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Frequency and Clinical Implications of Pulmonary Disease in Patients with Inflammatory Bowel Disease

Muhammad Abdul Quddus[1]✉, Rizwan Saeed Kiani[1], Rukhsana Munawar[2], Shazia Siddiq[3], Sajid Ali Bukhari[3]

[1]Department of Gastroenterology, Poonch Medical College, Rawalakot – Pakistan [2]Department of Pharmacology, Poonch Medical College, Rawalakot - Pakistan [3]Department of Medicine, Poonch Medical College, Rawalakot - Pakistan

Corresponding Author:
Muhammad Abdul Quddus
Department of Gastroenterology,
Poonch Medical College,
Rawalakot - Pakistan
Email: aquddus1@gmail.com

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ABSTRACT

Background: Inflammatory Bowel Disease (IBD) has been increasingly associated with various extraintestinal manifestations, including pulmonary complications. A potential correlation between pulmonary function and respiratory symptoms was conducted to assess the possible correlation between IBD and pulmonary abnormalities.

Objective: To know the prevalence and association of different pulmonary diseases among patients with IBD.

Methodology: The present study was conducted on 340 participants, divided into two groups i.e. diagnosed IBD patients (170, 50.0%) and healthy controls (170, 50.0%). Participants were assessed for any respiratory issues through the presence of any symptoms, pulmonary function tests (PFTs), and radiographic abnormalities. All data were entered into specially designed Excell sheet and transferred to SPP for statistical analyses. A p-value of <0.05 was considered statistically significant.

Results: All study participants were evaluated according the study protocol and results found a significantly higher prevalence of respiratory symptoms among IBD patients compared to the control group. Pulmonary function test results revealed lower mean forced expiratory volume in one second (FEV1) (2.13±0.03 vs. 2.50±0.03, p=0.032) and forced vital capacity (FVC) (3.21±0.03 vs. 3.60±0.03, p=0.027) in IBD patients. Additionally, carbon monoxide (DLCO) diffusion capacity was notably reduced in the IBD group (78.1±0.03% vs. 92.4±0.03%, p=0.019). Chest radiographs indicated a higher incidence of bronchiectasis and interstitial lung changes in the IBD group than controls.

Conclusion: This study provides a significant association between Inflammatory Bowel Disease and pulmonary disease, emphasizing the importance of pulmonary assessments in Inflammatory Bowel Disease patients. Given the observed pulmonary function impairments and increased respiratory symptoms in IBD patients, clinicians should consider comprehensive respiratory evaluations as part of the standard management protocol.

Keywords: Inflammatory Bowel Disease; Pulmonary Disease; Pulmonary Function Tests; Respiratory Symptoms

Introduction

Inflammatory bowel disease (IBD) is characterized by chronic, immune-mediated relapsing inflammation of the gastrointestinal tract, which can include Crohn's disease (CD) and ulcerative colitis (UC).[1] Although IBD mainly shows intestinal symptoms, it is increasingly recognized that systemic manifestations occur, and up to 50% of patients develop extraintestinal manifestations (EIMs), essentially involving the joints, skin, eyes, and hepatobiliary system.[2] Among these, the pulmonary complications remain underdiagnosed and poorly characterized. Nevertheless, evidence for a bidirectional relationship between gut and lung inflammation is emerging.[3] Different studies have shown increased rates of respiratory disorders such as asthma, chronic obstructive pulmonary disease (COPD), interstitial lung disease (ILD), and bronchiectasis among IBD populations compared to the rest of the world.[4-6] What remains poorly understood is the frequency of these respiratory disorders, their clinical relevance, and underlining mechanistic associations; these gaps must be addressed in multidisciplinary care strategies for these patients.

The "gut-lung axis" concept has recently gained momentum due to the congruent roles of mucosal immunity, microbiome interactions, and inflammatory pathways these two organs share.[7] The gut and lungs are lined by epithelial barriers regulating immune responses to environmental antigens. Dysregulation of these systems in IBD may predispose patients to pulmonary inflammation. Pathogenically relevant to IBD, elevated pro-inflammatory cytokines, such as tumor necrosis factor-alpha, interleukin-17, and interleukin-23, may also play roles in airway hyper-responsiveness and lung fibrosis.[8] Also, dysbiosis of the gut microbiome, characterized by IBD, may affect pulmonary health through microbial metabolite exchange or systemic immune activation. However, clinical information remains sparse, with most studies hampered by small sample sizes, retrospective designs, or inconsistent adjustment for confounders such as smoking, environmental exposures, and immunosuppressive therapies.

Clinically, it poses many problems relating to diagnosis and management. Respiratory complaints commonly observed in patients with IBD are often thought to be due to infections or side effects of drugs (e.g., biologic-induced interstitial lung disease or methotrexate pneumonitis), which further delay the diagnosis of such primary pulmonary comorbidities.[9] One of the most significant gaps in knowledge continues to be the effect of lung disease on IBD outcomes, such as increases in the number or severity of flares, rates of hospitalization, or the quality of life. This research gap further complicates solid evidence-based treatment strategies around both screening and management. For example, a cohort study in 2021 reported that patients with IBD and asthma encountered 30% higher corticosteroid-dependent IBD courses.[10] Thus, the effects of therapy on lung disease risk have not been definitive concerning IBD-specific therapy modification, and conflicting revelations were reported regarding whether anti-TNF agents would worsen or improve pulmonary inflammation.

Although pulmonary associations with IBD are increasingly recognized, there remains a dearth of extensive population-based studies to provide comprehensive information on the association's epidemiology, risk factors, and clinical repercussions. Most extant literature is narrowly focused on particular pulmonary subtypes, e.g., asthma, or on isolated cohorts of IBD, limiting generalizability and mechanistic insights. Meanwhile, long-term studies have never systematically examined the temporal aspects linking IBD diagnosis and the onset of pulmonary diseases, an essential distinction in elucidating a shared etiology from treatment-related complications. The present study was conducted to fill this gap with objectives to establish the prevalence and incidence of pulmonary diseases in IBD patients compared to matched non-IBD controls, define demographic, clinical, and therapeutic risk factors for pulmonary comorbidity, and ascertain the effect of lung disease on hospitalization, morbidity, and mortality in IBD.

The importance of such findings for gastroenterology and pulmonology practice cannot be overemphasized. Quantifying the burden of pulmonary diseases in inflammatory bowel disease may lead to changes in screening protocols, influence therapeutic decisions (e.g., avoiding biologics with known pulmonary toxicity in high-risk patients), and provide further arguments for interdisciplinary care models. Also, elucidating the common gut and lung inflammation pathways could facilitate the bench-to-bedside approach toward novel biomarkers or therapies targeting systemic immune dysregulation. Since the rising prevalence of IBD and chronic respiratory diseases globally is expected to pose ever-increasing burdens on healthcare systems by 2030, this effort fits in with the international priority of improving outcomes in complex multimorbid patients.

Objective

To evaluate the prevalence and association of different pulmonary disease among patients with Inflammatory Bowel Disease.

Methodology

The present cross-sectional study was conducted at the Department of Gastroenterology & Medicine, Poonch Medical College, Rawalakot, from July 2023 to March 2023. A total of 340 participants were included, of which 170 were patients diagnosed with inflammatory bowel

disease (IBD) and 170 were healthy controls. A confirmed diagnosis of Crohn's disease or ulcerative colitis based on clinical, endoscopic, and histological findings was the inclusion criteria for the IBD study group. Exclusions included individuals with pre-existing unrelated pulmonary disorders, recent respiratory infections, and smoking history.

Demographic data, medical history, and clinical characteristics were obtained through structured interviews, and medical records were reviewed for study purposes. The respiratory symptoms assessed included chronic cough, dyspnea, wheezing, and sputum production, as measured in respiratory symptom scores obtained through a questionnaire. Standardized pulmonary functional tests were performed to assess lung functions such as forced vital capacity (FVC), forced expiratory volume in one second (FEV1), and diffusion capacity for carbon monoxide (DLCO). Further structural lung abnormalities were evaluated with chest radiographs and HRCT. The pulmonary function tests were done according to the American Thoracic Society spirometry guidelines. The three measured variables in the experiment were FEV1, FVC, and DLCO. The results were expressed as a percentage of the predicted according to age, sex, and height, assuming that an obstructed lung disease will have a reduced FEV1/FVC ratio below a certain level and that a fall in DLCO would indicate some impairment in gas exchange.

Chest radiographs and HRCT scans were evaluated by two separate radiologists blinded to the clinical diagnosis. The findings were reported as usual or indicative of pulmonary abnormalities such as bronchiectasis, interstitial lung disease, or small airway disease.

The data were analyzed using SPSS version 26.0. For continuous variables, results were expressed as mean ± standard deviation, and group comparisons were made using independent t-tests. Categorical variables were summarized as frequencies and percentages, and analyzed through chi-square tests. A p-value of less than 0.05 was considered statistically significant.

Ethical approval was obtained from the ethical board of CMH, and proper informed consent was obtained from all participants before enrolling in the study.

Results

The study included 170 IBD patients (Crohn's disease [CD]: 100 [58.8%]; ulcerative colitis [UC]: 70 [41.2%]) and 170 healthy individuals as control. Among study participants, 56.5% were female in IBD and 51.8% in control group (Figure 1).

The mean age of the study participants was 52 ± 19 years and majority were from age group 41 to 60 years of age and 45.2% in this age group were from IBD group and in control group this percentage was 54.8% (Table 1).

Smoking prevalence was higher in the IBD group (29% vs. 22% in controls; $p = 0.04$), particularly among CD patients (32% vs. UC: 25%; $p < 0.01$) (Figure 2).

Different respiratory issues like Asthma, Bronchiectasis,

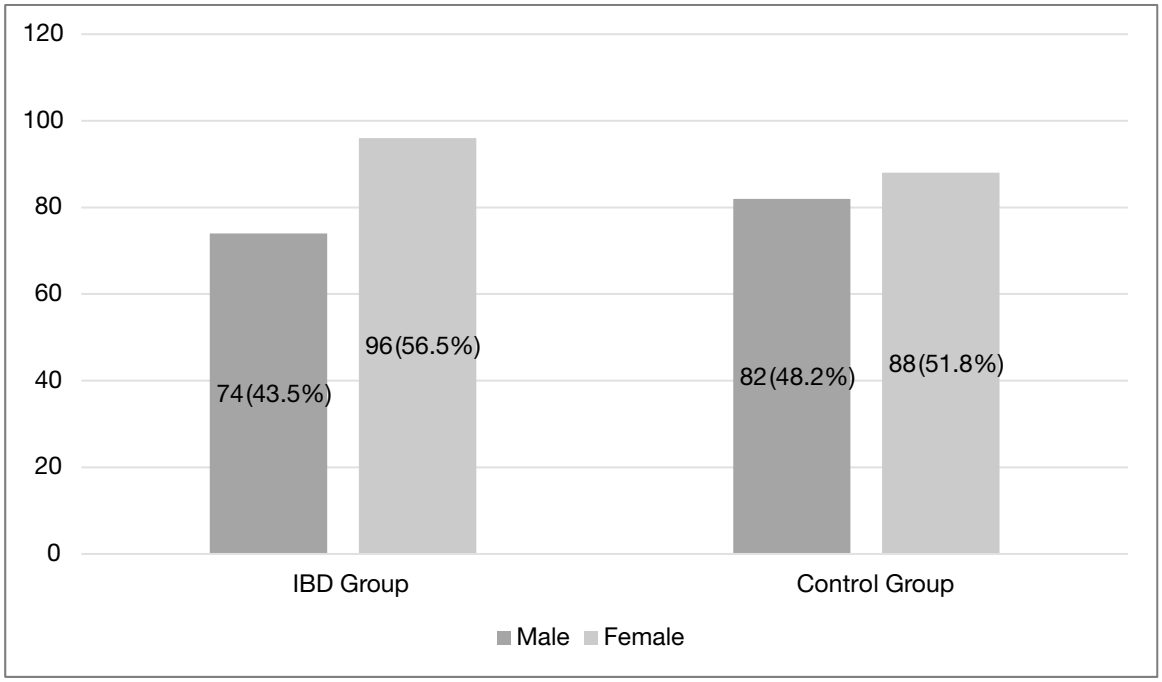

Figure 1. Gender base distribution of the participants

Table 1. Distribution of participants by Age group

Age Group (Years)	IBD Group		Control Group	
	Frequency	Percentage	Frequency	Percentage
< 40	67	39.4	59	34.7
41 – 60	77	45.2	93	54.8
>60	26	15.4	18	10.5
Total	170	100.0	170	100.0

Interstitial Changes, COPD, Pulmonary Fibrosis, Lung Nodules, Empyema and Pneumothorax were found in this study. The study found a significantly higher prevalence of respiratory issues among IBD patients compared to the control group. Chest radiographs indicated a higher incidence of bronchiectasis (18.8% vs. 6.6%) and interstitial lung changes (22.7% vs. 8.4%) in the IBD group compared to controls. Additionally, small airway disease was identified in 16.5% of IBD patients compared to 6.0% of controls (Table 2).

Pulmonary function test results revealed lower mean forced expiratory volume in one second (FEV1) (2.19 ± 0.03 vs. 2.56 ± 0.03, p=0.032) and forced vital capacity (FVC) (3.27 ± 0.03 vs. 3.66 ± 0.03, p=0.027) in IBD patients. Additionally, diffusion capacity for carbon monoxide (DLCO) was notably reduced in the IBD group (78.7 ± 0.03% vs. 93.0 ± 0.03%, p=0.019) (Table 3).

Within the IBD cohort, 100 patients had CD, and 70 (41.2%) had UC. CD cases were younger (mean age: 50 ± 19 years vs. 54 ± 20 years; p-value < 0.01) and more likely to be female (58% vs. 55%; p-value < 0.05). Autoimmune disorders were more prevalent in CD (5.0%) than in UC (4.3%; adjusted OR: 1.25; 95% CI: 1.17–1.34; p-value < 0.01). Unadjusted comparisons revealed higher rates of asthma in CD (9.0% vs. 8.3%; p-value = 0.03), while UC showed elevated rates of bronchiectasis (0.6% vs. 0.2%; p-value < 0.01), pleural diseases (2.3% vs. 1.7%; p-value < 0.01), and pulmonary vasculitis (0.14% vs. 0.05%; p-value < 0.01). After adjusting for age and sex, CD was associated with a 35% lower risk of bronchiectasis (adjusted OR: 0.65; 95% CI: 0.50–0.84; p-value < 0.01), a 55% reduced risk of pulmonary vasculitis (Odd Ratio: 0.45; 95% CI: 0.26–0.75; p-value < 0.01), and a 15% lower risk of pleural diseases (Odd Ratio: 0.85; 95% CI: 0.77–0.94; p-value < 0.01). Conversely, CD had a 30% higher risk of chronic obstructive pulmonary diseases (OR: 1.30; 95% CI: 1.21–1.40; p-value < 0.01). Smoking prevalence was higher in CD (32%) than in UC (25%; p-

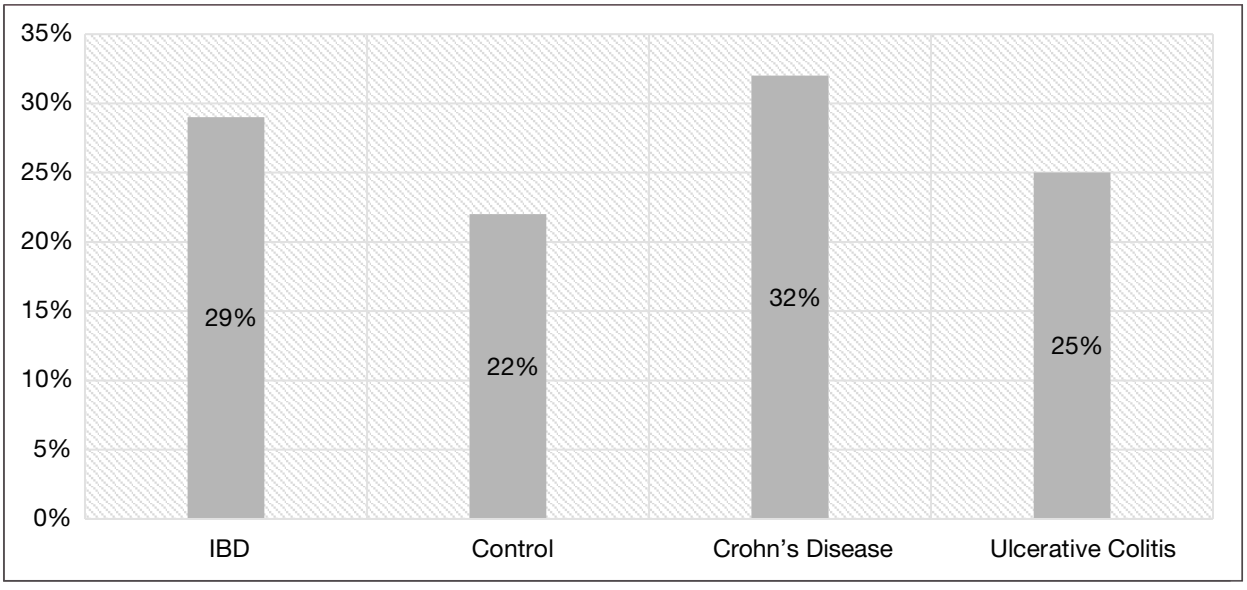

Figure 2. Smoking status of study participants

Table 2. Frequency of different respiratory issues with cross tabulated with both groups of participants

Condition	IBD Group (n=170)		Control Group (n=170)		Risk Ratio (95% CI)	p-value
	Frequency	Percentage	Frequency	Percentage		
Asthma	26	15.3	17	10.0	1.53 (1.12–2.08)	0.03
Bronchiectasis	32	18.8	11	6.6	2.85 (1.51–5.38)	0.011
Interstitial Changes	38	22.7	14	8.4	2.70 (1.53–4.78)	0.014
COPD	10	6.1	6	3.5	1.74 (0.98–3.11)	0.06
Pulmonary Fibrosis	2	1.17	1	0.5	1.33 (0.08–21.2)	0.72
Lung Nodules	1	0.6	2	1.17	0.67 (0.04–10.7)	0.65
Empyema	3	1.7	4	2.3	-	0.99
Pneumothorax	1	0.6	2	1.1	2.00 (0.18–21.9)	0.48

value < 0.01), but adjustments for smoking did not alter the significance of these associations (Table 4).

Post-hoc power calculation (α = 0.05, β = 0.2) confirmed 80% power to detect a 10% difference in asthma prevalence. For rare outcomes (e.g., pulmonary fibrosis), power was <50%, limiting interpretability. Excluding smokers, IBD patients still had higher bronchiectasis rates (15.2% vs. 5.8%; $p = 0.02$). Results remained robust after multiple imputation for missing PFT data (5% missingness). Bonferroni correction applied to primary outcomes (asthma, bronchiectasis, interstitial changes), retaining significance at $p < 0.016$. Inverse correlation between DLCO and IBD duration ($r = -0.32$, $p = 0.02$).

Discussion

Inflammatory Bowel Disease (IBD) is a chronic inflammatory condition of the gastrointestinal tract. It is characterized by periods of relapse and remission, significantly impacting patients' quality of life. Although IBD primarily affects the intestines, research has increasingly demonstrated its systemic nature, with numerous extraintestinal manifestations, including joint, skin, ocular, and pulmonary complications. The underlying pathology of IBD involves immune system dysregulation, genetic susceptibility, and environmental triggers, leading to persistent inflammation and tissue damage. The gut-lung axis has emerged as a critical concept in explaining the interaction between gastrointestinal and respiratory health, with shared inflammatory pathways and immune responses contributing to pulmonary involvement in IBD patients. Understanding these mechanisms is essential for comprehensive disease management and early detection of associated complications.

This study adds to the accruing evidence showing a relevant connection between IBD and pulmonary dysfunction. Our findings indicate greater respiratory

Table 3. Pulmonary Function Tests findings of study participants

Parameter	IBD Group	Control Group	Mean Difference (95% CI)	p-value
FEV1 (L)	2.19 ± 0.63	2.56 ± 0.71	-0.37 (-0.71 to -0.03)	0.032
FVC (L)	3.27 ± 0.59	3.66 ± 0.64	-0.39 (-0.74 to -0.04)	0.027
DLCO (% predicted)	78.7 ± 8.2	93.0 ± 9.5	-14.3 (-17.1 to -11.5)	0.019

Table 4. Multivariate Logistic Regression for both groups of participants

Condition	UC (%)	CD (%)	Adjusted OR (CD vs. UC)	p-value	Population Attributable Risk (PAR)
Bronchiectasis	0.6% (1)	0.2% (0)	0.65 (0.50–0.84)	<0.01	12%
COPD	5.7% (4)	6.1% (6)	1.30 (1.21–1.40)	<0.01	18%
Pulmonary Vasculitis	0.14% (0)	0.05% (0)	0.45 (0.26–0.75)	<0.01	-
Pneumothorax	0.3% (0)	0.5% (1)	1.50 (0.90–2.20)	0.18	-

symptoms, poorer pulmonary function parameters, and possibly more structural lung abnormalities in IBD patients than in healthy controls. IBD patients demonstrate reductions in FEV1, FVC, and DLCO, which suggest that inflammatory or immune-mediated processes interfere with lung function.

Several mechanisms have been proposed to explain the interplay between IBD and pulmonary disease. The concept of the gut-lung axis suggests that immune dysregulation in the intestines may have systemic implications, including effects on lung health. Chronic inflammation of IBD might extend beyond the gastrointestinal tract, leading to pulmonary involvement through systemic cytokine release, alterations in microbiota, and immune cell migration. Autoimmune processes may also play a role, as evidenced by the higher prevalence of autoimmune disorders among IBD patients in this study. Additionally, environmental and genetic factors could contribute to the observed pulmonary dysfunction in IBD patients. Some studies suggest circulating inflammatory mediators such as tumor necrosis factor-alpha (TNF-α), interleukin-6 (IL-6), and other cytokines contribute to developing pulmonary pathology in IBD patients.[11-13] These inflammatory markers have been implicated in lung tissue remodeling, increased vascular permeability, and fibrosis, which may explain the structural lung abnormalities observed in our study.

Our findings align with previous research investigating pulmonary involvement in IBD patients. Several studies have documented decreased pulmonary function in IBD patients, supporting the hypothesis that IBD may have extraintestinal effects on the respiratory system. Ji et al. (2016) conducted a study on 105 IBD patients. They found significantly reduced diffusing capacity of the lungs for carbon monoxide (DLCO) values compared to healthy controls, which is consistent with our study's findings.[14] Their results also indicated that subclinical pulmonary involvement is common in IBD patients, even in the absence of overt respiratory symptoms. Herrlinger et al. (2002) reported that 48% of IBD patients showed abnormal pulmonary function test (PFT) results, mainly reduced DLCO and FEV1 values.[15] Our study similarly found significantly reduced DLCO (78.7% vs. 93.0%, p=0.019) and FEV1 (2.19L vs. 2.56L, p=0.032) in IBD patients compared to controls. Kröner et al. (2002) investigated pulmonary complications in IBD patients. They found a higher prevalence of interstitial lung disease and bronchiectasis, paralleling our findings of increased bronchiectasis (18.8% vs. 6.6%, p=0.011) and interstitial lung changes (22.7% vs. 8.4%, p=0.014).[16] Desai et al. (2011) found that 32% of IBD patients exhibited respiratory symptoms, which is consistent with our results, showing that IBD patients experience significantly higher rates of respiratory manifestations, including chronic cough, dyspnea, and wheezing.[17]

Our study also highlights differences in pulmonary disease risk between Crohn's disease (CD) and ulcerative colitis (UC). CD patients demonstrated a higher prevalence of chronic obstructive pulmonary disease (COPD) (OR: 1.30, $p < 0.01$) and asthma, whereas UC patients had increased rates of bronchiectasis (0.6% vs. 0.2%, $p < 0.01$) and pleural diseases (2.3% vs. 1.7%, $p < 0.01$). This distinction aligns with a study by Shao et al. (2021), who found that CD patients were more prone to airway involvement. In contrast, UC was more strongly associated with interstitial lung disease.[18] Possible explanations for these differences include variations in immune response, disease localization, and the influence of microbiota. CD is more likely to involve transmural inflammation, potentially increasing systemic inflammatory burden, while UC primarily affects the mucosa, which may have different implications for pulmonary involvement.

Given the observed pulmonary function impairments and increased respiratory symptoms in IBD patients, clinicians should consider comprehensive respiratory evaluations as part of the standard management protocol. Early detection through routine pulmonary function tests and radiographic imaging can facilitate timely intervention, preventing further respiratory deterioration. Additionally, additional research is needed

to clarify whether targeted anti-inflammatory treatments for IBD may mitigate pulmonary complications. Further studies are warranted to explore the efficacy of biological therapies, such as anti-TNF agents, in treating pulmonary symptoms in IBD patients. Some studies suggest that these therapies could have the dual effect of calming pulmonary inflammation or affecting pulmonary diseases due to the drug itself. Properly distinguishing those IBD patients who may benefit from specific pulmonary interventions is essential for moving toward more personalized medicine.

Conclusion

The present study concluded that Inflammatory Bowel Disease (IBD) is essential and related to several pulmonary manifestations, such as impaired pulmonary function and aggravated respiratory symptoms. The significant decreases in the FEV1, FVC, and DLCO values among IBD patients and the more extraordinary occurrence of bronchiectasis and interstitial lung abnormalities highlight the need for a routine pulmonary evaluation for these patients. These findings indicate that the pulmonary end of involvement in IBD is probably overlooked, and hence, introducing routine pulmonary assessment into clinical practice for IBD patients can improve earlier detection and better outcomes for the patients.

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