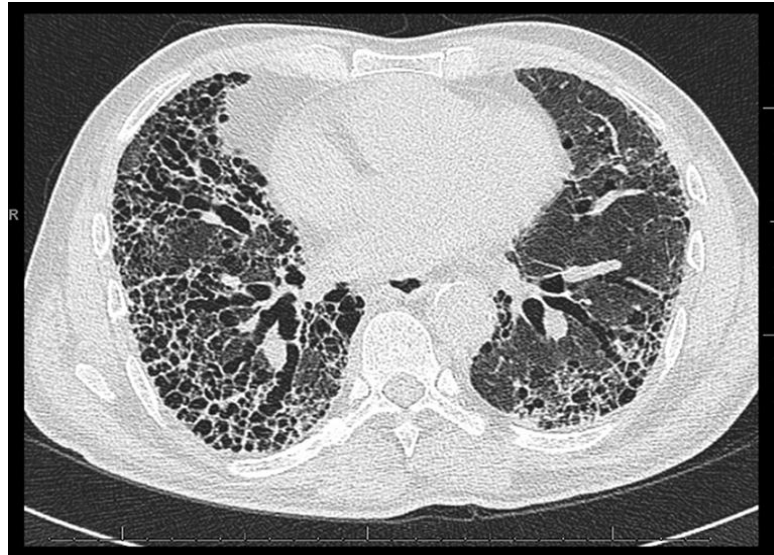


Figure 1.1: An HRCT of the lungs showing the classical UIP pattern: honeycomb transformation, the sub-pleural distribution and traction bronchiectasis can be discerned. HRCT, high resolution computed tomography; UIP, usual interstitial pneumonia.

From a treatment perspective, patients with UIP, especially those with IPF, may benefit from antifibrotic medications like pirfenidone and nintedanib, which have been shown to slow disease progression but not reverse existing fibrosis. By identifying UIP early through HRCT, clinicians can promptly initiate such treatments, potentially improving the quality of life and extending survival for these patients. However, UIP is associated with limited responsiveness to immunosuppressive therapies, which are more commonly used in other ILD subtypes, highlighting the importance of accurate pattern recognition on HRCT to guide treatment decisions (19).

Ground-Glass Opacities: Another characteristic of NSIP, which remains well appreciate on MHN, is the demonstration of ground-glass opacities on high-resolution computed tomography scans. These areas of hazy increased opacity do not obscure underlying structures and represent regions of partial inflammation or fibrosis. In NSIP, ground-glass opacities tend to be more diffuse and uniform, unlike the patchy distribution observed in UIP. This pattern suggests active inflammation, which is often reversible with appropriate treatment (21).

Unlike Usual Interstitial Pneumonia (UIP), Nonspecific Interstitial Pneumonia (NSIP) is rarely associated with honeycombing, and when present, it is typically less

extensive. The absence or minimal presence of honeycombing is a favorable prognostic marker, as it indicates less severe or potentially reversible lung damage (20). It supplies clinicians with invaluable information regarding lung architecture and disease extent, helping in making decisions about further diagnostic procedures and adjusting treatment (21).

HRCT can identify subtle early fibrotic changes, which are inapparent on routine imaging. Early detection is important because the process can then be intervened on before fibrosis becomes fixed and uncorrectable. Advanced fibrosis is resistant to treatment and, therefore, early detection by HRCT will enable clinicians to introduce therapies such as antifibrotic or immunosuppressive medications that can attenuate or reverse disease progression. Proactive therapy benefits the patient, maintains lung function, and optimizes quality of life.

HRCT not only remains a powerful diagnostic tool but also the foundation for chronic ILD management. The fact that HRCT can guide invasive diagnostic methods, track disease progression, and detect early fibrotic change allows early and effective treatment, thereby enhancing patient prognosis and outcome (23). There is a greater need for extensive studies examining HRCT as a first-line screening test in early fibrosing ILDs. Current research has largely been focused on the diagnosis of advanced-to-moderate fibrosis, with little evidence that it can detect early disease. Having standard protocols in place for routine use of HRCT in high-risk groups—those with a family history of pulmonary fibrosis or chronic occupational exposures—may improve detection rates early on and allow for timely therapeutic intervention (24). Japanese studies have indicated that IPF is higher in men and smokers, and diagnosis rates also rise as wider use of HRCT imaging occurs. In China, evidence is less readily available, yet hospital-based data estimates the incidence to be lower than in Western nations, with 5-10 cases per 100,000. Yet, industrial exposure-related ILDs like silicosis and asbestosis are more common in highly industrialized areas (29).

NSIP is less common than IPF but remains an important subtype of fibrosing ILDs. Prevalence estimates suggest that NSIP affects 2 to 5 per 100,000 people, but this number may be underreported due to diagnostic challenges. Data from the UK and other European countries suggest similar prevalence rates of 3 to 6 per 100,000, with more patients being diagnosed as diagnostic techniques like HRCT improve. NSIP is

considered relatively rare but more prevalent in middle-aged females. Estimates suggest 1 to 2 per 100,000 people are diagnosed with NSIP annually in Japan. Occupational ILDs, such as asbestosis and silicosis, are more prevalent in regions with significant industrial exposure. In countries with extensive mining, construction, and manufacturing industries, the burden of these diseases is much higher (30).

China has one of the highest rates of occupational lung diseases globally, with silicosis being a major concern. The reported prevalence varies by region, with some industrial provinces reporting rates as high as 6,000 per 100,000 workers in high-risk industries like mining and construction. India has a significant burden of occupational lung diseases, particularly silicosis, due to widespread mining and construction activities. While precise prevalence data are limited, hospital-based studies report high rates of silicosis in regions like Rajasthan, where stone-cutting industries are common (31).

Global prevalence rates for IPF vary significantly by region, with estimates ranging from 10 to 63 cases per 100,000 people. Higher prevalence rates are typically reported in developed countries, where aging populations and advanced diagnostic tools like HRCT are more common (28). Less prevalent than IPF, NSIP affects approximately 2 to 5 per 100,000 people globally, with higher rates of diagnosis occurring as awareness of ILDs increases. Occupational ILDs, particularly silicosis and asbestosis, are prevalent in regions with heavy industrial activity, such as China, South Africa, and India. Prevalence rates for silicosis can be extremely high in certain populations, such as gold miners, where up to 25% of workers may be affected (31).

Prevalence rates for fibrosing ILDs, especially IPF, show significant geographic variability. In countries like the United States and Europe, ageing populations and improved diagnostic tools have contributed to an increase in diagnosis rates (30).

In contrast, in regions with higher industrial exposure, occupational lung diseases like silicosis and asbestosis are more prevalent. As HRCT imaging becomes more widely accessible, earlier diagnosis and better prevalence estimates for fibrosing ILDs will likely continue to emerge worldwide (31).

The findings of this research will also contribute to the limited local literature on HRCT's diagnostic utility in fibrosing ILDs in Pakistan. In a setting where healthcare resources are often constrained, this study could emphasise the importance of

incorporating HRCT into standard clinical practice for managing ILDs, particularly by promoting early intervention to improve patient outcomes. This research is expected to provide valuable insights into the role HRCT can play in reducing mortality and morbidity associated with fibrosing ILDs in the local population, helping to bridge the gap in diagnostic and management strategies for these diseases.

AIM AND OBJECTIVES

1. To determine the prevalence of different HRCT patterns (UIP, NSIP, HP, organizing pneumonia, DIP, etc.) in patients with suspected ILD and association between specific HRCT patterns and final diagnoses of ILD.
2. To describe the short-term and long-term clinical outcomes of patients with different HRCT patterns.

Chapter 2

LITERATURE REVIEW

2.1. Interstitial Lung Diseases (ILDs)

A broad spectrum of pulmonary conditions, known as interstitial lung diseases (ILDs), primarily impact the lung interstitium, the area surrounding the alveoli, or air sacs, within the lungs. The complex workings behind ILDs often have an impact on both inflammatory and fibrotic processes, which can lead to ongoing lung scarring. ILDs show up in many ways, but they start with vague signs. These can include a long-lasting dry cough, trouble breathing during exercise, feeling tired, and sometimes chest pain (33 34). Because these early signs aren't clear-cut, it can take a while to figure out what's wrong making it hard to catch.

Studies on disease spread show that ILDs affect 20 to 100 out of every 100,000 people, with older folks more likely to get them (35). Of all the ILD types Idiopathic Pulmonary Fibrosis (IPF) is the most common making up a big chunk of cases. IPF causes lungs to work less and less over time leading to breathing failure and higher death rates. After doctors diagnose IPF, people live between three to five years, which shows how the disease moves (36 37). Other ILD types include those linked to connective tissue diseases, lung reactions to allergens, and sarcoidosis. Each of these looks different when doctors examine patients and take pictures of their lungs.

Even though we've learned a lot about what causes ILDs and how they work in the body, it's still tough to diagnose them. This is because they're so different from each other and their signs can look like other diseases (38).

2.2. Fundamentals of High-Resolution Computed Tomography

High-Resolution Computed Tomography (HRCT) has transformed lung imaging by enabling the detailed visualization of lung parenchyma. Unlike conventional CT scans, which are limited by lower spatial resolution and thicker slice thickness, HRCT employs thin-slice imaging (typically 1 mm or less) and advanced image processing algorithms to enhance contrast and minimize noise (54). This higher resolution makes

HRCT the modality of choice for imaging interstitial lung diseases (ILDs) since it facilitates the detection of subtle pathological changes in lung tissue.

HRCT is performed using axial images that may be reconstructed in sagittal and coronal planes, allowing for better evaluation of lung anatomy and pathology. The images are normally obtained at breath-hold to minimize motion artifacts and yield clean images (55). HRCT uses higher kilovolt peak (kVp) settings, which improve its sensitivity to early interstitial changes without limiting radiation exposure to acceptable levels. (56).

High-Resolution Computed Tomography (HRCT) provides improved visualization of lung architecture and is a crucial component in the assessment of Interstitial Lung Diseases (ILDs). In comparison to routine chest X-rays and conventional CT scans, HRCT more favorably possesses spatial resolution and thin slices, enabling precise measurement of lung pathology. The following considers the most important imaging features of HRCT and how they aid in the detection, characterization, and quantitation of fibrosing ILDs (57).

HRCT's feature of obtaining thin-slice images (1 mm or less) allows for high-definition imaging of lung parenchyma. Thin-slice technique reduces volume-averaging artifacts, which in normal CT scans obscure the fine details and make diagnosis impossible (58).

The higher resolution of HRCT allows for close inspection of the secondary pulmonary lobules, the basic lung building blocks. This level of detail is required for detecting subtle abnormalities that would not be detected by lower-resolution imaging (59). By facilitating such detailed visualization, HRCT differentiates among a number of interstitial lung patterns, such as reticulations, nodules, ground-glass opacities, and honeycombing. These findings provide important information regarding disease pathology (60).

Among the most important advantages of HRCT is the detection of early fibrotic changes before they are clinically evident or visible on chest X-rays. Ground-glass opacities (GGOs), poorly defined regions of increased lung density without completely obscuring underlying structures, typically represent early inflammation or interstitial thickening (60). Nonetheless, being subtle in nature, their high contrast and

fine resolution are critical to their correct identification. GGOs are especially crucial in early-stage diseases such as Nonspecific Interstitial Pneumonia (NSIP) and Hypersensitivity Pneumonitis (HP), where diagnosis at an early stage can have a great impact on patient prognosis and treatment (60).

HRCT is also superior in showing fine reticulations and subpleural lines, subtle signs of fibrosis that might not be visible on routine CT scans or chest X-rays. For instance, reticulations in the lower lung bases can herald the onset of Idiopathic Pulmonary Fibrosis (IPF), with clinicians able to introduce therapeutic measures that arrest the disease at this point (62).

2.2.1 Characterization of Imaging Patterns

HRCT is very important in identifying and distinguishing interstitial lung disease patterns

UIP (Usual Interstitial Pneumonia): This pattern includes reticular opacities, honeycombing, and traction bronchiectasis, with predominantly peripheral and basal distribution within the lungs. Honeycombing, seen as clusters of thick-walled air-filled cysts, is critical for the diagnosis of Idiopathic Pulmonary Fibrosis (IPF). When UIP is found on HRCT and is concordant with clinical and laboratory data, it can negate the need for a surgical lung biopsy.

NSIP (Nonspecific Interstitial Pneumonia): This pattern shows ground-glass opacities and fine reticulation, with some sparing of the peripheral lung regions. NSIP differs from UIP by the absence of honeycombing of advanced lung disease. It is important to recognize NSIP because it has a tendency to suggest a better prognosis than UIP.

OP (Organizing Pneumonia): It manifests as patchy, migratory lung consolidations that may mimic infection or carcinoma. HRCT assists in the diagnosis of OP by showing its propagation along the bronchi and lung periphery. Recognizing OP is crucial for making treatment choices, such as using corticosteroids.

2.3. Monitoring Disease Progression and Treatment Response

HRCT is priceless for longitudinal follow-up of ILDs. Serial HRCT scans can demonstrate changes in the extent or pattern of lung involvement over time, reflecting disease progression or response to treatment. For instance, decrease in ground-glass opacities or stabilization of reticular patterns following initiation of treatment is indicative of a good response, whereas increase in honeycombing or traction bronchiectasis reflects progression (71).

The capacity to monitor quantitative changes over time is particularly valuable in diseases such as IPF, where deterioration can be unpredictable and dramatic (72). By linking clinical outcome with serial HRCT results, clinicians are better able to individualize treatment plans and modulate therapy in a timely fashion (73).

2.4. Advanced Techniques and Technological Enhancements

New tech breakthroughs have boosted HRCT's power. Methods like ultra-high-resolution CT (UHRCT) now give thinner slices and sharper images than old HRCT helping doctors spot tiny lung changes (74). Also dual-energy CT adds info about lung blood flow and tells apart scarring from swelling (75). These new ideas are stretching what HRCT can do letting doctors catch tricky lung problems earlier and more .

HRCT's imaging skills make it key to check and treat ILDs. Its sharp picture's ability to see different lung disease patterns, and use in both quality and quantity checks help get diagnoses right and make patients better. How it helps catch problems, describe diseases, and keep track over time shows why it's so important in today's lung care (77).

2.5. Strengths and Limitations

The benefits of HRCT in the evaluation of ILDs are numerous. It possesses high spatial resolution and the ability to see fine lung architecture, which is very helpful in early detection and differentiation of interstitial patterns (78). HRCT is also non-invasive, which is a good guess for patients, particularly those that may require imaging to be repeated over time to evaluate disease or response to treatment (79).

Furthermore, the use of HRCT can reduce the need for invasive procedures, such as lung biopsies, which carry inherent risks (80).

2.6. HRCT in Early Detection of Fibrosing ILDs

2.6.1. Significance of Early Detection

The importance of early diagnosis in fibrosing interstitial lung diseases (ILDs) must not be overstated since the sooner the conditions are detected, the higher the patient outcomes, survival rate, and quality of life. High-resolution computed tomography (HRCT) plays a pivotal role in early diagnosis of ILDs because HRCT can detect subtle structural abnormalities in the lungs that would be undetected by routine imaging techniques such as chest X-rays (88). Early diagnosis allows for early treatment, which can decelerate the progression of the disease and limit the risk of permanent damage (89).

Fibrosing ILDs including idiopathic pulmonary fibrosis (IPF), nonspecific interstitial pneumonia (NSIP), and connective tissue disease-associated ILDs (CTD-ILDs) typically advance to advanced stages when patients become symptomatic with clinically severe features (the window of opportunity for therapeutic intervention to succeed may be missed). HRCT's ability to pick up parenchymal changes in their early stages, i.e., ground-glass opacities and subpleural reticulations, can enable an earlier diagnosis so that more intensive treatment protocols can be implemented at a time when they will prove most useful (90).

2.7. Impact on Patient Management and Monitoring

Early identification and separation of ILD by HRCT have a big impact on the management of the patient. Treatment initiated early may alter the progression of the disease, leading to better long-term results and decelerated advancement of the disease. It has been shown by studies that administration of antifibrotic agents, pirfenidone, and nintedanib is of greatest benefit if administered early during the disease, before extensive fibrosis (80). This is particularly the case for IPF, where delaying treatment until advanced disease decreases therapy effect and survival (101).

HRCT is also vital in monitoring the progression of the disease and drug response. Follow-up HRCT scans allow visualizing temporal dynamics, including declining reticulations, honeycombing development, or traction bronchiectasis, which may indicate worsening fibrosis (102). This attribute enables clinicians to adjust treatment regimes based on image findings, ensuring optimal patient management (103).

The objective information of HRCT findings can subsequently be combined with clinical and functional assessment to achieve an integrative assessment of disease status. A patient with very minimal clinical findings but worsening findings on imaging performed on HRCT, for instance, may be considered for up-titration of treatment or evaluation for other potential causatives such as infection or drug-induced injury (103).

2.8. Clinical Studies Supporting HRCT in Early Detection

Different studies have established the utility of HRCT in the early detection of ILD and in directing patient care. Johkoh et al.'s (83) longitudinal research found that patients at risk for developing advanced fibrosing ILD can be identified by HRCT imaging prior to the presence of significant symptoms. These findings have informed guidance on the utilization of HRCT in individuals presenting with risk factors or suggestive but non-specific signs (104).

Walsh et al. demonstrated in a study that early HRCT features of fibrotic ILD, such as ground-glass opacities and fine reticulations, correlated with faster decline in lung function over a two-year follow-up in patients than those without such evidence. This justifies the employment of HRCT for risk stratification and for guiding earlier, individualized treatment (105).

HRCT's imaging capability is a revolutionary driver in the early treatment and diagnosis of fibrosing ILDs. By facilitating the identification of subclinical disease, discrimination of specific ILD patterns, and creation of a basis for early treatment, HRCT is an indispensable diagnostic and monitoring device in the clinician's arsenal. Its high-resolution imaging not only increases diagnostic accuracy but also the quality of patient care through early and informed therapeutic measures.

2.9. Pattern Recognition in HRCT

One of the strongest points of HRCT is the ability to differentiate between the various subtypes of ILDs on the basis of pattern recognition. This ability is crucial because subtypes of ILD can have varying prognoses and responses to therapy. HRCT provides high-resolution images that highlight characteristic patterns in the lung parenchyma, which allows clinicians to make definitive diagnoses that direct therapy and patient management (106).

Each subtype of ILD presents with distinct imaging features that, when identified, aid in distinguishing one condition from another. For instance, the presence of certain patterns such as honeycombing, ground-glass opacities, and reticulations on HRCT can guide the diagnosis toward specific types of fibrosing ILDs, such as idiopathic pulmonary fibrosis (IPF) or nonspecific interstitial pneumonia (NSIP) (106). This differentiation is particularly important because treatment protocols differ significantly; while antifibrotic therapies are central to IPF management, immunosuppressive treatment is more commonly used for NSIP (106).

2.10. Fundamentals and Findings

The use of high-resolution computed tomography (HRCT) in the differentiation between ILD subtypes has been studied at length, with significant advancements being made in patient management and diagnostic accuracy. This section reports landmark studies that describe the diagnostic potential, accuracy, and clinical importance of HRCT in ILD differentiation.

Lynch et al. (2017) – The Impact of HRCT on Histopathological Correlation Lynch et al. conducted one of the most important studies demonstrating the diagnostic benefit of HRCT in ILDs, which quantified the relationship between histopathological and HRCT findings. The study, in a population of 250 patients with a suspected ILD, demonstrated that HRCT had a reliable accuracy in diagnosing idiopathic pulmonary fibrosis (IPF) in cases where imaging clearly identified a usual interstitial pneumonia (UIP) pattern. Their findings indicated that a confident UIP diagnosis on HRCT had a predictive value of over 90%, suggesting that HRCT alone could suffice in many cases, reducing the need for invasive lung biopsies (107).

This study also revealed the importance of differentiating UIP from other patterns such as nonspecific interstitial pneumonia (NSIP). Lynch et al. indicated that while NSIP might share certain imaging features with UIP, including reticulations and ground-glass opacities, the absence of honeycombing and abnormality distribution were the distinguishing factors (107). These findings not only validated HRCT as an effective diagnostic tool but also supported the use of its application to speed up the diagnosis process, ultimately leading to sooner treatment initiation and improved patient outcomes.

Kawamura et al. (2016) – Sensitivity and Specificity in ILD Differentiation Kawamura et al. discussed HRCT's diagnostic value in UIP differentiation from NSIP and other forms of ILDs in a research that quantified its sensitivity and specificity. This was a multicenter study, where data were obtained from over 300 patients with ILD being seen in ILD specialty clinics. Their study revealed that HRCT was approximately 85% sensitive and 92% specific for the presence of UIP if used in combination with clinical parameters such as age of the patient, symptoms, and comorbidities (108).

The research emphasized the significance of specialist interpretation because UIP disentanglement from chronic HP or fibrotic NSIP can be difficult, especially where imaging results were similar. Kawamura et al. added that incorporation of clinical data, for instance, history of exposure in suspected HP, improved diagnostic precision and enabled more targeted management strategies (108). The research called for the integration of HRCT into a multidisciplinary team (MDT) approach in order to optimize diagnostic accuracy and improve patient management.

Walsh et al. (2020) – Mixed Patterns in ILD Walsh et al. conducted a seminal study on the recognition of mixed patterns in ILD, recognizing that some patients lack distinct imaging features which belong to a single subtype. The research on over 200 patients with various forms of fibrosing ILD depicted how mixed imaging patterns were not uncommon and were a significant diagnostic challenge (108).

Walsh's team introduced an HRCT-based approach that recognized the significance of subtle imaging features, such as the coexistence of UIP features (e.g., honeycombing) with ground-glass opacities typical of NSIP. The presence of such intricate patterns has been said to be linked to different prognostic results, noting that imaging complexities could have an impact on treatment regimens. Patients exhibiting signs of

combined UIP and NSIP, for example, were typically candidates for both antifibrotic and immunosuppressive therapies (109). This study noted the importance of HRCT's high-resolution imaging in identifying complicated cases, which allows for more personalized treatment planning.

Flaherty et al. (2019) – The Call for Standardization Recognizing variation in the interpretation of HRCT, Flaherty et al. focused on the challenges with differing levels of radiologist experience and how it affects diagnosis. Flaherty et al. compared HRCT reports of over 500 patients in over one center and noted significant variation in the interpretation of the same HRCT findings (109).

Flaherty's study emphasized the importance of standardized imaging protocols as well as greater training of radiologists to reduce subjective reading. The study further emphasized that variation in diagnosing subtypes such as NSIP vs UIP could lead to mismanagement, particularly where less experienced ILD evaluators in radiology were involved. Their recommendations stressed the importance of developing standardized HRCT reading protocols as well as MDTs to maximize diagnostic accuracy (110).

Jacob et al. (2021) – HRCT in Prognostication and Therapy Guidance Jacob et al. thoroughly assessed the prognostic role of HRCT when they examined how certain HRCT features correlated with disease progression and survival in ILD patients. It was a retrospective cohort study involving more than 400 patients, emphasizing key imaging features such as honeycombing, traction bronchiectasis, and the extent of ground-glass opacities (110).

Jacob's findings showed that honeycombing present extensively on HRCT placed a patient at very much increased risk of accelerated progression of disease and mortality compared with patients who have predominantly ground-glass opacities or reticulations alone without honeycombing (110).

This observation was vital as it emphasized the application of HRCT not only for diagnostic but also for risk stratification. These imaging markers could be utilized by clinicians to detect patients at high risk who could potentially be given precedence for lung transplantation or clinical trials (109). The study further illustrated that treatment response, measured by the resolution of ground-glass opacities, could be used to indicate a successful therapeutic response and thus facilitate treatment monitoring and alterations.

Richeldi et al. (2021) – Early Treatment and HRCT Findings Richeldi et al. further explored the relationship between HRCT-detected early fibrotic changes and treatment response in a large study. In their research, they focused on early-stage IPF patients who underwent HRCT screening and were subsequently treated with antifibrotic therapy. The study found that patients with subclinical UIP on HRCT—who had not yet developed significant symptoms—experienced slower disease progression if treatment was started early (180).

This study highlighted the preventive value of HRCT, where early detection translated into better management outcomes. Richeldi’s work strengthened the argument for routine HRCT use in at-risk populations, such as those with a family history of ILD or autoimmune disorders, to facilitate early intervention and improve long-term prognosis (108).

Silva et al. (2020) – HRCT in Connective Tissue Disease-Associated ILD Silva et al. examined the utility of HRCT for the diagnosis and management of ILD secondary to connective tissue diseases (CTD-ILD). Their study included 350 patients with systemic sclerosis, rheumatoid arthritis, and other autoimmune disorders. Their research highlighted how HRCT was capable of differentiating UIP and NSIP patterns in this group, thereby guiding particular treatment interventions (109).

The findings did confirm that systemic sclerosis patients tended to demonstrate an NSIP pattern on HRCT, and this was correlated with a better prognosis compared with the UIP pattern (89). This difference was significant since the treatment strategy was influenced, and UIP patients sometimes received more vigorous treatment, such as potential antifibrotic use (109). Silva et al. This study also revealed the importance of differentiating UIP from other patterns such as nonspecific interstitial pneumonia (NSIP). Lynch et al. indicated that while NSIP might share certain imaging features with UIP, including reticulations and ground-glass opacities, the absence of honeycombing and abnormality distribution were the distinguishing factors (107). These findings not only validated HRCT as an effective diagnostic tool but also supported the use of its application to speed up the diagnosis process, ultimately leading to sooner treatment initiation and improved patient outcomes.

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Implications of These Studies:

Collectively, the observations from these milestone studies underscore the indispensable role that HRCT plays in the diagnosis, differential diagnosis, and management of ILDs. The data demonstrate that not only can HRCT reduce the reliance on invasive procedures like lung biopsies, but that it can guide prompt and correct therapeutic decisions as well. Additionally, the ability of HRCT to identify mixed patterns and subtle differences between ILD subtypes means that radiologists need to undergo continuing education and training to deliver quality diagnostic work.

Application of uniform HRCT protocols and increased collaboration among members of MDTs, fostered through these investigations, are mandatory steps towards increased diagnostic accuracy and quality care. Second, the prognostic details gleaned through HRCT images will facilitate patients to be prioritized for augmented observation and timelier intervention to ultimately increase the rate of survival.

HRCT has cemented its place as a stalwart in the management of ILD through thorough research that has established its diagnostic validity, prognostic relevance, and role in therapeutic planning. The way forward for future research will involve further technological advancement in HRCT, e.g., through AI application, in order to enhance its utility for diagnosis.

While HRCT is highly valuable in the diagnosis and ILD subtype differentiation, there are certain inherent limitations. Overlapping imaging features can preclude accurate diagnosis, particularly when there is more than one pattern involved. Chronic HP, for example, may have imaging features indistinguishable from UIP, such as reticulations and honeycombing, and one cannot differentiate between the two without appropriate clinical correlation (110).

Moreover, interpretation of HRCT is very specialized and requires a great deal of experience and expertise. Differences in training among radiologists and subjective interpretation can lead to diagnostic variations. Improved training programs and standardized imaging protocols have been proposed to enhance diagnostic reproducibility (109,110).

2.11. Evaluating Treatment Efficacy

HRCT findings can serve as a surrogate marker for therapeutic response. Changes in HRCT patterns, such as reduction in ground-glass opacities or traction bronchiectasis, can suggest a favorable response to antifibrotic agents or corticosteroids.

Silva et al. (2020) had investigated the association of HRCT findings with the response to therapy in a paper on patients being treated with antifibrotic therapy. The paper concluded that those in whom fibrotic changes had been detected earlier on HRCT, who received treatment early on, had lower progression of the disease on the follow-up studies compared to individuals who received late treatment for the disease (109). This reinforces the notion that HRCT can help assess the timing of treatment interventions and guide therapy adjustments.

Chapter 3

METHODOLOGY

3.1. Research design:

This study was Cross-sectional study with a prospective component.

3.2. Clinical setting:

The study was conducted at the Radiology Department of Arif Memorial Teaching Hospital, Lahore, Pakistan.

3.3. Sample size:

$$\text{Sample Size} = \frac{Z^2 \cdot P(1-P)}{d^2}$$

Sample size turned out to be 128 patient.

3.4. Sampling Technique:

Non-probability convenient sampling techniques was used.

3.5. Duration of study:

The duration of my study was 4 months.

3.6. Selection criteria:

3.6.1. Inclusion criteria:

Adults aged above 17 years.

Patients with clinical suspicion of ILDs as per the referring physician.

Patients who are scheduled to undergo HRCT of the chest.

Patients who provide informed consent to participate in the study.

3.6.2. Exclusion criteria:

Other primary lung disease patients that can cause confounding results (e.g., active malignancy, severe COPD).

Those for whom HRCT is not feasible because of non-respiratory reasons (such as intractable claustrophobia).

Pregnant or planning pregnancy in the course of the study.

3.7. Ethical Consideration

The study was scrutinized and validated by the Ethics Review Committee of Superior University, Lahore. All participants' consent was taken before their involvement in the research. The patient data was anonymized and securely stored to maintain confidentiality and abide by data protection law.

3.8 Data Collection Procedure

3.8.1. HRCT Scan Acquisition

HRCT scans were obtained by means of standardized imaging protocols to provide consistency and accuracy. The protocols involved high-resolution parameters within-slice imaging and correct windowing techniques to maximize lung parenchyma visualization. Scans will be obtained on the latest multi-detector CT scanners to obtain the best image quality.

We use Hitachi Eclos 16-slice CT scan machine for HRCT chest, typical parameters include a slice thickness of 0.625-1.25 mm, a scan time of 0.5-1 second, kVp of 120, and mAs of 100-200. The field of view (FOV) is typically 35 cm, and the matrix size is 768x768. A high spatial frequency reconstruction algorithm is usually used, and the window setting is lung window. The patient is typically positioned supine, and full inspiration is recommended.

Here's a more detailed breakdown:

Image Acquisition:

- Slice Thickness: 0.625-1.25 mm (thin sections for high-resolution imaging).
- Scan Time: 0.5-1 second (depending on the scan type and patient size).
- kVp: 120 (to optimize image quality and minimize radiation dose).
- mAs: 100-200 (to control the amount of radiation and image contrast).
- Collimation: 1.5-3 mm (to define the slice thickness).
- Matrix Size: 768 x 768 (or the largest available for the scanner).
- FOV: 35 cm (field of view encompassing the entire chest).

- Reconstruction Algorithm: High spatial frequency (for sharp details).
- Patient Position: Supine (most common) or prone (if suspected ILD).
- Level of Inspiration: Full inspiration (to visualize the lungs properly).

Image Display:

- Window: Lung window (to optimize visualization of lung parenchyma).

3.8.2. Image Review and Interpretation

HRCT images were to be independently evaluated and interpreted by senior radiologists with expertise in thoracic imaging. The radiologists were to examine each scan for typical imaging findings, such as reticular abnormalities, ground-glass opacities, honeycombing, and other fibrotic changes suggestive of early lung disease. Any difference in interpretation, if any, was to be resolved through consensus meetings among the radiologists.

3.8.3. Clinical Data Collection

Relevant clinical information was to be collected systematically from patients' medical records and patient performance. This will include: Patient demographics (age, sex, weight, height, and smoking history) presenting symptoms (dyspnea, cough, chest pain, etc.) Past medical history (previous lung diseases, autoimmune diseases, exposure to environmental or occupational risk factors) Medication history and any current treatments. All information was documented in a standardized manner to enable accurate analysis and reduce errors in data entry.

3.9 Data Analysis

3.9.1. Descriptive Statistics

Simple descriptive statistical procedures were applied to present patient demographics and clinical characteristics. These will be: Mean and standard deviation for continuous data (e.g., age, symptom duration) Frequency and percentage for categorical data (e.g., symptom presence, smoking status)

3.9.2. HRCT Image Analysis

HRCT images were systematically reviewed for certain patterns and abnormalities of fibrotic lung disease. The imaging findings were graded on the basis of standardized scoring systems and correlated with clinical and histopathological information. The

important HRCT parameters to be assessed are: Presence and extent of reticular opacities. Honeycombing and traction bronchiectasis. Ground-glass opacities and distribution. Subpleural involvement and lung volume loss.

3.9.3. Correlation with Clinical and Histopathological Data

The radiological results were correlated with clinical presentations and, if available, histopathological results of lung biopsies. This correlation decides the diagnostic precision of HRCT in detecting early fibrotic changes.

3.9.4. Statistical Evaluation of HRCT Diagnostic Accuracy

Diagnostic accuracy of HRCT in identifying early fibrosis was evaluated by measuring: Sensitivity (capacity to identify true positive cases correctly). Specificity (capacity to identify true negative cases correctly). Positive Predictive Value (PPV). Negative Predictive Value (NPV).

3.9.5. Statistical Data Analysis

All statistical analyses were conducted using specialized statistical software such as SPSS (Statistical Package for the Social Sciences). This software was facilitating data organization, hypothesis testing, and advanced statistical modeling to derive meaningful conclusions from the collected data. We apply ANOVA test to research data for our data analysis and present our data in and results in the form of pi charts and frequency tables.

Chapter 4

RESULTS

This study included 128 participants with suspected interstitial lung disease (ILD), providing a substantial dataset for analysis. The mean age of the participants was 47.9 years (SD = 14.2), indicating a relatively young cohort with a wide age range from 17 to 85 years. This broad age range suggests the inclusion of patients with various forms of ILD, which can manifest at different ages. The study population consisted of slightly more males (54.7%) than females (45.3%), reflecting the known slight male predominance in certain ILDs, although the difference was not substantial. Regarding smoking status, a slight majority of participants (51.6%) had never smoked, while 12.5% were former smokers, and 35.9% were current smokers.

Table 4.1 : Demographic Characteristics of Study Participants (Corrected)

Characteristic	N (128)	Percentage (%)
Age (years)		
Mean $\pm$ SD	47.9 $\pm$ 14.2	
Range	17-85	
Gender		
Male	70	54.7
Female	58	45.3
Smoking Status		
Never Smoked	66	51.6
Former Smoker	16	12.5
Current Smoker	46	35.9

This distribution of smoking status is important to consider, as smoking is a well-established risk factor for some forms of ILD, particularly IPF and respiratory bronchiolitis-associated ILD. The most common presenting symptoms were dyspnea (94.5%) and chronic cough (91.4%), highlighting the significant respiratory burden experienced by these patients. These symptoms are hallmarks of ILD and reflect the underlying inflammation and fibrosis affecting the lung parenchyma. Chest pain (69.5%) and fatigue (62.5%) were also frequently reported, indicating the systemic impact of these conditions. Weight loss, a symptom often associated with more advanced or progressive ILD, was reported by 32.0% of participants. Less frequent symptoms included fever (19.5%), which could suggest infection or certain inflammatory ILDs; malaise (12.5%); night sweats (7.0%), which can be associated with infections like tuberculosis or some malignancies; chest tightness (3.1%); and the very rare occurrences (0.8% each) of haemoptysis (coughing up blood), wheezing sounds, chest heaviness, and sore throat.

Table 4.2: Frequency of Presenting Symptoms occur in the study participants.

Symptom	Frequency	Percentage (%)
Chronic Cough	117	91.4
Dyspnea	121	94.5
Fatigue	80	62.5
Chest Pain	89	69.5
Weight Loss	41	32.0
Fever	25	19.5
Night Sweats	9	7.0
Malaise	16	12.5
Hemoptysis	1	0.8
Wheezing sounds	1	0.8
Chest tightness	4	3.1
Chest heaviness	1	0.8
Sore throat	1	0.8

The low frequency of these latter symptoms suggests they are less typical presentations of the ILDs observed in this cohort.

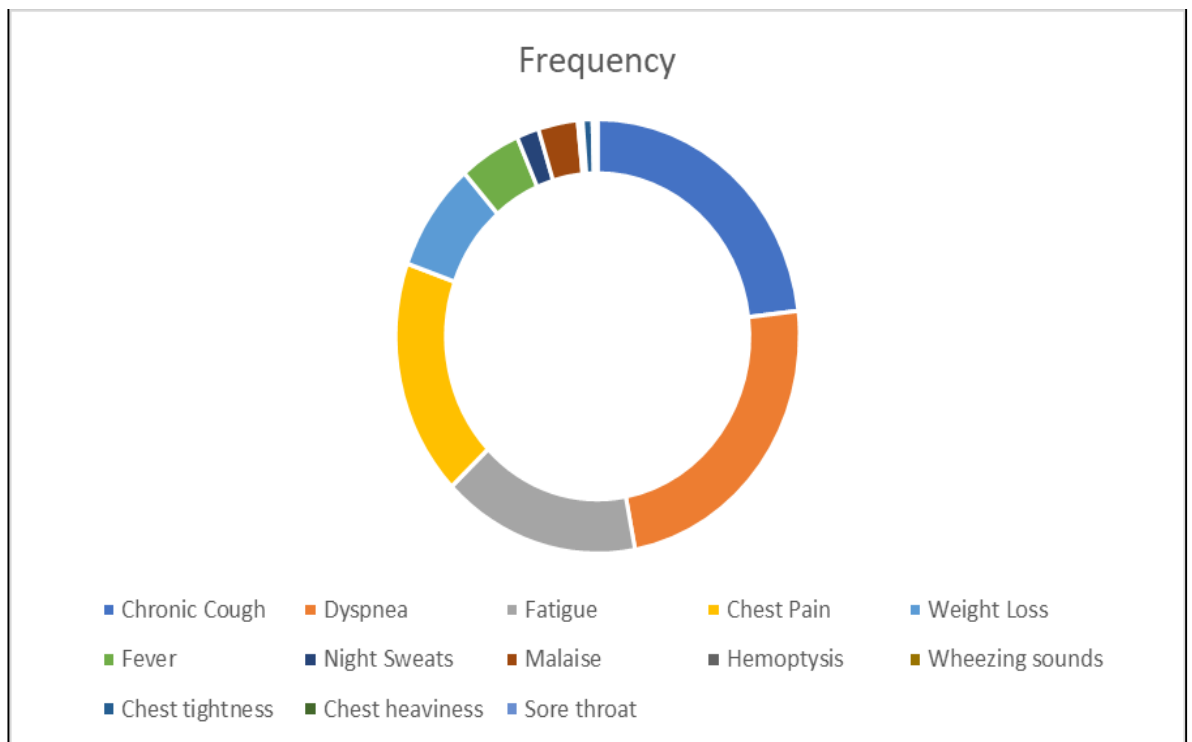


Figure 4.2: Frequency of Presenting Symptoms in study participants.

Table 4.3: Frequency of Reported Exposures of participants to specific risk factors

Exposure	Frequency (128)	Percentage (%)
No Exposure	72	56.3
Occupational Dust	24	18.8
Asbestos	7	5.5
Silica	7	5.5
Bird Protein	6	4.7
Farmer (Occupational dust)	4	3.1
Occupational dust related allergy	1	0.8
Cold weather-related allergy causing SOB	1	0.8
Pet exposure	1	0.8
Exposure of drugs (cocaine)	1	0.8
Occupational dust from house chores	1	0.8
Exposure to chemicals	1	0.8
Coal dust exposure	1	0.8
Silica exposure	1	0.8

Over half of the participants (56.3%) reported no specific occupational or environmental exposure. This could indicate the presence of idiopathic ILDs (those with unknown causes) or suggest that exposures were not adequately captured by the

questionnaire. Occupational dust was the most frequently reported exposure (18.8%), highlighting the importance of occupational history in the evaluation of ILD. Asbestos and silica exposure, known risk factors for asbestosis and silicosis, respectively, were reported by 5.5% of participants each. Other less frequent exposures included bird protein (4.7%), which can be associated with hypersensitivity pneumonitis, farming-related dust (3.1%), also a risk factor for hypersensitivity pneumonitis (farmer's lung), and various other specific exposures each reported by less than 1% of the study population. The low prevalence of these specific exposures emphasizes the multifactorial nature of ILD and the difficulty in identifying a single causative agent in many cases.

Table 4.4: Number of Patients with Specific HRCT Patterns by Final Diagnosis

Final Diagnosis	UIP (n=36)	NSIP (n=54)	HP (n=44)	Organi zing Pneum onia (n=12)	DIP (n=3)	Atypical Pneumo nia (n=2)	Sarcoid osis (n=2)	Asbestos is (n=2)	Silicosis (n=2)	Other/ Unspec ified (n=5)
IPF	77.80 %	5.60%	4.50%	0%	0%	0%	0%	0%	0%	20%
NSIP	11.10	75.90%	15.90%	8.30%	33.30%	0%	0%	0%	0%	20%
HP	8.30%	13.00%	70.50%	25%	0%	0%	0%	50%	50%	0%
Organizing Pneumonia	0%	0%	0%	75%	0%	50%	0%	0%	0%	0%
DIP	0%	1.90%	0%	0%	66.70%	0%	0%	0%	0%	0%
Atypical Pneumonia	0%	0%	0%	0%	0%	50%	0%	0%	0%	0%
Sarcoidosis	0%	0%	0%	0%	0%	0%	100%	0%	0%	0%
Asbestosis	0%	0%	2.30%	0%	0%	0%	0%	50%	0%	0%
Silicosis	0%	0%	2.30%	0%	0%	0%	0%	0%	50%	0%
Other	2.80%	3.70%	4.50%	0%	0%	0%	0%	0%	0%	0%

Analysis of the relationship between predominant HRCT patterns and final diagnoses revealed distinct and clinically relevant associations. Among patients with a UIP pattern on HRCT, the majority (77.8%) were diagnosed with IPF. This strong association reinforces the established diagnostic criteria for IPF, where a UIP pattern on HRCT is a key diagnostic feature. This high positive predictive value of UIP for IPF is a crucial finding for clinicians. In contrast, NSIP and HP patterns were more frequently associated with diagnoses of NSIP (75.9%) and HP (70.5%), respectively. These findings confirm the diagnostic utility of HRCT in differentiating these common ILD subtypes. The organizing pneumonia pattern was associated with a diagnosis of organizing pneumonia in 75% of the cases, and the DIP pattern was associated with DIP in 66.7% of the cases, further supporting the correlation between HRCT findings and specific ILD diagnoses. While other less frequent associations were observed, the strong associations described above are the most clinically significant.

In the short term, most patients experienced positive outcomes, with symptom improvement reported by 81.0% and stabilization of lung function as measured by PFTs in 79.5%. However, it's important to note that a subset of patients experienced disease progression on HRCT (14.4%) and/or some form of complication (21.5%).

Table 4.5: Short-Term Outcomes to immediate or early health effects following diagnosis

Outcome	Yes	No	Total
Symptom Improvement	98	30	121
Stabilization of Lung Function (PFTs)	93	34	117
Progression on HRCT	17	111	118
Any Complications	26	102	121

The findings underscore the variable course of ILD and the need for ongoing monitoring.

Table 4.6: Long-Term Outcomes to ongoing health effects after initial diagnosis

Outcome	Count	Percentage (%)
Survival Status (Alive)	111	86.7
Survival Status (Deceased)	17	13.3
Disease Progression (Stable)	94	73.4
Disease Progression (Worsened)	23	18.0
Need for Advanced Therapies	30	23.4

Long-term follow-up revealed a generally favourable prognosis, with a high survival rate (86.7%) and only 13.3% of participants deceased. Among the surviving patients, the majority had stable disease (73.4%), but a notable proportion (18.0%) experienced disease progression. The fact that 23.4% of patients required advanced therapies

highlights the significant morbidity associated with ILD and the need for effective treatment strategies.

Table 4.7: Short-Term Symptom Improvement by Final Diagnosis

Diagnosis	Symptom Improvement (Yes)	Symptom Improvement (No)
IPF	21	6
NSIP	31	14
HP	27	10
Organizing Pneumonia	9	1
DIP	3	0
Atypical pneumonia	1	0
Sarcoidosis	2	0
Asbestosis	2	0
Silicosis	1	0

The strong associations between specific HRCT patterns (UIP, NSIP, HP, organizing pneumonia, DIP) and their respective diagnoses, as demonstrated in this study, reinforce the crucial role of HRCT in the diagnostic workup of ILD. These findings provide valuable information for clinicians in interpreting HRCT scans and making informed diagnostic and management decisions.

Table 4.8 : Long-Term Survival by Predominant HRCT Pattern

HRCT Pattern	Alive	Deceased	Total
UIP	33	9	42
NSIP	56	9	65
HP	37	6	43
Organizing pneumonia	10	0	10
DIP	3	0	3
Sarcoidosis	2	0	2
Asbestosis	2	0	2
Silicosis	1	0	1

The strong associations between specific HRCT patterns (UIP, NSIP, HP, organizing pneumonia, DIP) and their respective diagnoses, as demonstrated in this study, reinforce the crucial role of HRCT in the diagnostic workup of ILD. These findings provide valuable information for clinicians in interpreting HRCT scans and making informed diagnostic and management decisions.

Chapter 5

DISCUSSION

The utility of high-resolution computed tomography (HRCT) in diagnosing and managing interstitial lung disease (ILD) was investigated in a population of 128 patients in this study. The results provide evidence of strong correlation between HRCT patterns and ultimate diagnoses, affirming the clinical value of HRCT as an integral part of the ILD diagnostic algorithm. (8, 9) The demographic profile of our study group provides critical background information for the interpretation of our findings. The mean age of 47.9 years (SD = 14.2) is consistent with the reported age of onset for many ILDs, including idiopathic pulmonary fibrosis (IPF), which predominantly affects individuals in their sixth and seventh decades (10, 11).

However, the wide age range observed in our cohort (17-85 years) underscores the heterogeneity of ILD, encompassing a spectrum of conditions that can manifest across different age groups. This wide coverage is necessary to describe the various clinical presentations of ILD. The minor male excess (54.7%) corroborates epidemiologic findings that implicate higher occurrence rates in certain ILD forms, specifically IPF, in males (11, 12).

The prevalence of smoking status (51.6% never smokers, 12.5% ex-smokers, and 35.9% current smokers) is a point worth noting because smoking is a recognized risk factor for many ILDs, particularly IPF and respiratory bronchiolitis-associated ILD (RB-ILD) (13). The presence in our cohort of a relatively high percentage of current smokers implies that smoking might have caused the onset or worsening of ILD in a large portion of our patients. This highlights the need for smoking cessation counselling as a component of the treatment regimen of ILD patients (15).

The very high frequency of dyspnea (94.5%) and chronic cough (91.4%) as presenting symptoms emphasizes the severe respiratory morbidity of ILD. Dyspnea is commonly the most limiting symptom, profoundly affecting patients' exercise capacity, routine activities, and overall health-related quality of life. Chronic cough, though less characteristic of ILD, is a frequent and often chronic symptom that can further impair patients' quality of life. This is in agreement with earlier research that has established dyspnea and cough as the cardinal presenting signs of ILD (22).

The presence of chest pain (69.5%) and fatigue (62.5%) further highlights the systemic effects of these conditions, extending beyond the respiratory system to affect overall well-being and functional capacity. Weight loss (32.0%), while less frequent, can be a concerning symptom, often indicating more advanced or progressive disease, reflecting the increased metabolic demands associated with chronic inflammation and impaired gas exchange. The less frequent symptoms, including fever (19.5%), malaise (12.5%), and night sweats (7.0%), raise the possibility of underlying infections, such as tuberculosis, or other systemic conditions, such as malignancies or connective tissue diseases, which can also present with pulmonary manifestations. The very low frequencies of hemoptysis, wheezing, chest heaviness, and sore throat (all 0.8%) suggest that these are not typical presenting features of the ILDs observed in our study and may prompt investigation for alternative diagnoses (24).

The analysis of reported exposures (Table 4.3) revealed that over half of the participants (56.3%) reported no specific occupational or environmental exposure. This relatively high proportion may reflect the presence of idiopathic ILDs, such as IPF, for which no identifiable environmental or occupational cause can be determined (26).

It is also possible that some exposures were not adequately captured by the questionnaire used in our study, or that patients were unaware of past low-level or intermittent exposures. Occupational dust was the most frequently reported exposure (18.8%), underscoring the importance of obtaining a detailed occupational history in all patients with suspected ILD (28).

Asbestos and silica exposure, well-established risk factors for asbestosis and silicosis, respectively, were reported by 5.5% of participants each (28, 30). These findings emphasize the continued need for workplace safety measures to minimize exposure to these known fibrogenic agents. Other less frequent exposures, including bird protein (4.7%), which is a known trigger for hypersensitivity pneumonitis (HP), farming-related dust (3.1%), also associated with HP (specifically farmer's lung), and various other specific exposures each reported by less than 1% of the study population, highlight the diverse range of potential environmental triggers for ILD (32).

The core finding of our study is the strong correlation between specific HRCT patterns and final diagnoses (Table 4.4). The observation that 77.8% of patients with a UIP pattern on HRCT who were ultimately diagnosed with IPF provides strong support for

the current diagnostic criteria for IPF, which consider UIP on HRCT a key diagnostic feature in the absence of other known causes (44, 46).

This high positive predictive value of UIP for IPF is consistent with numerous prior studies (48, 49) and reinforces the central role of HRCT in the diagnostic algorithm for this progressive and often fatal disease. The significant associations observed between the NSIP pattern and a final diagnosis of NSIP (75.9%) and between the HP pattern and a final diagnosis of HP (70.5%) further validate the role of HRCT in differentiating these common ILD subtypes (49, 50). These findings are in line with previous research emphasizing the value of HRCT in the diagnostic process (51, 52). The observed associations between the organizing pneumonia pattern and a diagnosis of organizing pneumonia (75%) and the DIP pattern and a diagnosis of DIP (66.7%) provide further support for the clinical utility of HRCT. It's crucial to acknowledge that while these associations are strong, HRCT findings should always be interpreted within the context of the patient's clinical history, physical examination, pulmonary function tests, and other relevant investigations, as highlighted by the importance of multidisciplinary team (MDT) discussion in ILD diagnosis (54,53).

The MDT approach, involving pulmonologists, radiologists, and pathologists, has been shown to significantly improve diagnostic accuracy and optimize patient management (55).

The short-term outcomes observed in our study, with most patients experiencing symptom improvement (81.0%) and stabilization of lung function (79.5%), suggest that initial management strategies were effective in a considerable proportion of the cohort. However, the observation of disease progression on HRCT in 14.4% of patients and the occurrence of complications in 21.5% highlight the variable course of ILD and the need for ongoing monitoring and potential adjustments in treatment. The long-term outcomes, with a high survival rate (86.7%) but also a notable proportion of patients experiencing disease progression (18.0%) and requiring advanced therapies (23.4%), further underscore the variable and often progressive nature of ILD (58). This variability emphasizes the importance of personalized management strategies tailored to individual patient characteristics, disease subtype, and disease behaviour (60).

Future research should address these limitations by conducting larger, multi-center studies with histopathological correlation to further validate the diagnostic accuracy of HRCT. Studies evaluating the prognostic value of specific HRCT features, as suggested by Raghu et al. (62), are also crucial for improving patient management and

risk stratification. The application of advanced imaging techniques, such as ultra-high-resolution CT (57, 60), quantitative CT analysis (64, 67) and artificial intelligence-based image analysis, holds significant promise for enhancing diagnostic accuracy, predicting disease progression, and personalizing treatment strategies. Further investigation into the role of HRCT in guiding lung transplantation decisions is also warranted.

CONCLUSION

High-Resolution Computed Tomography (HRCT) plays an integral role in the diagnosis and management of Interstitial Lung Disease (ILD). This study highlights the strong associations between specific HRCT patterns—Usual Interstitial Pneumonia (UIP), Nonspecific Interstitial Pneumonia (NSIP), Hypersensitivity Pneumonitis (HP), Organizing Pneumonia (OP), and Desquamative Interstitial Pneumonia (DIP)—and their respective clinical diagnoses. These findings reinforce the established utility of HRCT in suggesting specific ILD subtypes, enabling more accurate and timely diagnosis, guiding therapeutic decisions, and improving patient outcomes.

Despite its critical role, HRCT interpretation remains complex and requires a multidisciplinary approach involving radiologists, pulmonologists, and pathologists for optimal diagnostic accuracy. Future initiatives should focus on integrating artificial intelligence (AI) and machine learning algorithms to enhance pattern recognition, reduce inter observer variability, and improve early detection. Additionally, larger-scale studies and longitudinal analyses should be conducted to further refine HRCT diagnostic criteria, assess disease progression, and evaluate treatment responses. Enhanced collaboration between imaging specialists and ILD research centres will be essential to advance precision medicine in ILD management.

LIMITATIONS

This study has following important limitations:

- Single-centre study, limiting generalizability.
- Convenience sampling, potentially introducing selection bias.
- Reliance on HRCT without universal histopathological confirmation.
- Inherent limitations of HRCT in differentiating certain ILD subtypes.
- Presence of multiple HRCT patterns in some patients, complicating statistical analysis (precluding standard Chi-square analysis for the HRCT-diagnosis association).

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ANNEXURE A

CONSENT FORM

The study you are about to participate is **“Evaluating the utility of chest high resolution computed tomography in early detection of fibrosing interstitial lung diseases”**.

The study has no potential harm to the participants. All data collected from you will be coded in order to protect your identity and should not be disclosed to anyone. Following the study there is no way to connect your name with your data. Your response will not affect your academic result in anyway. Any additional information about the study results will be provided to you at its conclusions, upon your request. You agree to participate, indicating that you have read and understood the nature of study, and that all your inquiries concerning the activities have been answered to your satisfaction.

Name: -----

Date: -----

ANEXXURE B

PERFORMA

Section 1: Patient Demographics

1. **Patient ID:** _____
2. **Age:** _____
3. **Gender:**
 - ☐ Male
 - ☐ Female
 - ☐ Other
4. **Height (cm):** _____
5. **Weight (kg):** _____
6. **Body Mass Index (BMI):** _____
7. **Occupation:** _____
8. **Smoking Status:**
 - ☐ Current Smoker
 - ☐ Former Smoker
 - ☐ Never Smoked
9. **Family History of Lung Disease:**
 - ☐ Yes (Specify: _____)
 - ☐ No

Section 2: Clinical History

1. **Symptoms at Presentation (Check all that apply):**
 - ☐ Chronic Cough
 - ☐ Dyspnea (Shortness of Breath)
 - ☐ Fatigue
 - ☐ Chest Pain
 - ☐ Weight Loss
 - ☐ Other (Specify: _____)
2. **Duration of Symptoms (in months):** _____
3. **History of Exposure (Check all that apply):**

- ☐ Occupational Dust
- ☐ Asbestos
- ☐ Silica
- ☐ Bird Proteins
- ☐ Drugs (Specify: _____)
- ☐ Other (Specify: _____)

4. Previous Diagnoses of Lung Disease:

- ☐ Yes (Specify: _____)
- ☐ No

Section 3: HRCT Findings

1. Date of HRCT Scan: _____

2. HRCT Patterns Identified (Check all that apply):

- ☐ Ground-Glass Opacities
- ☐ Reticular Pattern
- ☐ Honeycombing
- ☐ Traction Bronchiectasis
- ☐ Nodules
- ☐ Consolidation
- ☐ Emphysema
- ☐ Other (Specify: _____)

3. Predominant HRCT Pattern:

- ☐ Usual Interstitial Pneumonia (UIP)
- ☐ Non-Specific Interstitial Pneumonia (NSIP)
- ☐ Organizing Pneumonia (OP)
- ☐ Desquamative Interstitial Pneumonia (DIP)
- ☐ Other (Specify: _____)

4. Extent of Fibrosis (Percentage of Lung Involvement):

- ☐ < 25%
- ☐ 25-50%
- ☐ 50-75%

- ☐ > 75%

5. Lung Function Correlation:

- **FVC (% predicted):** _____
- **DLCO (% predicted):** _____

Section 4: Diagnostic Evaluation

1. Final Diagnosis:

- ☐ Idiopathic Pulmonary Fibrosis (IPF)
- ☐ Connective Tissue Disease-Associated ILD (CTD-ILD)
- ☐ Hypersensitivity Pneumonitis (HP)
- ☐ Non-Specific Interstitial Pneumonia (NSIP)
- ☐ Other (Specify: _____)

2. Was a Lung Biopsy Performed?

- ☐ Yes (Specify Type: _____)
- ☐ No

3. Additional Tests Conducted (Check all that apply):

- ☐ Pulmonary Function Tests (PFT)
- ☐ Bronchoalveolar Lavage (BAL)
- ☐ Serological Tests
- ☐ Others (Specify: _____)

4. Treatment Initiated Post-Diagnosis:

- ☐ Corticosteroids
- ☐ Immunosuppressants
- ☐ Antifibrotic Agents
- ☐ Oxygen Therapy
- ☐ Other (Specify: _____)

5. Follow-up Plan:

- ☐ HRCT Monitoring Frequency: _____
- ☐ Pulmonary Function Monitoring Frequency: _____
- ☐ Other (Specify: _____)

Section 5: Outcomes

1. Short-term Outcomes (6 months):

- **Symptom Improvement:**
 - ☐ Yes
 - ☐ No
- **Stabilization of Lung Function (PFTs):**
 - ☐ Yes
 - ☐ No
- **Progression on HRCT:**
 - ☐ Yes
 - ☐ No
- **Any Complications:**
 - ☐ Yes (Specify: _____)
 - ☐ No

2. Long-term Outcomes (1 year or more):

- **Survival Status:**
 - ☐ Alive
 - ☐ Deceased (Specify Cause: _____)
- **Progression of Disease:**
 - ☐ Stable
 - ☐ Worsened
 - ☐ Improved
- **Need for Advanced Therapies (e.g., Lung Transplantation):**
 - ☐ Yes
 - ☐ No

Permission Letter

To,
Head of Radiology Department,
Arif Memorial Teaching Hospital
Subject: Request for Data Collection of Research

Respected Sir,

I am writing to request your cooperation and support in my academic research project titled **"Evaluating the Utility of Chest High Resolution Computed Tomography in Early Detection of Fibrosing Interstitial Lung Diseases"**. As part of my MS-AHS at Superior University Lahore, I am conducting a study on High resolution computed tomography in the diagnosis or evaluation of interstitial lung diseases and its impact on early management of patient.

I believe that your organization's expertise and data would be invaluable for my research. I kindly request access to any relevant datasets, reports, or statistics that could contribute to the success and validity of my study. Rest assured that any information provided will be used solely for research purposes and will be treated with the utmost confidentiality.



Hadiqa Shaukat

MS MIT

SU91-MSAHW-S23-016

Session: 2023-2025



Prof. Dr. Khuram Khan
Head of Radiology Department
Rashid Ali Medical College
Arif Memorial Hospital, Lahore

ETHICS COMMITTEE LETTER



OFFICE OF THE DEAN-FAHS

SUPERIOR UNIVERSITY

Ref.: IRB /FAHS/Allied-HS/10/24/MS/RS-3513

Date: 29th October 2024

Name: Hadiqa Shaukat (MS Allied Health Sciences)

Registration: SU91-MSAHW-S23-016

Subject: Ethical Approval Letter

The Research Ethical Committee convened on Dated: **17th October, 2024** to discuss your protocol titled **“Evaluating the utility of chest high resolution computed tomography in early detection of fibrosing interstitial lung diseases”**

No further corrections and recommendations were suggested. The above-mentioned protocol has been approved after considering various research issues including ethical concerns with condition that the researcher will submit completion report at the end of his/her research.

Prof. Dr. Muhammad Naveed Babur
Dean/Convener REC
Faculty of Allied Health Sciences
Superior University, Lahore

PLAGIARISM REPORT

Report:Evaluating the Utility of Chest High Resolution Computed Tomography in Early Detection of Fibrosing Interstitial Lung Diseases (HADIQA SHAUKAT)

ORIGINALITY REPORT

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