ORIGINAL ARTICLE

# Pulmonary function tests in ulcerative colitis

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**Background:** Pulmonary impairment in patients suffering ulcerative colitis (UC) has been suggested by several investigators using standard pulmonary function tests (PFTs). This changes in pulmonary function associated with minimal respiratory symptoms have been documented, especially in patients with active disease. The aim of this prospective study was to determine airway resistance and lung volumes in patients with UC who have no respiratory symptoms in comparisons to a healthy control group. **Materials and Methods**: We evaluated a total of 30 patients with UC by means of spirometry, body plethysmography, and impulse oscillometry. The patients were not complaining of any pulmonary symptoms and did not present any history of previous respiratory diseases. As controls we examined 30 healthy subjects matched for gender, age, and smoking status. The relationship between PFT, lung volume, and airway resistance; and the activity, localization, and duration of the UC disease were analyzed. **Results**: There was a significant difference between airway resistances (kPa/L/s) measured by body plethysmography in patients with UC and those of the controls (R5hz; 0.60 ± 0.44 vs. 0.39 ± 0.13; $P < 0.001$) and R20hz (0.37 ± 0.19 vs. 0.29 ± 0.1, $P = 0.02$). There were no correlation between PFT, airway resistance and site and scoring activity ($P > 0.05$). **Conclusion**: Despite the lack of pulmonary symptoms, increased airway resistance was found in UC patients. We also have not found correlation between PFT, lung volume and airway resistance values and scoring of UC activity.

**Key words:** Body plethysmography, impulse oscillometry, ulcerative colitis

**How to cite this article:** Amra B, Ataabadi G, Emami MH, Hassanzadeh A, Golshan M, Soltaninejad F. Pulmonary function tests in ulcerative colitis. J Res Med Sci 2014;19:605-9.

## INTRODUCTION

The chronic inflammatory bowel disease (IBD), ulcerative colitis (UC) which is a diffuse process, involving the superficial mucosa of the colon is one of the common morbidities affecting many people throughout the world.[1] Although, the etiology of UC is unknown, genetic and environmental factors are thought to be responsible in the pathophysiology of UC.[2] Despite the known systemic manifestation of UC and a number of reports linking lung disease and UC, this association is often overlooked as an extra-intestinal manifestation of UC.[3-5] IBD is associated with a variety of extra-intestinal manifestations, although the lungs are not generally considered as a common site of involvement.[4,6] Some observations suggest that mucosal inflammation of the gastrointestinal tract can spill over to the airways.[5,7] Involvement of airway's epithelium is sometimes seen in association with UC, raising the possibility of a systemic mechanism affecting both bronchial and colonic epithelium.[7] An increased bronchial hyper-responsiveness in patients with IBD in the absence of bronchopulmonary symptoms and with normal baseline lung function had been reported.[8] Some patients might have abnormal pulmonary function and alveolar lymphocytosis in the absence of symptoms referring to respiratory system, and may not refer to a pulmonary physician.[3]

The association between IBD and pulmonary involvement has not been well-clarified and not emphasized; therefore, clinicians may not pay attention to pulmonary involvement in the IBD patients:[9] Furthermore, some observations suggest that an inflammation exists in the airways that is not detectable by routine pulmonary function tests (PFTs).[6,10] Body plethysmography is the gold standard for assessment of airway resistance. This method measures resistance of the entire airway from the mouth to the "average" alveolus. Impulse oscillometry (IO) is an alternative method, which measures airway resistance by sending a low energy sound wave produced by a loudspeaker into the lungs of a spontaneously breathing subject and looking for changes in flow in response to the dilatory effect of the applied energy.[11]

Although previous studies evaluated the relationship between UC and PFT, but no studies consider all

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**Received:** 30-11-2013; **Revised**: 07-01-2014; **Accepted**: 24-04-2014

above tests (IO, body plethysmography and spirometry) in asymptomatic patients. Therefore, the purpose of this study was to evaluate possible changes in airway resistance of patients suffering UC with no pulmonary symptoms. We used both body plethysmography and IO to determine the airway resistance and compare it with control group.

## MATERIALS AND METHODS

Ethical Committee of the institution approved the research protocol (Research project Number: 386393) and a written consent was signed by the participants or the gradients. Thirty consecutive suffering UC patients referring to the Department of Gastroenterology of the University Hospitals of Isfahan, Iran, were included in the study, if:

1. The diagnosis of UC established by the characteristic history coupled with a typical endoscopic appearance of the mucosa and confirmatory histology seen on colonic biopsy.[12]
2. They did not present any chronic pulmonary symptoms, including: chronic cough, phlegm, or dyspnea and did not represent any history of chronic lung diseases such as: Asthma, tuberculosis, chronic bronchitis, etc. Since mild obstructive lung disease in UC patients was attributed to smoking and allergy,[13] smokers and asthmatic patients were not included. Furthermore, patients with occupation in high-risk jobs for respiratory system were not included.

The patients have been treated with mesalazine (9 patients), sulfasalazine (6 patients), Asacol (4 patients), azathioprine + mesalazine (9 patients), azathioprine + sulfasalazine (1 patient) and azathioprine + Asacol (1 patients). None of them have received corticosteroid or methotrexate.

A group of 30 healthy age and sex matched individuals referred for checkup were enrolled as controls. The members of this group did not have any of the symptoms to be suspected for UC.

The disease was either active or quiescent. Disease activity in UC patients was evaluated with the simple clinical colitis activity index (SCCAI), as described by Walmsley *et al*.[14] Evaluation of disease activity was done at the time of pulmonary function measurements. In SCCAI, bowel movements per day, blood in stool, fever, tachycardia, anemia, erythrocyte sedimentation rate, and endoscopic appearance were evaluated. In study that was performed by Alavi Foumani *et al*.[10] UC activity was assessed by Rachmilewitz clinical activity index. Index ≥4 and index <4 were recognized as active and inactive respectively.

All patients underwent for spirometry and body plethysmography and IO tests as followings:

### Spirometry and body plethysmography

Lung volumes and subdivision indices were measured, using a body plethysmography machine (ZAN500 bodybox; nSpire Health, Inc., UK) according to the published standards and criteria.[15,16] After obtaining spirometric measurements, the subject was allowed to rest for 5 min before proceeding to the measurement of lung subdivisions. Briefly, the subject was taught the panting technique, while breathing through the mouthpiece of the body plethysmograph. The door was then closed and the measurements including residual volume (RV), functional residual capacity (FRC), and total lung capacity (TLC) were made. The results were corrected for body temperature, pressure, saturation automatically by the body-box software. All of the measurements were made by one trained technician. The output report of each subject was scrutinized qualitatively by one pulmonary physician (B.A.) before inclusion for statistical analysis.

### Forced oscillation technique

The equipment used for IO (IO Jaeger, Würtzburg, Germany) consisted of an impulse generator (a loudspeaker), a pneumotachograph, and a pressure transducer. The impulse interval was set at the default level of 0.33 s with a pulse length of 45 m. The superimposed pressure oscillations during normal volume spontaneous breathing are composed of several frequencies, allowing the assessment of resistance and reactance at several frequencies simultaneously. The frequency range of the signal was from 0 to 30 Hz, and we recorded R and X at 5 and 25 Hz.[17] we used two methods to improve accuracy of measurement and avoid over and under estimation. This is useful especially in subjects without good cooperation.

### Statistical analysis

Data were collected in a checklist. Statistical analysis was performed using the statistical package SPSS version 16 (SPSS Inc., Chicago, IL, USA) software. Data were expressed as mean ± standard deviation the Mann-Whitney test was used to assess differences in the laboratory parameters between the groups, and Spearman's correlation was used to analyze the correlation between the parameters. All the *P* values were two tailed: $P < 0.05$ were considered as statistically significant.

## RESULTS

Demographic characteristics of case and control groups have been presented in [Table 1].

**Table 1: Demographic characteristics of patients with UC and controls (mean ± SD)**

| Variable | UC | Controls | *P* value |
|---|---|---|---|
| Mean age, year (mean ± SD) | 36.06±10.19 | 36.2±10.63 | 0.48 |
| Male/female | 12/18 | 12/18 | |
| BMI (kg/m$^2$) (mean ± SD) | 24.6±4.2 | 26±3.86 | 0.09 |

BMI = Body mass index; UC = Ulcerative colitis; SD = Standard deviation

Pulmonary function tests were abnormal in 16 of 30 patients. Most common finding was decrease of forced expiratory flow (FEF) 25-75 (FEF 25-75 <60% of predicted value based on sex, age and height). There was a significant difference in the airway resistance between the patients with UC and control group ($P < 0.01$) [Table 2].

Mean values of maximal mid expiratory flow (MMEF) 25-75 in case and control groups were 3.28 ± 1.33 and 3.94 ± 1.92, respectively with significant statistical difference ($P = 0.021$). Mean values of forced expiratory volume in 1 s/forced vital capacity ($FEV_1$/FVC) in case and control groups were 82.34 ± 4.49 and 83.89 ± 2.91 respectively with significant statistical difference ($P = 0.05$). Results regarding different variable measure as shown in Table 2.

Patients were divided to three groups based on site of bowel disease: Left sided colitis (16 patients), pancolitis (8 patients) and proctosigmoiditis (6 patients). There was no significant difference between site of colon involvement and PFT abnormality ($P > 0.05$).

Relationship between the airway resistance and the disease activity index in UC as shown in [Table 3].

Since all patients were new case of UC, we didn't investigate relationship between duration of bowel disease and PFT.

**Table 2: Pulmonary function tests of patients with UC and controls**

| Variable | UC | Controls | *P* value |
|---|---|---|---|
| FVC (L) | 3.85±1.08 | 4.05±0.9 | 0.23 |
| $FEV_1$ (L) | 3.18±0.94 | 3.39±0.76 | 0.17 |
| $FEV_1$/FVC | 82.34±4.49 | 83.89±2.91 | 0.05 |
| FEF 25-75% (L/s) | 3.38±1.33 | 3.94±1.22 | 0.02 |
| RV | 2.9±0.82 | 2.13±0.95 | 0.19 |
| TLC | 6.04±1.4 | 6.15±0.97 | 0.36 |
| Specific airway resistance (SRaw) | 1.1±0.31 | 0.86±0.16 | 0.00 |
| Total airway resistance (SRaw) | 0.34±0.1 | 0.86±0.16 | 0.00 |
| R5hz (kPa/L/s) | 0.60±0.44 | 0.39±0.13 | 0.00 |
| R20hz (kPa/L/s) | 0.37±0.19 | 0.29±0.1 | 0.02 |
| X5hz (kPa/L/s) | −0.26±0.39 | −0.29±0.1 | 0.07 |

Data are expressed as mean ± SD. $P < 0.05$ was considered significant. FVC = Forced vital capacity; $FEV_1$ = Forced expiratory volume in 1 s; RV = Residual volume; TLC = Total lung capacity; R = Resistance; SD = Standard deviation; UC = Ulcerative colitis; FEF = Forced expiratory flow

**Table 3: Correlations with scoring activity of UC with pulmonary function tests**

| Variable | R value | *P* value |
|---|---|---|
| FVC (L) | −0.76 | 0.44 |
| $FEV_1$ (L) | −0.52 | 0.60 |
| $FEV_1$/FVC | −0.30 | 0.76 |
| FEF 25–75% (L/s) | −0.28 | 0.77 |
| Raw | −0.30 | 0.76 |
| SRaw | −0.72 | 0.47 |
| R5hz (kPa/L/s) | −0.89 | 0.37 |
| R20hz (kPa/L/s) | −0.78 | 0.43 |
| X5hz (kPa/L/s) | −0.94 | 0.06 |

Comparison between ulcerative colitis patients and controls with Mann-Whitney test. UC = Ulcerative colitis; FVC = Forced vital capacity; $FEV_1$ = Forced expiratory volume in 1 s; SD = Standard deviation; FEF = Forced expiratory flow

## DISCUSSION

The aim of this prospective study was to determine airway resistance and lung volumes in patients with UC who have no respiratory symptoms in comparisons to a healthy control group. This study was the first study that used both IO and body plethysmography to measure airway resistance in UC patient.

Respiratory function abnormalities are not uncommon in patients with UC.[18-34]

The presence of subclinical pulmonary disease in patients with minimal respiratory symptoms had been suggested; however, the pulmonary function abnormalities had revealed inconsistent results.[15] In fact, some authors could not detect differences in routine PFT between IBD patients and controls, while others suggested various changes, including a decrease in gas transfer factor, an increased FRC and increased RV during periods of active bowel disease,[20] decrease in MMEF rate, and an increased frequency of bronchial hyperresponsiveness.[7] The most frequently reported findings in UC are decrease of $FEV_1$/FVC and TLC, increase in RV and FRC.[17] However, such changes have been thought to appear, especially during exacerbations of underlying UC.[15] Douglas *et al*. found PFT abnormalities in 32% of patients with IBD and decreased lung transfer factor in 16%.[20] One previous study stated that the most prevalent abnormalities in lung function are decrease in diffusing capacity and increase in RV/TLC ratio.[8] This might mean that a restrictive pulmonary impairment is predominant in UC patients. This observation is not supported in our study.

In our study, in a group of UC patients obviously with less severe disease, a mild and statistically significant reduction of FEF 25-75 in patients with UC was found in comparison with the control group, the findings are less concerning than those suggested by the mentioned authors. However, our study revealed that even in such a UC population with less severe disease and no respiratory symptoms increased airway resistance can be detected by both body plethysmography and IO. Interestingly in our study, PFT and airway resistance abnormalities were not correlated with scoring of disease activity, meaning that pulmonary involvement is independent of the bowel disease activity. The main question addressed by this study was whether airway resistance was affected in patients with UC. The main finding was that UC is indeed accompanied by increased airway

resistance by IO and body plethysmography. We found that patients with UC showed increased R5, specific airway resistance despite their normal baseline spirometry values. Contrarily, no significant change was found in spirometry values between patients and control subjects, a finding suggesting *t* that increased resistance is an earlier finding disclosing pulmonary involvement in UC. In another study[10] the most common abnormal PFTs in UC patients were air trapping (increase of RV/TLC) and small airway obstructive pattern (decrease of FEF 25-75). Lung involvement in UC also presented with high-resolution computed tomography abnormalities up to 50% of patients in a study.[35]

In our study, all patients were new case of UC and therefore, we didn't investigate relationship between duration of bowel disease and PFT. In another study,[10] 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, and duration of UC.

Pulmonary involvement seems to be a more frequent extra-intestinal manifestation of UC than thus far supposed. The causes or confounding factors are uncertain.

## CONCLUSION

This study has shown that there is increased airway resistance and also dysfunction of the small airways in patients with UC despite their normal PFTs. However, further studies that include transbronchial biopsies are needed to verify the precise nature of our observations.[3]

We suggest that all patients with UC should be regularly evaluated for possible pulmonary involvement.

## AUTHORS' CONTRIBUTIONS

BA, MG, GA, ME, FS contributed to the design of the work. AH analyzed data and interpreted the work. FS and GA drafted the work. BA, FS, MG, AH, and ME were involved in revising article. All authors approved the version to be published and agreed to be accountable for all aspects of the work.

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**Source of Support:** Nil, **Conflict of Interest:** None declared.