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ORIGINAL ARTICLE

Pulmonary manifestations in inflammatory bowel disease: a prospective study

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Abstract
Background Although pulmonary abnormalities have been recognized in patients with inflammatory bowel diseases (IBD), their prevalence and clinical significance are not known.
Aim To study the prevalence and clinical significance of pulmonary abnormalities in patients with IBD.
Methods Ninety-five non-consecutive patients with IBD (12 Crohn's disease, 83 ulcerative colitis; mean age 41.9 [SD 13] years; 47 women) were prospectively studied from January 2007 to March 2010. Pulmonary function tests (PFT) and high-resolution CT (HRCT) chest were performed in them. PFT were compared to those in 270 healthy (control) subjects matched for age, sex and smoking status.
Results Twenty-seven (28.5%) patients and 11 (4%) control subjects had abnormal PFT ($p<0.0001$). Small airway obstruction was seen in 18 patients, restrictive defect in six and mixed defect in three. Twenty-one (22%) patients had abnormal HRCT findings – bronchiectasis and nodules (nine patients each, including one with nodules who later developed active tuberculosis after infliximab therapy), parenchymal bands (8), mediastinal lymphadenopathy (five, including two with tuberculosis on histology and culture), emphysema (5), brochiolitis (2), pleural effusion or thickening (2), pericardial effusion (2), patchy consolidation (1), ground-glass opacities (1) and lung metastasis (1). Three patients had symptoms (one asthma, two cough).
Conclusion PFT and HRCT chest showed abnormality in about one-quarter of patients with IBD. A majority of patients with these abnormalities were asymptomatic.

Keywords Diffusion abnormality · Interstitial lung disease · Lung function tests · Pulmonary involvement

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Introduction

The pathogenesis of inflammatory bowel diseases (IBD), including ulcerative colitis (UC) and Crohn's disease (CD), involves interaction between environmental, genetic, microbial and immunoregulatory factors; disordered innate immunity also plays a role [1]. Similarities in the structure of the intestine and bronchus and their common origin from the primitive foregut may provide a basis for the development of inflammatory changes in the bronchus in patients with IBD [1, 2].

Lung involvement in IBD was first reported in 1976 in a series of six patients [3] and has been increasingly reported in recent years [4]. This may be overt or subclinical, and can be grouped as large and small airway disease, parenchymal lung disease, and reduced diffusion capacity of the lungs [5]. Most patients have normal chest X-ray, and abnormalities are detected on high-resolution CT (HRCT) of the chest [6, 7]. The pulmonary manifestations do not correlate with the duration of IBD, and are variously reported as occurring frequently during active disease, occurring independent of disease activity, and even in

post-colectomy patients [7–9]. There is no difference in their prevalence between patients with UC and Crohn's disease [9]. Although interstitial lung disease has been reported in those treated with medications that are used in the therapy of IBD, such as sulfasalazine, 5-aminosalicylic acid preparations and methotrexate, lung involvement in IBD is considered a distinct entity [10–12].

The prevalence of lung abnormalities in IBD has varied in reports, and clinical significance is not clear. We conducted this prospective study to determine the prevalence of lung abnormalities on HRCT and pulmonary function tests (PFT) in patients with IBD, and to assess their clinical significance.

Methods

The prospective study was carried out at our tertiary-care hospital, between January 2007 and March 2010. Patients with IBD, aged more than 18 years, and willing to participate were included in the study. Patients with ankylosing spondylitis or other extra-pulmonary diseases restricting lung expansion, those with lung disease due to other causes, severe systemic disease and pregnant women were excluded. PFT and HRCT chest were done in all patients.

Lung volumes were measured by helium dilution method on a Jaeger M S PFT system (ERICH JAEGER GmbH, Hoechberg, Germany). Each patient underwent standard PFT for forced expiratory volume in 1 s (FEV_1), forced vital capacity (FVC), total lung capacity (TLC) and residual volume (RV) and a transfer coefficient for carbon monoxide (DLCO) by a single breath test. The individuals were classified as normal when all measurements were >70% of predicted values. A restrictive defect was considered when FEV_1 and FVC were reduced (<70% of predicted) with FEV_1/FVC ratio >70% of predicted, and obstructive defect when FEV_1 was reduced with normal FVC and FEV_1/FVC ratio was <70% of predicted. The criterion for small airway obstruction was FEF_{25-75} below 60% predicted. Mixed defect was defined as a combination of obstructive (FEV1/FVC below 70%) and restrictive (DLCO below 70%) [6]. The PFT records of 270 subjects attending our health-check clinic, and matched for age, sex and smoking status, were taken as control.

HRCT was performed using GE 64 SLICE VCT machine. Inspiratory scan protocol consisted of slice thickness of 1.25 mm at interval of 10 mm, KV 140, mA 250, rotation time 0.4 s, rotation length FULL, scan type AXIAL. Expiratory scan protocol was same as above but done at interval of 40 mm. The average radiation dose was 1.2–1.4 mSV. Obstructive airway criteria included air trapping on expiratory scans with attenuated vessels within the air–trapped lung. This may be associated with bronchial wall thickening. HRCT was not done in control subjects.

The study protocol was approved by the institution's ethics committee, and written informed consent was obtained from each study patient. Statistical analysis was performed by using Fisher's exact test for categorical variables.

Results

Ninety-five patients meeting the study criteria and consenting to participate were enrolled. Twelve of them had Crohn's disease and 83 had ulcerative colitis. There were 47 women (six with CD, 41 UC). They were aged mean 41.9 (SD 13) years, with range 19 to 81 years. Median duration of disease was six (range 1 to 30) years. Of 12 patients with Crohn's disease, eight had inflammatory disease, and two each had fistulizing and stricturing disease. Of the 83 patients with ulcerative colitis, ten had proctitis, 29 had procto-sigmoiditis, 28 had left–sided disease and 16 pancolitis.

PFT was abnormal in 27 of 95 patients and 11 of 270 control subjects ($p<0.0001$; two-tailed Fisher's exact test). Abnormal PFT included small airway obstruction in 18 (mild in two, moderate in 16), restrictive defect in six (mild

Table 1 Comparison of findings on PFT and chest CT in UC and CD in this and earlier studies

	Patients (*n*)		Control subjects (*n*)	Abnormal PFT		Abnormal CT	Symptoms
	UC	CD		UC	CD		
Tzanakis et al. [10]	85	47	36	17.6%	19%	Not done	
Herrlinger et al. [13]	31	35	30	39%	45%	Not done	
Songur et al. [8]	23	13	14	58%		52%	44%
Sarioglu et al. [15]	15	2	No	5.8%		88.2%	23%
Tunc et al. [14]	32	20	No	6.25%	25%	50% UC, 60% CD	
Yilmaz et al. [17]	30	9	20	56%		64%	25.6%
Present study 2010	83	12	270 (PFT)	28.5%		22%	3%

PFT pulmonary function tests, *UC* ulcerative colitis, *CD* Crohn's disease

in three, moderate in three) and mixed obstructive and restrictive defect in three (moderate obstruction and restriction in two, moderate obstruction and mild restriction in one). Of the 61 patients in whom data were available, 11 (18%) had abnormalities in alveolar diffusion of carbon monoxide (DLCO) on PFT.

Twenty-one patients (22%) had abnormal findings on HRCT. These included bronchiectasis and nodules (nine patients each), parenchymal bands (8), mediastinal lymphadenopathy (5), emphysema (5), brochiolitis (2), pleural effusion (likely related to hypoalbuminemia) (1) or pleural thickening (1), pericardial effusion (2), patchy consolidation (1), ground-glass opacities (1) and lung metastasis (1). One patient with pulmonary nodule later developed active tuberculosis after receiving infliximab therapy. Of five patients with lymphadenopathy, two proved to have tuberculosis on tissue histology and culture. Abnormalities on chest X-ray were seen in only two of these 21 patients. Seven (7.3%) patients had abnormal PFT and HRCT and ten (10.5%) had abnormal PFT and DLCO.

Three patients had respiratory symptoms (one had bronchial asthma and two had recurrent cough). Of the latter, one had diffuse small airway disease and the other had moderate airway obstruction with good reversibility and moderately severe restrictive defect. All three patients needed treatment.

Discussion

An early study found PFT abnormalities in 18% of patients with ulcerative colitis and 19% with Crohn's disease [3]. A later study reported the prevalence of abnormal PFT to be as high as 39% in UC and 45% in CD [13]. Songur et al. [8] reported abnormal CT and PFT in more than 50% of patients with IBD (Table 1) [13–15]. In an Indian study that looked at pulmonary and hematologic abnormality in 51 patients with IBD, 14 (27%) patients had abnormal PFT [16], similar to our findings. All patients were asymptomatic. Ours is probably the largest prospective study of lung abnormalities in IBD; no earlier study compared PFT in age–, sex–, and smoking– matched control subjects.

We found abnormal PFT in 28.5% of patients with IBD; reported figures in literature range from 5% to 58%. This prevalence was significantly higher than that in the control subjects (4%). Twenty-two per cent of the patients had abnormal HRCT. This prevalence is less than in earlier studies (22% to 88%), but the pattern of abnormalities is similar to that in earlier reports [8, 14, 15, 17]. The HRCT abnormalities reported in IBD include bronchiectasis, air trapping, tree–in– bud appearance (branching pattern of small nodules), ground–glass appearance, peribronchial thickening and reticular pattern. This study and the earlier Indian study [16] found lower prevalence of 22% and 27%, respectively, as compared to other studies that have shown HRCT abnormalities from 52% to 88%. A majority of patients with HRCT abnormality had no respiratory symptoms.

An important issue in our study was whether the finding can be solely attributed to IBD. A majority of our patients had pulmonary findings for which no other cause could be found. However every effort must be made to rule out other causes, especially infective, before attributing them to IBD.

Three of 95 patients in our study had symptoms that needed treatment. Three earlier studies reported higher prevalence of symptoms (44%, 23%, and 25.6%) [10, 15, 17]. We suspect that the small number of patients with symptoms in our study could be due to intermittent steroid use, although we do not have supporting data.

We do not recommend routine PFT in patients with IBD. However, of concern in our setting is the incidental detection of tubercular lymphadenopathy in two patients, one of whom had normal chest X-ray. A third patient, with pulmonary nodules on HRCT, manifested with sputum-positive tuberculosis after two doses of infliximab; his chest X-ray was also normal initially. These findings may suggest a need for HRCT in all patients with IBD in whom biological therapy is planned, especially in regions with high prevalence of tuberculosis.

In summary, we found PFT abnormality in more than one-quarter of patients with IBD, which was greater than the prevalence in control subjects. HRCT chest showed abnormality in nearly as many patients. Three of 95 patients had respiratory symptoms. We do not recommend routine pulmonary function testing in patients with IBD, but HRCT may be indicated before institution of biological therapy especially in regions with high prevalence of tuberculosis.

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