Trends in Medical and Biological Sciences

Journal homepage: https://scholarsacademiaworld.com/index.php/TMBS

High-Resolution CT Characterization of Radiologic Phenotypes among COPD Patients in Sindh, Pakistan

Shazma Tahseen [1]
[1] Department of Information Technology, Liaquat University of Medical and Health Sciences (LUMHS), Jamshoro, Pakistan
shazma.tehsen@lumhs.edu.pk

ARTICLE INFO

Received:
February 1, 2025
Revised:
February 16, 2025
Accepted:
March 4, 2025
Available Online:
March 25, 2025

Keywords:
COPD, HRCT, emphysema, chronic bronchitis, phenotypes, Pakistan

Corresponding Author:
Shazma Tahseen
shazma.tehsen@lumhs.edu.pk

ABSTRACT

Background: Chronic obstructive pulmonary disease (COPD) is a leading cause of morbidity and mortality worldwide, particularly in low- and middle-income countries (LMICs), where environmental exposures and limited healthcare access exacerbate disease burden [1–3,4]. COPD exhibits marked structural and clinical heterogeneity, with emphysema and chronic bronchitis as its principal phenotypes. High-resolution computed tomography (HRCT) offers detailed visualization of structural lung changes, aiding phenotypic characterization and prognosis [10–13].

Objective: To characterize radiologic phenotypes of COPD among patients in Sindh, Pakistan, and examine their distribution across different age groups using HRCT in conjunction with clinical assessment, spirometry, and chest radiography.

Methods: A cross-sectional observational study was conducted at the Department of Respiratory Medicine, NRIGH, Sindh, Pakistan, enrolling 90 consecutive patients aged 35–75 years with confirmed COPD. Patients underwent detailed clinical evaluation, pulmonary function testing, chest radiography, and HRCT imaging. HRCT scans were analyzed to identify emphysema subtypes, small airway disease, and other structural abnormalities.

Age-related differences in phenotypes were assessed using Z-tests for proportions.

Results: The mean age of participants was 54.8 years, with 75.6% aged 41–60 years. Predominant emphysema was observed in 56.7% of patients, chronic bronchitis in 36.7%, and mixed patterns in 6.6%. Chronic bronchitis was more frequent in patients ≤50 years, whereas emphysema predominated in those >50 years ($p < 0.05$). HRCT revealed centrilobular emphysema (46.7%), small airway disease (40.0%), panacinar (16.7%) and paraseptal emphysema (8.9%), with occasional ground-glass opacities, interstitial lung disease, and mass lesions. Spirometry confirmed persistent airflow limitation with minimal bronchodilator reversibility, and radiographic findings correlated with structural phenotypes.

Conclusion: COPD in this cohort demonstrates significant structural and phenotypic heterogeneity, with emphysema predominating in older adults and chronic bronchitis in younger patients. HRCT is a valuable adjunct to spirometry and radiography for accurate phenotypic characterization, early detection of comorbidities, and individualized management. These findings highlight the importance of imaging-based phenotyping to inform clinical decision-making in resource-limited LMIC settings.

Introduction

COPD is a major cause of morbidity and mortality among the chronic respiratory diseases (CRDs) in the world. Even though CRDs, including asthma, tuberculosis, and pneumonia, are considered most significant health issues, COPD has a progressive progression and a significant amount of burden, particularly in low- and middle-income countries (LMICs) [1,2]. WHO statistics also indicate that about 90 percent of deaths caused by COPD among people below the age of 70 years in LMICs [1].

Pathophysiologically, COPD is typified by a lasting and, to a large extent, incurable airflow constriction, which is caused by chronic airway inflammation and airway pathology, as well as airway tissue destruction [1]. The key factors that contribute to risk are tobacco smoking, household air pollution associated with the use of bio-mass fuel and work-related exposures to dust and chemical substances [3,1]. Symptoms of the chronic cough, sputum production, and progressive dyspnea are common clinical manifestations of patients who do not fully improve with the use of bronchodilator therapy [1].

COPD remains a growing burden on the global level. The 2021 Global Burden of Disease (GBD) report approximated prevalent cases of COPD to be 213 million with almost 3.72 million deaths in the same year due to the disease [4]. These statistics underscore the high rates of prevalence as well as the enormous health and economic burden of COPD in the world [4]. According to the projections made in the modeling studies, the COPD cases are projected to increase to about 600 million by 2050, with the LMICs and women disproportionately increased [5].

COPD is a major but little known public health issue in Pakistan. The estimates of national prevalence indicate that approximately 2 percent of adults are infected, though very many cases are not diagnosed because of the lack of access to spirometry and the lack of awareness [6,7]. In the Pakistani case, the problem of risk factors is aggravated by extensive biomass fuel use, the high prevalence of tobacco use, and rising levels of industrial pollution, particularly in those provinces of the country that rapidly urbanize, such as Sindh [8,9].

COPD is characterized by a high level of structural heterogeneity in addition to clinical symptoms and spirometric measurements. Its two significant pathological components, which include chronic bronchitis and emphysema, have different manifestations in patients. Long-standing productive cough is a clinical characteristic of chronic bronchitis and final destruction of the alveolar walls resulting to air trapping and loss of gaseous exchange surface, is a characteristic of emphysema. Emphysema is further divided into centrilobular, panacinar and paraseptal subtypes, based on how the alveoli are involved. Other structural alterations are small airway fibrosis, mucous hypersecretion, airways wall remodeling, ventilation-perfusion mismatch, and remodeling of the pulmonary vascularity [10,11].

High-resolution computed tomography (HRCT) is very important in the dissection of this structural complexity. HRCT is able to identify and measure the subtypes of emphysema, airway wall thickening, and mosaic attenuation indicative of small airway disease, ground-glass opacities and incidental findings (nodules or masses) unlike spirometry or plain chest radiography [12,13]. Notably, imaging-defined phenotypes based on HRCT have proven to be prognostic: mixed phenotypes of emphysema and airway disease have been linked to increased exacerbations, faster progression of lung function, and increased comorbidity burden [11,10].

Although HRCT-based phenotyping of COPD has a clinical and prognostic value, the HRCT-based phenotyping of COPD in Pakistan, especially in Sindh, with both a high environmental risk and a paucity of imaging studies, is underresearched. The definition of radiologic phenotypes in this group would provide important information about the heterogeneity of diseases, help treat them more accurately, and identify complications (including pulmonary hypertension or lung cancer) at an earlier stage. Thus, the proposed research is expected to employ HRCT to establish and measure radiologic phenotypes in COPD patients in Sindh, and identify how these phenotypes change with age, thus guiding more specific clinical interventions within a resource-limited environment.

Method and Materials

This observational cross-sectional study was carried out on a one-year follow up period within the Department of Respiratory Medicine, NRIGH, Sindh, Pakistan. There were a total of 90 patients, both genders diagnosed with chronic obstructive pulmonary disease (COPD) that were recruited consecutively [18].

The inclusion criteria included patients between the ages of 35 and 75 with a known diagnosis of COPD according to spirometric-defined criteria, having a stable condition without any acute exacerbation within the last six weeks, and being willing to sign informed written consent [18,19]. The exclusion criteria was comprised of comorbid cardiovascular conditions like ischemic heart disease, and presence of respiratory conditions like active tuberculosis, post-tuberculosis sequelae, bronchiectasis, or interstitial lung disease [7,8].

Each participant was questioned in a detailed clinical evaluation (medical history, physical examination, and other lab tests) [18,20]. All patients underwent testing of the pulmonary functioning (PFT) and COPD was diagnosed based on Global Initiative for Chronic Obstructive Lung Disease (GOLD): the ratio of post-bronchodilator FEV1 and FVC less

than 0.7, with the limited reversibility defined as less than 200 mL or less than 12 percent change of the baseline following the administration of bronchodilators [18,21,22].

All patients were subjected to initial imaging (Standard chest radiography (CXR)) imaging. Individuals whose radiographic features were in line with COPD and did not show any other pulmonary pathology were subjected to high-resolution computed tomography (HRCT) of the chest [12,13]. Two-dimensional echocardiography (2D-ECHO) was used in situations of clinical suspicion or X-ray evidence of pulmonary hypertension [12]. Radiographic alterations that were commonly seen on CXR were hyperinflation, flattened diaphragm, bullous alterations, a tubular cardiac silhouette, an augmented retrosternal air space and tapering of the pulmonary vasculature [18,23].

Analysis of HRCT scans was performed to describe the structural changes in the lung and identify radiologic phenotypes. The subtypes of emphysema, small airway disease and ground-glass opacities (GGOs) were key HRCT findings. GGOs, the areas of higher lung density where the underlying bronchial and vascular systems can be observed, can signal the occurrence of inflammatory or interstitial alterations in the early stages, partial filling of the alveoli, or both interstitial pathology [16,17]. The results of HRCT were essential clues to COPD phenotypic expression that allows distinguishing between major emphysematous and airway disease patterns and has prognosis and individual management implications [10,11,12].

The demographic and imaging data were analyzed in percentages. A proportion Z-test was used to test the difference in ages between the patients with predominant chronic bronchitis and predominant emphysema. It is important to study the relative role of these phenotypes because chronic bronchitis, emphysema do not share pathophysiology and clinical manifestation and radiologic presentation which directly determines the choice of specific therapeutic approaches [10,11,18].

Results

This cross-sectional observational study was conducted on 90 sequentially recruited male and female patients with a diagnosis of chronic obstructive pulmonary disease (COPD) at the Department of Respiratory Medicine, NRIGH, Sindh, Pakistan [18]. The participants were aged between 35 and 75 years, with an average age of 54.8 years. Most patients fell within the age range of 41–60 years [6,9]. Depending on the clinical examination and HRCT, patients were categorised into three main phenotypes: emphysema, chronic bronchitis, and mixed pattern [10,11,12].

Table 1: Age Distribution of COPD Patients (n = 90)

Age Group (Years)	No. of Patients	Percentage (%)
35–40	6	6.7
41–50	36	40.0
51–60	32	35.6
61–70	14	15.6
71–75	2	2.2
Total	90	100.0

Interpretation:
The majority of the patients (75.6) fell into the category of 41-60, so middle-aged adults were the most vulnerable group to COPD in this group. This is similar to the findings of global and regional studies that revealed that COPD is most common in the fifth and sixth decades of life because of cumulative smoking and environmental pollution exposure [3,9].

Table 2: Distribution of COPD Phenotypes

Phenotype	No. of Patients	Percentage (%)
Predominant Emphysema	51	56.7
Predominant Chronic Bronchitis	33	36.7
Mixed Pattern	6	6.6
Total	90	100.0

Interpretation:
The most common phenotype was predominant emphysema, and the subsequent one was chronic bronchitis. A few mixed patterns were observed. This is indicative of the progressive aspect of COPD, where the airway-predominant disease can develop into emphysema with age and extended exposure to noxious particles [14,18].

Table 3: Age Distribution in Chronic Bronchitis Patients

Age Group (Years)	No. of Patients	Percentage (%)
≤50	22	66.7
>50	11	33.3
Total	33	100.0

Table 4: Age Distribution in Emphysema Patients

Age Group (Years)	No. of Patients	Percentage (%)
≤50	18	35.3
>50	33	64.7
Total	51	100.0

Interpretation (Tables 3 & 4)

Younger patients (≤50 years) had chronic bronchitis and older patients (>50 years) had emphysema. Statistical significance was confirmed using the Z-test ($p < 0.05$). This finding has shown an age-associated distribution of COPD phenotypes, which is in line with the literature outlining chronic bronchitis as an earlier airway-based disease and emphysema as a later parenchymal-based disease [15,18].

Table 5: HRCT Findings in COPD Patients

HRCT Finding	No. of Patients	Percentage (%)
Centrilobular Emphysema	42	46.7
Panacinar Emphysema	15	16.7
Paraseptal Emphysema	8	8.9
Small Airway Disease (BWT + Mosaic)	36	40.0
Ground-Glass Opacities (GGO)	6	6.7
Interstitial Lung Disease (ILD)	3	3.3
Mass Lesions	3	3.3

Interpretation:
Uncommon observations, such as GGOs, ILD, and mass lesions, indicate the usefulness of HRCT to identify comorbid or overlapping pulmonary diseases, which can influence treatment and prognosis [16,17].

Table 6: Spirometric and Radiological Correlation

Parameter	Mean / Frequency
Post-BD FEV_1/FVC	< 0.7
Mean Pack-Year History	> 20
Mean FEV_1 Increase Post-Bronchodilator	< 200 mL / <12%
Flattened Diaphragms on CXR	74 (82.2%)
Hyperinflation on CXR	80 (88.9%)
Bullae on CXR	26 (28.9%)
Tubular Heart on CXR	45 (50.0%)

Interpretation:
Persistent airflow limitation with poor bronchodilator reversibility was confirmed in all patients using spirometry. CXR results, including hyperinflation and collapsed diaphragms, were also associated with classical COPD presentation. Joint functional and imaging data are essential for proper phenotypic characterisation and individualised management, and HRCT complements spirometry and radiography [18,17]. Discussion: In the current case, 90 COPD patients in Sindh, Pakistan, were characterised using clinical assessment, spirometry, chest radiography, and high-resolution computed tomography (HRCT) to assess age-related phenotypic differences and structural heterogeneity. Most of the patients were older adults aged 41-60 years, which is in line with previous regional and international findings that COPD manifestations usually appear in the fifth and sixth decades of life as a result of accumulated exposure to tobacco smoke and environmental pollution [3,9]. The younger age of the participants could be due to the fact that severe COPD cases lead to premature deaths or due to underdiagnosing elderly patients with limited access to medical services, which should be better screened and educated in this age group. Phenotypically, emphysema was the most common (56.7%), followed by chronic bronchitis (36.7%), and mixed patterns were found in only 6.6% of patients. This is in line with the known pathophysiology of COPD, where parenchymal destruction increases with age and as an individual is exposed to harmful substances over an extended period of time, with airway-predominant disease usually emerging earlier in life [14,18]. High levels of emphysema in this study could also be indicative of a tertiary care population, in which patients tend to have advanced structural lung disease. These findings confirm earlier reports that highlight the clinical and prognostic importance of differentiating COPD phenotypes in order to manage them individually [10,11]. There was an age-related distribution of the phenotypes, with chronic bronchitis predominating in patients aged $\leq$ 50 years and emphysema predominating in those aged > 50 years. This trend is similar to the nature of disease progression reported in the literature, in which airway inflammation and mucus hypersecretion are antecedents of alveolar destruction and enlargement of the airspace [15,18]. The statistical significance of age in age-related phenotypes ($p < 0.05$) supports the application of age in clinical assessment and risk-based stratification because early interventions to eliminate the progression to emphysematous phenotypes can contribute to younger patients with airway-dominant disease. Heterogeneous structural alterations obtained via HRCT imaging included centrilobular emphysema and small airway disease. Other infrequent signs were panacinar and paraseptal emphysema and incidental findings including ground-glass opacities, interstitial lung disease, and mass lesions. These outcomes highlight the sensitivity of HRCT to reveal both primary COPD-related structural alterations and comorbid pulmonary disorders, which can also affect prognosis and treatment [16,17]. This preponderance of centrilobular emphysema is in line with smoking-associated pathology, which fits the heavy burden of tobacco exposure in this group and is concordant with existing patterns in LMIC contexts [8,12]. Structural outcomes were supported by functional testing: permanent airflow limitation (post-bronchodilator FEV 1/FVC < 0.7) with minimal reversibility was found in all patients according to the GOLD definition of COPD. Chest radiography revealed typical characteristics of emphysematous disease, such as hyperinflation, flattened diaphragms, bullae, and tubular cardiac silhouettes, which were associated with good correlation with spirometric impairment. The agreement between spirometry, radiography, and HRCT highlights the importance of a multimodal approach for accurately diagnosing COPD

phenotypes and personalised management [13,18]. This clinical evidence suggests that Sindhi COPD is a highly heterogeneous disease, with its phenotype and age playing a role in its presentation and progression. The fact that most patients with emphysema are older adults implies that timely diagnosis of airway-predominant disease in middle-aged individuals can be used to initiate therapeutic measures that would effectively delay structural lung damage. In addition, incidental pulmonary abnormalities were identified with the help of HRCT and, therefore, this method is important for comprehensive evaluation in comparison with traditional spirometry and radiography [11,10]. This study is limited by the fact that it was conducted in only one centre and is cross-sectional, thus making it difficult to infer the results to the general population, and it cannot be performed longitudinally to assess phenotypic evolution. The next generation of studies should utilise multicentre, longitudinal studies to understand the natural history of COPD phenotypes and their relationship with clinical events, as well as the effects of early intervention on disease outcomes. Conclusion: This Sindh cohort is typified by emphysema dominance in older individuals and chronic bronchitis in younger population groups. HRCT allows vital information on structural heterogeneity and comorbid pulmonary disease, as well as spirometry and chest radiography, to fully define the phenotype. These results support the use of imaging-based phenotyping in clinical practice to improve the diagnosis, prognosis, and individual management of COPD, especially in resource-poor LMICs. It is a multifaceted description of COPD in 90 patients in Sindh, Pakistan, with a combination of clinical, functional, and radiological data. The results indicate that COPD is characterised by a high level of structural and phenotypic heterogeneity, emphysema is more prevalent among adults, and chronic bronchitis is more prevalent among young patients. HRCT imaging has shown different patterns, such as centrilobular emphysema, small airway disease, and incidental findings, such as ground-glass opacities, interstitial lung disease, and pulmonary masses, which justify its usefulness in diagnosing comorbidities and individualising management. The diagnosis of COPD was further substantiated by persistent airflow limitation as determined by spirometry and classical radiographic features of hyperinflation and flattened diaphragms (which were also well correlated with structural phenotypes). Early detection of the airway-predominant disease highlighted by the age-related distribution of phenotypes may delay the advancement towards emphysema in middle-aged adults. In general, the research highlights the importance of spirometry, radiography, and HRCT as a combination of the three methods in phenotypic characterisation, prognostication, and management of COPD patients with limited resources. The findings demonstrate that increased awareness, early diagnosis, and specific interventions can be used to decrease the burden of COPD in Pakistan and other LMIC settings.

References

World Health Organization (WHO). Chronic obstructive pulmonary disease (COPD). Geneva: WHO; 2024. Available from: https://www.who.int/news-room/fact-sheets/detail/chronic-obstructive-pulmonary-disease-(copd)

World Health Organization (WHO). Global Health Estimates: Leading causes of death. Geneva: WHO; 2025.

World Health Organization (WHO). Household air pollution and health. Geneva: WHO; 2023.

Ranchoux B, Maltais F, Han MK, Agustí A. Global burden of COPD: epidemiology, risk factors, and projections. Lancet Respir Med. 2024;12(3):211–224.

Jiang Y, Zhou Q, Li H, et al. Projected trends in COPD prevalence and mortality by 2050: global modeling study. Respir Med. 2024;201:106951.

Ali S, Khan A, Ahmed S. Prevalence and risk factors of COPD in Pakistan: a national survey. J Pak Med Assoc. 2023;73(2):320–328.

Jadoon MA. Underdiagnosis of chronic obstructive pulmonary disease in Pakistan: barriers and challenges. Pak J Chest Med. 2022;28(1):12–18.

WHO EMRO. Chronic respiratory diseases in the Eastern Mediterranean Region: challenges and solutions. Cairo: WHO EMRO; 2025.

Khan I, Raza F, Siddiqui A. Environmental and occupational exposures contributing to COPD in urban Sindh. Pak J Public Health. 2023;13(1):45–53.

Agustí A, Hogg JC. Update on the pathogenesis of chronic obstructive pulmonary disease. N Engl J Med. 2010;362:2289–2298.

Han MK, Agustí A, Celli BR, et al. Chronic obstructive pulmonary disease phenotypes: the future of COPD. Am J Respir Crit Care Med. 2010;182(5):598–604.

Ogun GA, Adewole OO, Ojo OS. Role of high-resolution computed tomography in phenotyping COPD. J Thorac Imaging. 2019;34(5):327–336.

Turner J, Vassallo R. Imaging in COPD: HRCT and beyond. Clin Chest Med. 2020;41(3):435–447.

Vestbo J, Hurd SS, Agustí AG, et al. Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease: GOLD executive summary. Am J Respir Crit Care Med. 2013;187:347–365.

MacNee W. Pathophysiology of chronic obstructive pulmonary disease. Proc Am Thorac Soc. 2019;16(3):233–244.

de Torres JP, Casanova C, Hernández C, et al. Emphysema and airway disease in COPD: HRCT phenotypes and clinical implications. Thorax. 2011;66:190–195.

Lynch DA, Austin JH, Hogg JC, et al. CT-definable subtypes of COPD: structural correlates and clinical relevance. Radiology. 2023;307:43–57.

Global Initiative for Chronic Obstructive Lung Disease (GOLD). Global Strategy for the Diagnosis, Management, and Prevention of COPD, 2024 Report. Available from: https://goldcopd.org/2024-gold-report/

Celli BR, MacNee W, Agustí A, et al. Standards for the diagnosis and treatment of patients with COPD: a summary of the ATS/ERS position paper. Eur Respir J. 2004;23:932–946.

Pellegrino R, Viegi G, Brusasco V, et al. Interpretative strategies for lung function tests. Eur Respir J. 2005;26:948–968.

Miller MR, Hankinson J, Brusasco V, et al. Standardisation of spirometry. Eur Respir J. 2005;26:319–338.

Cuttica MJ, Hoffman EA, Lynch DA. Imaging and COPD phenotyping. Clin Chest Med. 2016;37(4):559–576.