# Effect of obstructive airway disease in patients with non-cystic fibrosis bronchiectasis

Mohammed Khalid, MD, FCCP; Sarfraz Saleemi, MBBS, MSc, MRCP (UK); Mohammed Zeitouni, MD, FCCP; Saleh Al Dammas, MD, FCCP; Muhammad Rehan Khaliq, MBBS, MRCP (UK)

**Background:** Extensive research has been devoted to cystic fibrosis-related brochiectasis, compared with non-cystic fibrosis bronchiectasis but the latter is more common and results in significant morbidity and mortality. We assessed the relationship between pulmonary function test (PFT) findings and sputum bacteriology, blood gases, number of hospital admissions and mortality in patients with non-cystic fibrosis bonchiectasis (NCFB).

**Methods:** We conducted a retrospective review of 88 consecutive patients admitted with exacerbation of bronchiectasis over 5 years from 1996 to 2001. Demographic and clinical data collected included gender, age, pulmonary functions, arterial blood gases, sputum bacteriology during stable and exacerbation periods, and number of hospital admissions due to exacerbation of bronchiectasis. A comparison was made between patients having obstructive airway disease (OAD group) and patients with normal or restrictive pulmonary functions (non-OAD group).

**Results:** OAD in patients with NCFB adversely affected clinical outcome. There was a significant increase in *Pseudomonas* colonization (60.3% vs. 16%; $P<0.0003$), hypercapnic respiratory failure (63.4% vs. 20%; $P<0.0003$), and mean number of admissions due to exacerbation (6 vs. 2; $P<0.0001$) in the OAD group as compared with the non-OAD group. Although mortality was increased in the OAD group, the difference was not statistically significant.

**Conclusion:** Patients with NCFB who have OAD have a significantly higher rate of colonization with *Pseudomonas aeruginosa* (PSA), hypercapnic respiratory failure, a greater number of hospital admissions due to exacerbation of bronchiectasis, and a higher mortality compared with patients with restrictive or normal pulmonary functions.

**Key words:** Non-cystic fibrosis bronchiectasis, obstructive airway disease, pulmonary function tests, morbidity, mortality

*From the Section of Pulmonology, Department of Medicine, King Faisal Specialist Hospital and Research Centre, Riyadh, Saudi Arbaia*

*Correspondence to:*
*Dr. Mohammad Khalid*
*Head, Section of Pulmonology*
*MBC 46*
*King Faisal Specialist Hospital & Research Centre*
*P.O.Box 3354, Riyadh 11211*
*E-mail: mkhalid@kfshrc.edu.sa*

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Bronchiectasis is defined as permanent and irreversible dilatation of bronchi leading to retention of respiratory secretions and recurrent infective exacerbations.[1] Non-cystic fibrosis bronchiectasis (NCFB) is a common pulmonary health problem associated with significant morbidity and mortality in underdeveloped countries.[2] It is also a growing concern in industrialized countries where the high incidence of HIV is a major factor in its causation.[3-5] Extensive research has been devoted to cystic fibrosis-related bronchiectasis, but non-cystic fibrosis bronchiectasis is much more common and results in significant mortality and morbidity Especially important are pulmonary function tests and bacteriological aspects, which are important determinants of prognosis in patients suffering from this debilitating and often difficult to treat medical condition. Patients with NCFB predominantly have obstructive airway disease (OAD), which usually results in colonization with different organisms, most notably *Pseudomonas aeruginosa*.[6-7] Colonization in turn causes more airway damage, resulting in further airway obstruction, worsening hypoxemia and hypercapnia, and increasing morbidity and mortality.[8] The purpose of this study was to identify the effect of obstructive airway disease on morbidity and mortality in patients with NCFB. This was the first study of the effect of obstructive airway disease on morbidity and mortality in Saudi patients with NCFB.

## Methods

We performed a retrospective review of medical records of patients with an established diagnosis of NCFB during a 5-year follow-up period from 1996 to 2001 at King Faisal Specialist Hospital and Research Center, a tertiary care medical facility. The diagnosis of bronchiectasis was established by the presence of dilated bronchi on X-ray or on computerized tomography (CT) of the chest. Patients who were diagnosed as having cystic fibrosis by appropriate tests were excluded. Investigations of the etiology of bronchiectasis in this group were reviewed. Patients in whom no underlying

etiology was found were labeled as NCFB of unknown etiology. Pulmonary function tests (PFTs) performed on NCFB patients during the follow-up period were analyzed to find the type of airway defect and were grouped into obstructive (OAD) and non-obstructive (non-OAD) groups. Patients with mixed obstructive and restrictive defect were grouped along with OAD. The non-OAD group included patients with restrictive or normal PFTs. Bronchodilator response to the beta-agonist, salbutamol (standard beta-agonist used in our PFT laboratory), was determined as a measure of reversibility according to American Thoracic Society criteria of more than 12% and a 200 mL increase in FEV1 after inhaled beta-agonist in all patients with OAD.[9] Patients in the OAD group were classified as having mild, moderate and severe obstruction according to their $FEV_1$ values: 65-80%, 33-64% and <33% predicted, respectively.[9] All sputum cultures during the study period were analyzed and patients having *Pseudomonas aeruginosa* (PSA) in sputum cultures more than once were labeled as PSA colonized. All sputum cultures during their last exacerbation period were also identified to see the bacteriological aspect of exacerbation. OAD group and non-OAD group were compared in terms of sputum bacteriology, arterial blood gas analysis, hospital admissions and mortality. Fisher's Exact test was used to compare the characteristics of the two groups and to calculate two-tailed *P* values on the GraphPad's QuickCalcs system. Mean values were compared using the paired t test.

## Results

Eighty-eight consecutive patients with a mean age of 46 years (range 17-81) were included in this retrospective study. Fifty-five patients (62%) had no known etiology for their NCFB. We postulated that it was related to childhood respiratory tract infections. NCFB in 26 patients (29.5%) was due to old pulmonary tuberculosis (TB). Only 7 patients (8%) had rare underlying causes, namely immune deficiency, immotile cilia syndrome and allergic bronchopulmonary aspergillosis. Sixty-three patients (71.5%) had obstructive airway disease or mixed airway disease (OAD group) on PFT ($FEV_1$<80% predicted), of which only 7 patients (11.1%) had a significant response to the beta-agonist (salbutamol) inhaler (more then 12% and 200 mL increase in $FEV_1$ as defined by the American Thoracic Society) (Table 1). Forty-four patients in the OAD group (69.8%) had severe obstruction ($FEV_1$<33%). Twenty-five patients (27.5%) had either restrictive or normal PFT (non-OAD group). Multiple sputum cultures showed that 38 patients in the OAD group (60.3%) were PSA colonized while only 4 (16%) were PSA colonized in the non-OAD

**Table 1.** Demographic and cinical features of patients in the obstructive (OAD) and non-obstructive (non-OAD) airway disease groups.

| | OAD (n=63) n (%) | non-OAD (n=25) n (%) | *P* values |
|---|---|---|---|
| Males | 24 (38.1) | 14 (56) | |
| Females | 39 (61.9) | 11 (44) | |
| Age (range) (years) | 48 (17-81) | 38 (17-71) | |
| Etiology | | | |
| Unknown | 41 (65.1) | 14 (56) | 0.47 |
| Post tuberculosis | 18 (28.6) | 8 (32) | 0.953 |
| Rare causes* | 4 (6.3) | 3 (12) | 0.655 |
| Hypercapnic RF | 40 (63.4) | 5 (20) | 0.0003 |
| PSA colonized | 38 (60.3) | 4 (16) | 0.0003 |
| Sputum culture during last exacerbation | | | |
| *P. aeruginosa* | 34 (53.9) | 4 (16) | 0.003 |
| *H. influenzae* | 4 (6.3) | 7 (28) | 0.016 |
| *S. pneumonae* | 3 (4.7) | 5 (20) | 0.067 |
| *S. aureus* | 1 (1.6) | 0 (0) | 0.50 |
| *M. catarrhalis* | 2 (3.2) | 4 (16) | 0.09 |
| Mean number of exacerbations | 6 | 2 | <0.0001 |
| Mortality† | 6 (9.5) | 1 (4) | 0.669 |

*Includes immune deficiency, immotile cilia syndrome and allergic bronchopulmonary aspergillosis
†Deaths due to bronchiectasis over 5 years
PSA, *Pseudomonas aeruginosa*

group ($P$<0.0003). Sputum cultures during exacerbation in the OAD group grew PSA in 34 (53.9%) patients while 4 patients (16%) in the non-OAD group grew PSA during exacerbation ($P$<0.003). Arterial blood gas analysis showed that 40 patients (63.4%) in the OAD group had hypercapnia ($PCO_2$ more than 6 kPa) as compared to 5 patients (20%) in the non-OAD group ($P$<0.0003). The mean number of admissions due to exacerbations in the OAD group was 6 as compared to 2 in non-OAD group $P$<0.0001. Six patients (9.5%) in OAD group died over a 5-year period versus 1 (4%) in the non-OAD group. OAD was a major determinant of morbidity and mortality in patients with NCFB.

## Discussion

Non-cystic fibrosis bronchiectasis, a common pulmonary problem in developing countries, causes progressive pulmonary disease and respiratory failure and is associated with significant morbidity and mortality. Because of the pulmonary infections associated with AIDS, NCFB will be of growing concern in developed countries as well.[10-11] Our study addresses many unresolved issues related to this significant pulmonary problem and emphasizes the need for future research to improve the quality of life and survival of patients with NCFB. In our review we observed that a significant number of patients with NCFB have OAD, based on their PFTs.[11] Patients with OAD are more frequently colonized with *P. aeruginosa*, suffer a higher incidence of hypercapnic respiratory failure, require more frequent hospitalizations and have increased mortality.[12-13]

We believe that an increased degree of airway obstruction, by causing greater stagnation of secretions and thus producing a fertile ground for colonization with different bacteria (most significantly with *P. aeruginosa*), was responsible for poor pulmonary hygiene. *P. aeruginosa* colonization leads to increased inflammation of the airways causing increased obstruction. Various proteolytic enzymes, produced by bacteria and different inflammatory cells, lead to progressive destruction of airways and pulmonary parenchyma resulting in respiratory failure.[14-16] In our review, once patients were colonized with *P. aeruginosa*, almost all their exacerbations were due to the same organism, thus emphasizing the need for early institution of an anti-pseudomonal therapy in this particular group of patients. This could be of significant benefit in respect to outcome during acute exacerbation and would be necessary to break the vicious cycle of airway destruction due to recurrent exacerbations. The proper and timely use of antibiotics can help in slowing the progression of the disease and possibly improve long-term survival. Also, long-term use of anti-pseudomonal antibiotic therapy, either by inhalation or oral, may be of benefit in this subgroup of patients, as shown in some studies.[17-19]

A large number of our patients with NCFB failed to show a bronchodilator response to a beta-agonist (salbutamol). This was most likely due to persistent infection and inflammation caused by colonized organisms. Repeated exacerbations of bronchiectasis cause an increase in sputum quantity, and retention of these thick purulent secretions leads to airway obstruction. This is in contrast to bronchial asthma where airway inflammation and smooth muscle spasm play a major role in airway obstruction.[20-21]

Although some case reports suggest a beneficial response to beta-agonists like salbutamol in NCFB by increasing mucociliary clearance, but these reports are not substantiated by any large clinical trials. Until proven otherwise we believe that beta-agonists have a minimal role in management of NCFB except in patients who show a significant bronchodilator response to beta-agonists.[22]

Long-term use of anti-inflammatory drugs like inhaled steroids should have a beneficial effect, as shown in some reports,[23-24] as should chest physiotherapy and uses of devices like flutter valves, in increasing mucociliary clearance.[25-26] A large-scale study is needed to establish the long-term benefit of anti-inflammatory drugs like steroids and other anti-inflammatory agents as well as chest physiotherapy. These treatment modalities may prevent progression of obstructive airway disease, decrease airway colonization with *P. aeruginosa*, and reduce morbidity and mortality in patients with NCFB.

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