Pulmonary Function Test Results In Patients with Ulcerative Colitis

SA Alavi Foumani¹, F Mansour-Ghanaei²*, MR Zahedpour-Anaraki³, M Yousefi-Mashhour², F Joukar², S Besharati², M Bozorgnia⁴

¹Department of Respirology, Pulmonary and Respiratory Disease Research Center, ²Department of Gastroenterology and Hepatology, Gastrointestinal and Liver Diseases Research Center (GLDRC), Guilan University of Medical Sciences, Rasht, ³Department of Respirology, Pulmonary and Respiratory Disease Research Center, Tehran University of Medical Sciences, Tehran, ⁴Department of Radiology, Guilan University of Medical Sciences, Rasht, Guilan, Iran

Abstract

Background: Pulmonary complication of IBD includes airway inflammation involving small and large airways, pulmonary paranchymal disease and serositis. The aim of this study was to determine the prevalence of Pulmonary Function Test (PFT) abnormality in ulcerative colitis (UC) patients.

Methods: During spring and summer of 2006, PFT (spirometry and body box plethysmography) of 50 UC patients were compared with 50 healthy persons matched for age and sex (control). Data collection form including demographic specification and UC condition were filled.

Results: Mean age of patients was 37.2 years (SD=14.5). Active UC was seen in 24% of patients while 18% of patients suffered from severe UC. PFT results included 42% air trapping (only increase in residual volume/total lung capacity), 20% small airway obstructive pattern (only decrease in maximal expiratory flow at 25-75% of vital capacity), 12% restrictive ventilation defect, 2% obstructive airway, 2% hyperinflation and 6% upper airway obstructive pattern. There was a significant relationship between small airway obstructive pattern and duration of UC and no relationship was noticed between other pulmonary disorders and severity, activity, duration of UC.

Conclusion: According to high prevalence of air trapping, small airway disease may be the prominent feature of lung involvement in UC patients. Therefore a meticulous work up for respiratory diseases is necessary in UC patients.

Keywords: Pulmonary function test; Ulcerative colitis; Inflammatory bowel disease

Introduction

Inflammatory bowel disease (IBD) is a general term for a group of chronic inflammatory disorders of unknown etiology involving the gastrointestinal tract. Chronic IBD may be divided into two major groups, ulcerative colitis (UC) and Crohn's disease (CD).¹ UC is a chronic inflammatory process which diffusely affects the superficial mucosa of the colon and extends proximally from the anal verge up to the cecum.²

Almost every organ system can be involved, principally eyes, skin, joints, kidneys, liver and biliary tracts, and vasculature (or vascular system) are the most common sites of systemic IBD and their involvement is dependent on different mechanisms.^{3,4} Pulmonary disease has been described much less frequently than other organ systems. Lung and gastrointestinal systems are originated from primitive gut and they have same pathogenetic changes in these patients. Major patterns of pulmonary disease associated with inflammatory bowel disease (IBD) are pleuritis, airway disease; particularly non-asthmatic airways disease with productive cough, interstitial lung

^{*}Correspondence: Fariborz Mansour-Ghanaei, MD, Gastrointestinal and Liver Diseases Research Center, Guilan University of Medical Sciences, Razi Hospital, PO Box 41448-95655, Rasht, Iran. Tel: +98-131-5535116, Fax: +98-131-5534951, e-mail: <u>ghanaei@gums.ac.ir</u> Received: January 10, 2009 Accepted: May 17, 2009

disease, necrobiotic nodules, pulmonary eosinophilia, thromboembolic disease, vasculitis, granulomatous lung disease, etc.^{5,6} Also, case reports do not show a uniform picture of disease and describe various entities including bronchial hyperresponsiveness,⁷ bronchitis and bronchiectasis,⁸⁻¹¹ inflammatory tracheal stenosis,¹² and interstitial pneumonitis¹³ as well as bronchiolitis obliterans- organizing pneumonia.¹⁴⁻¹⁶ Some authors reported pulmonary impairment in IBD patients to be related to disease activity as well.^{17,18} Apart from extraintestinal activity, side effects of treatment may contribute to pulmonary dysfunction in IBD patients.^{19,20} These manifestations will be categorized by disease mechanism into drug-induced disease, anatomic disease, over-lap syndromes, autoimmune disease, physiologic consequences of IBD, pulmonary function test abnormalities, and nonspecific lung disease.²¹ Investigation of pulmonary function in IBD patients by standard lung function tests has revealed inconsistent results. Whereas some authors could not detect differences in routine pulmonary function tests between IBD patients and controls,^{22,23} others documented a reduced lung transfer factor for carbon monoxide (DLCO), especially in patients with active IBD and a high incidence of pulmonary function abnormalities were identified, despite the lack of radiological alterations and pulmonary symptoms, in ulcerative colitis patients.²⁴ The aim of this study was to determine the prevalence of pulmonary function test in UC patients compared with age and sex matched healthy persons.

Materials and Methods

Fifty patients with UC (case group) were enrolled during spring and summer of 2006. Fifty healthy persons served as a control group. Fifty UC patients of Guilan (north province in Iran) Gastrointestinal and Liver Diseases Research Center of Guilan University of Medical Sciences (case group) and 50 healthy persons (control group) introduced to a respirologist for pulmonary function test (PFT). The control group was from hospital staff that was matched in age and sex. The mean age in UC patients was 34.9 years, and the mean age in control patients was 35.2 years. The mean duration of disease in UC patients was 6.9 years (range: 0.1-25). Thirty-two of 50 patients received aminosalicylates (between 2 and 4 g/day) for at least 5 days and 35/50 patients were on corticosteroids (mean dose: 35 mg; range: 2.5-100 mg). None of the patients had ever received methotrexate. The study was approved in Ethics Committee of Gastrointestinal and Liver Diseases Research Center of Guilan University of Medical Sciences. A written consent form was obtained from each patient.

Reasons for exclusion from the study were major surgery, infectious bronchitis, pneumonia, and asthma, COPD (chronic obstructive pulmonary disease) detected by respirologist and recent or past history of smoking and lack of compliance in performing lung function test.

At prestudy visit, in addition to medical history, physical examination and colonoscopy, the patients' baseline disease state was scored. This index encompassed data from the previous week and included number of stool weekly, amount of blood in stools, abdominal pain or cramps, physician assessment of patient's condition, body temperature, extra-intestinal manifestations, erythrocyte sedimentation rate and hemoglobin concentration. UC activity was assessed by the Rachmilewitz clinical activity index (CAI). Clinical activity index 24 and index <4 was recognized as active and inactive UC respectively. Disease severity in patients with UC was assessed using the Truelove and Witts classification. This score includes stool frequency, fever, the occurrence of blood in stool, and, for laboratory findings, the Hb value and erythrocyte sedimentation rate. This classification divides patients into three groups: mild, moderate and severe. Patients with Truelove indices of mild were considered to be in remission and patients with indices moderate or severe had active disease. After written informed consent was obtained eligible patients were performed PFT.

Spirometry was used to determine forced expiratory volume in 1 s (FEV1), vital capacity (VC), forced vital capacity (FVC), maximal expiratory flow at 25-75% of vital capacity (MMEF₂₅₋₇₅), residual volume (RV), total lung capacity (TLC), residual volume/total lung capacity (RV/TLC). PFT was abnormal when VC, FVC and FEV1< 80% or MMEF₂₅₋₇₅<65% of predicted value. Results were expressed as the percentage of the normal value for gender, age, and height (percent predicted). PFT demonstrated obstruction and restriction ventilatory defect regarded to ATS (American Thoracic Society). Small airway obstruction pattern was defined if MMEF₂₅₋₇₅<65% of predictive value and upper airway obstruction pattern was identified based on the flow volume curve configuration. There was air trapping when RV/TLC were more than 40% of predictive value respectively.

Data were compared between two groups. Categorical variables were compared using a χ^2 and t tests and Pearson correlation coefficients were used for continuous data. All analyses were performed using the statistical package SPSS (version 10.0 for Windows, Chicago, Illinois, USA). *P* value < 0.05 was considered to be statistically significant.

Results

Thirty nine percent of patients were male and 61% were female. Mean duration of UC was 7.5 years (SD=6.7). Active UC was seen in 24% of patients and 76% were in remission. Nine (18%) patients had severe UC and 30% and 52% had moderate and mild UC respectively. The results of PFT showed air trapping with a significant increase only in RV/TLC and was seen in 21 of the 50 patients (42%) versus 10 (20%) healthy persons (p=0.021). Small airway obstructive pattern with only decrease in MMEF₂₅₋₇₅ was noticed in 10 (20%), restrictive ventilation defect in 6 (12%), obstructive airway in 1 (2%), hyperinflation in 1 (2%) and upper airway obstructive pattern in 3 (6%) patients (Table 1). The pulmonary function abnormalities were obstructive pattern (air trapping; 100%), small airway obstruction (20%), mixed ventillatory defect, restrictive and obstructive (24%) and

Table	1:	PFT	results	in	UC	and	the	control	aroups
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Table 1. 11 1 results in 66 and the control groups								
PFT Results	UC group No (%)	Control group No (%)	P value					
air trapping	21 (42)	10 (20)	0.02					
small airway obstructive pattern	10 (20)	10 (20)	0.09					
Mild restrictive ventilation defect	6 (12)	0 (6)	0.2					
Obstructive defect	1 (2)	0 (0)	0.3					
hyperinflation	1 (2)	0 (0)	0.3					

Table	2:	PFT	result	in	UC	patients	&	control	group

Group	UC (Std.	Control (Std.	P value
Mean of	Deviation)	Deviation)	
PFT parameter	_		
VC MAX(liters)(predicted value)	89.6(3.4)	90.2(6.9)	0.8
FVC(liters)(predicted value)	91.1(1.10)	88.2(2.9)	0.4
FEV ₁ (liters)(predicted value)	90.5(1.4)	90.7(3.5)	0.9
FEV ₁ /FVC(percentage)	85.2(1.5)	88.0(1.8)	0.04
MMEF(L/S)(predicted value)	79.8(1.5)	84.3(4.1)	0.3
RV(liter)(predicted value)	116.8(0.9)	105.9(2.6)	0.1
TLC(liter)(predicted value)	93.9(3)	94.0(6.4)	0.9
RV/TLC(percentage)	38.2(5.3)	31.6(4.8)	0.004

extra restrictive ventillatory defect (1 patient). Mean of FEV₁/FVC in UC patients was significantly lower and RV/TLC in UC group was significantly higher than control group (p=0.047, 0.004 respectively) (Table 2). Duration of UC had reversed correlation with FEV₁/FVC (r=-0.3, p=0.014) (Figure 1) and direct correlation with RV/TLC (r=0.3, p=0.005) (Figure 2). There was a significant correlation between small airway obstructive pattern and duration of UC (p=0.05) but no significant correlation between other pulmonary disorders with condition of UC (severity, activity and duration).



Fig. 1: Correlation between UC duration and FEV_1/FVC .



Fig. 2: Correlation between UC duration and RV/TLC

Discussion

We investigated the prevalence and type of abnormal pulmonary function in patients with UC in comparison with healthy controls. We detected abnormal results in pulmonary function tests (defined as 80% of predicted values) in a surprisingly large proportion of UC patients (100%). Tzanakiz et al. study suggests that there is no difference in routine PFTs between UC patients and normal controls.²³ Kuzela et al. shown lung function abnormalities were significantly more frequent in patients with inflammatory bowel disease as compared to controls.²⁵ In Godget et al. study, PFT abnormalities were found in 30 (55%) subjects.²⁶ Herrlinger et al. showed that UC lung function tests significantly decreased in comparison to the control group. This could be shown for FEV1 (17% in UC).²⁷ Abnormal lung function tests were more prevalent in the IBD patients than in the controls that was seen in Ceyhan et al. study and the mean FEV1 was 3.1±0.9 liters (96±18% predicted), and did not result in statistically significant differences in comparison with controls.²⁸ In our study, the mean of FEV1 was 90.51 and 90.71 in UC and control groups respectively. Mohammed-Hussein showed that 15 out of 26 patients with UC (57.6%) exhibited

at least one pathological pulmonary function test (<80% of predicted value). Small airway obstruction was reported in the 15 patients, restrictive dysfunction in 30.7% and obstructive dysfunction in 11.5%. The impairment of PFTs was significant and more pronounced in patients with active disease, FVC (-14% of predicted), FEV1 (-9% of predicted) and FEF_{25-75%} (-32% of predicted).²⁹ Tunc *et al.* demonstrated that among the patients with ulcerative colitis, 6.2% had an obstructive and/or restrictive ventilatory defect.³⁰ Air trapping in our UC group was significantly more than control group (p=0.039). Songur et al. study showed that RV/TLC was significantly higher than those of controls.³¹ In our study, RV/TLC was 38.2 and 31.6 in UC and control groups respectively. Mean of RV/TLC in UC group was significantly higher than control group (p=0.004). The influence of disease activity on pulmonary function tests in IBD patients is still under debate and an influence of disease activity was not noticed. In our study, There was a significant correlation between small airway obstructive pattern and duration of UC (p < 0.05) but no significant correlation between other pulmonary disorders with condition of UC (severity, activity and duration). Regarding our findings except small airway obstructive pattern, there was no correlation between pulmonary abnormalities and severity, activity and duration of UC.

According to high prevalence of air trapping, small airway disease may be the prominent feature of lung involvement in UC patients. Therefore a meticulous work up for respiratory diseases is necessary in UC patients.

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Conflict of interest: None declared.

References

 Aghazadeh R, Zali MR, Bahari A, Amin K, Ghahghaie F, Firouzi F. Inflammatory bowel disease in Iran: A review of 457 cases. J Gastroenterol Hepatol 2005;20:1691-5. [16] 246187] [doi:10.1111/j.1440-1746. 2005.03905.x]

2 Rahimi R, Nikfar S, Abdollahi M. Meta-analysis technique confirms the effectiveness of anti-TNF-alpha in the management of active ulcerative colitis when administered in combination with corticosteroids. *Med Sci Monit* 2007;**13**:PI13-8. [175 99035]

- Rogler G, Schölmerich J. Extraintestinal manifestations of inflammatory bowel disease. *Med Klin (Munich)* 2004;99:123-30. [15024484] [doi:10. 1007/s00063-004-1003-2]
- 4 Danese S, Semeraro S, Papa A, Roberto I, Scaldaferri F, Fedeli G, Gasbarrini G, Gasbarrini A. Extraintestinal manifestations in inflammatory bowel disease. World J Gastroenterol 2005;11:7227-36. [16 437620]
- 5 Ceyhan B. Inflammatory bowel disease and lung. *Tuberk Toraks* 2006;**54**:292-8. [17001550]
- 6 Raj AA, Birring SS, Green R, Grant A, de Caestecker J, Pavord ID. Prevalence of inflammatory bowel disease in patients with airways disease. *Respir Med* 2008;102:780-5. [18321696] [doi:10.1016/j.rmed.2007. 08.014]
- 7 Mansi Á, Cucchiara S, Greco L, Sarnelli P, Pisanti C, Franco MT, Santamaria F. Bronchial hyperresponsiveness in children and adolescents with Crohn's disease. Am J Respir Crit Care Med 2000;161: 1051-4. [10712362]
- 8 Kelly MG, Frizelle FA, Thornley PT, Beckert L, Epton M, Lynch AC. Inflammatory bowel disease and the lung: is there a link between surgery and bronchiectasis? Int J Colorectal Dis 2006;21:754-7. [16625374] [doi: 10.1007/s00384-006-0094-9]
- 9 Xia K, Wolf J, Friedman S, Carr-Locke DL. Granulomatous tracheobronchitis associated with Crohn's disease. *MedGenMed* 2004;6:18. [15208530]
- 10 Black H, Mendoza M, Murin S. Thoracic manifestations of inflammatory bowel disease. *Chest* 2007;131: 524-32. [17296657] [doi:10.1378/ chest.06-1074]
- 11 Mahadeva R, Walsh G, Flower CD, Shneerson JM. Clinical and radiological characteristics of lung disease in inflammatory bowel disease. *Eur Respir J* 2000;15:41-8. [10678619] [doi:10.1183/09031936.00.15104100]
- 12 Kuźniar T, Sleiman C, Brugière Ó, Groussard O, Mal H, Mellot F, Pariente R, Malolepszy J, Fournier M. Severe tracheobronchial stenosis in a patient with Crohn's disease. Eur Respir J 2000;15:209-12. [10678648]
- 13 Le Roux P, Boulloche J, Briquet MT, Guyonnaud CD, Le Luyer B. Respiratory manifestation of Crohn's

disease. Apropos of a case in an adolescent. *Rev Mal Respir* 1995; **12**:59-61. [7899671]

- 14 Karadag F, Ozhan MH, Akçiçek E, Günel O, Alper H, Veral A. Is it possible to detect ulcerative colitisrelated respiratory syndrome early? *Respirology* 2001;6:341-6. [11844 126] [doi:10.1046/j.1440-1843.2001. 00347.x]
- 15 Baron FA, Hermanne JP, Dowlati A, Weber T, Thiry A, Fassotte MF, Fillet G, Beguin Y. Bronchiolitis obliterans organizing pneumonia and ulcerative colitis after allogeneic bone marrow transplantation. Bone Marrow Transplant 1998;21:951-4. [9613791] [doi: 10.1038/sj.bmt.1701198]
- 16 Bentur L, Lachter J, Koren I, Ben-Izhak O, Lavy A, Bentur Y, Rosenthal E. Severe pulmonary disease in association with Crohn's disease in a 13-year-old girl. *Pediatr Pulmonol* 2000;29:151-4. [10639206] [doi:10. 1002/(SICI)1099-0496(20002)29:2 <151::AID-PPUL10>3.0.CO:2-WI
- 17 Agrawal D, Rukkannagari S, Kethu S. Pathogenesis and clinical approach to extraintestinal manifestations of inflammatory bowel disease. *Minerva Gastroenterol Dietol* 2007; 53:233-48. [17912186]
- 18 Munck A, Murciano D, Pariente R, Cezard JP, Navarro J. Latent pulmonary function abnormalities in children with Crohn's disease. *Eur Respir J* 1995;8:377-80. [7789480] [doi:10.1183/09031936.95.08030377]
- 19 Casey MB, Tazelaar HD, Myers JL, Hunninghake GW, Kakar S, Kalra SX, Ashton R, Colby TV. Noninfectious lung pathology in patients with Crohn's disease. Am J Surg Pathol 2003;27:213-9. [12548168] [doi:10. 1097/00000478-200302000-00010]
- 20 Stein RB, Hanauer SB. Comparative tolerability of treatments for inflammatory bowel disease. *Drug Saf* 2000;23:429-48. [11085348] [doi:10. 2165/00002018-200023050-00006]
- 21 Storch I, Sachar D, Katz S. Pulmonary manifestations of inflammatory bowel disease. *Inflamm Bowel Dis* 2003;9:104-15. [12769444] [doi:10. 1097/00054725-200303000-00004]
- 22 Johnson NM, Mee AS, Jewell DP, Clarke SW. Pulmonary function in inflammatory bowel disease. *Digestion* 1978;**18**:416-8. [35436] [doi:10. 1159/000198228]
- 23 Tzanakis N, Bouros D, Samiou M,

Panagou P, Mouzas J, Manousos O, Siafakas N. Lung function in patients with inflammatory bowel disease. *Respir Med* 1998;**92**:516-22. [9692115] [doi:10.1016/S0954-61 11(98)90301-8]

- 24 Marvisi M, Borrello PD, Brianti M, Fornarsari G, Marani G, Guariglia A. Changes in the carbon monoxide diffusing capacity of the lung in ulcerative colitis. *Eur Respir J* 2000; 16:965-8. [11153600] [doi:10.1183/ 09031936.00.16596500]
- 25 Kuzela L, Vavrecka A, Prikazska M, Drugda B, Hronec J, Senkova A, Drugdova M, Oltman M, Novotna T, Brezina M, Kratky A, Kristufek P. Pulmonary complications in patients with inflammatory bowel disease. *Hepatogastroenterology* 1999;46: 1714-9. [10430329]
- 26 Godet PG, Cowie R, Woodman RC, Sutherland LR. Pulmonary function abnormalities in patients with ulcerative colitis. *Am J Gastroenterol* 1997; 92:1154-6. [9219789]
- 27 Herrlinger KR, Noftz MK, Dalhoff K, Ludwig D, Stange EF, Fellermann K. Alterations in pulmonary function in inflammatory bowel disease are frequent and persist during remission. *Am J Gastroenterol* 2002;97:377-81. [11866276] [doi:10.1111/j.1572-02 41.2002.05473.x]
- 28 Ceyhan BB, Karakurt S, Cevik H, Sungur M. Bronchial hyperreactivity and allergic status in inflammatory bowel disease. *Respiration* 2003; 70:60-6. [12584393] [doi:10.1159/ 000068407]
- 29 Mohamed-Hussein AA, Mohamed NA, Ibrahim ME. Changes in pulmonary function in patients with ulcerative colitis. *Respir Med* 2007;101: 977-82. [17049827] [doi:10.1016/j.rmed.2006.09.005]
- Tunc B, Filik L, Bilgic F, Arda K, Ulker A. Pulmonary function tests, high-resolution computed tomography findings and inflammatory bowel disease. Acta Gastroenterol Belg 2006; 69:255-60. [17168120]
 Songür N, Songür Y, Tüzün M,
- 31 Songür N, Songür Y, Tüzün M, Doğan I, Tüzün D, Ensari A, Hekimoglu B. Pulmonary function tests and high-resolution CT in the detection of pulmonary involvement in inflammatory bowel disease. J Clin Gastroenterol 2003;37:292-8. [1450 6385] [doi:10.1097/00004836-200 310000-00006]