

Bronchiectasis in northern Iraq clinical and bacteriological characteristics during acute exacerbation

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ABSTRACT

Context: Bronchiectasis is a relatively common disease in developing countries. The pathogens responsible for its acute exacerbations vary from one area to another.

Objectives: To study the characteristics of patients with bronchiectasis in Northern Iraq, and to identify the types of pathogens responsible for the acute exacerbations.

Design: Case series study.

Setting: Respiratory Care Unit and general medical wards in Ibn-Sina Teaching Hospital in Mosul, during the years 2002-2004.

Patients and Methods: Fifty patients with bronchiectasis (16 males and 34 females) presenting during an acute exacerbation underwent clinical and radiological evaluation with sputum Gram (Gm) stain and culture.

Results: The cause of the disease was readily identifiable in 36% of patients. Tuberculosis was the predominant aetiology. *Streptococcus pneumoniae* and *klebsiella pneumoniae* were the commonest pathogens. Gm negative bacilli were responsible for 36% of cases overall, and were especially important in those with long standing disease (≥ 15 years). *Pseudomonas aeruginosa* was related to more extensive disease. Most of the isolates were sensitive to ciprofloxacin and cefotaxime.

Conclusion: Gm negative bacilli should be considered in antibiotic selection during acute exacerbation of bronchiectasis, especially in long standing and extensive disease.

Keywords: bronchiectasis, Gram negative bacilli

الخلاصة

السياق: توسع القصبات مرض شائع نسبياً في البلدان النامية. الجراثيم المسببة للنوبات الحادة تختلف من بلد إلى آخر.

الهدف: دراسة خصائص مرضى توسع القصبات في شمال العراق والتعرف على الجراثيم المسببة للنوبات الحادة للمرض.

التصميم: دراسة حالات متسلسلة.

مكان وزمان إجراء البحث: العناية التنفسية المركزة وردهات الباطنية في مستشفى ابن سينا في الموصل شمال العراق خلال السنوات 2002-2004.

المشاركين في البحث: خمسون مريضاً مصاباً بتوسع القصبات (16 ذكراً و 34 أنثى) تمت دراستهم أثناء نوبات المرض الحادة حيث خضع المرضى للمعاينة السريرية والفحوصات الإشعاعية مع إجراء فحص القشع بصيغة غرام وزرعه.

النتائج: كانت أسباب المرض ظاهرة في 36% من الحالات فقط، وكان التدرن هو السبب الرئيسي. وأظهر فحص القشع أن المكورة السبحية الرئوية هي مقدمة الجراثيم المسببة للنوبات الحادة تليها الكليبيسيلا الرئوية، وأن العصيات سالبة الغرام مسؤولة عن 36% من الحالات وخاصة عند المرضى الذين قد مضى على مرضهم 15 سنة أو أكثر. أكثر الجراثيم التي تم عزلها من قشع المرضى كانت حساسة لعقار السبروفلوكساسين والسيوفوتاكسيم.

الاستنتاج: عند علاج النوبات الحادة لتوسع القصبات يجب اختيار المضادات الحيوية التي تغطي بفاعليتها الجراثيم سالبة الغرام وخاصة بالنسبة للمرضى المصابين بالمرض لفترة طويلة والحالات المتقدمة من المرض.

Bronchiectasis is still a relatively common disease in developing countries and its infective exacerbation is an important cause of hospital admission⁽¹⁾.

Contrary to healthy non-smokers, whose lower airways are sterile^(2, 3), patients with bronchiectasis often have their lower respiratory tract colonized with potentially pathogenic microorganisms (PPMs) even during the "stable" periods (i.e., in between exacerbations)⁽³⁾.

Although the role of these PPMs in bronchiectasis is not fully established, evidence suggests their contribution to persistent inflammation and enzymatic destruction promoting progressive tissue damage and airway obstruction⁽⁴⁾. During exacerbations of the disease, these pathogens are responsible for the acute inflammatory process⁽⁵⁾.

Studies all over the world have shown different patterns of bacteriological profile of sputum culture during exacerbation⁽⁶⁾.

This study aims at evaluating the characteristics of patients with bronchiectasis in the north of Iraq and the apparent underlying causes, and to determine the types of pathogenic microorganisms during exacerbations of the disease and their antibiotic sensitivity, in order to guide antibiotic selection. Findings are compared with other studies, and the significance of bacterial isolates is discussed.

PATIENTS AND METHODS

Fifty patients with bronchiectasis (16 males and 34 females) were included in the study. Their mean age (\pm SD) was (47.08 \pm 19.2) ranging from 10-93 years. The patients were received in Ibn-Sina Teaching Hospital in Mosul during the years 2002-2004 and were admitted in the Respiratory Care Unit or the general medical wards; some of them were investigated as outpatients. The hospital serves as a referral centre for Nineveh Governorate and receives patients from other areas in the north of Iraq.

The diagnosis of bronchiectasis was based on a history of chronic productive cough, with or without haemoptysis, dyspnoea or wheezing, together with compatible findings on clinical examination, supported by a chest radiograph, and in some patients by a chest CT scan (14 patients).

All patients were received during an acute exacerbation defined by the presence of at least four of the criteria derived from O'Donnell *et al*⁽⁷⁾, and listed in Table 1. The patients were questioned about the duration

of their bronchiectatic symptoms. A detailed past history was taken, with a special emphasis on childhood infection like measles, whooping cough and pneumonia. History and radiological evidence of previous tuberculosis was particularly emphasized. Patients less than 30 years old, with suggestive clinical picture underwent sweat chloride test to exclude cystic fibrosis. Assessment of underlying causes however, did not include detailed laboratory, including immunological, investigations that are required to diagnose rarer causes. Chest radiographs and CT scan images were also reviewed to assess the percentage of patients with extensive cystic bronchiectasis, and the presence or absence of pneumonic consolidation.

Bacteriological studies: Sputum samples were obtained prior to antibiotic therapy. Gm staining was performed first, and only sputum samples of Murray-Washington classification⁽⁸⁾ degree IV or V were processed (degree IV: 10-25 epithelial cells and > 25 leukocytes; degree V: < 10 epithelial cells and > 25 leukocytes per low magnification field). Sputum samples were then cultured on blood, McConkey and chocolate agar. The first two were incubated aerobically, whereas chocolate plate was put in 10% CO₂ using a candle jar, all in a temperature range of 35-36C, for at least 48 hours of incubation. Classical bacteriological identification was followed including morphological and routine biochemical tests (i.e., catalase, oxidase, and urase tests)

Antibiotic sensitivity was assessed according to the clinical laboratory standards⁽⁹⁾. The antibiogram was identified in accordance to the standards of sensitivity testing.

Microorganisms that were considered non pathogenic included *Streptococcus viridans*, *Niesseria spp*, *Corynebacterium spp*, *Candida spp.*, *Enterococcus spp*, and coagulase negative staphylococci⁽¹⁰⁾. Other microorganisms were considered potentially pathogenic.

Statistical evaluation: Data were analyzed using Chi square test.

RESULTS

Of the fifty patients studied, 16 were males (32%) and 34 were females (68%). The duration of their bronchiectatic symptoms varied from a minimum of 2 years to as long as 50 years (mean of 13.64 \pm 11.62). However, the majority of patients (33) had symptoms of fewer than 15 years (66%), and only 17 patients (34%) had been complaining from the disease for at least 15 years. (Table 2).

Table (1): Symptoms of acute exacerbation of bronchiectasis*

Change in sputum production
Increased dyspnoea
Increased cough
Fever (temperature, >38.0°C)
Increased wheezing
Malaise, fatigue, lethargy, or decreased exercise tolerance
Reduced pulmonary function
Radiographic changes consistent with a new pulmonary process
Changes in chest sounds

* O'Donnell et al⁽⁹⁾**Table (2): Baseline characteristics of the 50 patients evaluated**

Characteristics	Values
Age (years): mean (SD)	47.08(+19.25)
Sex	
Males	16(32%)
Females	34(68%)
Duration (years)	
Mean (SD)	13.64(+11.62)
< 15 years	33(66%)
≥15 years	17(34%)
Aetiology	
Unknown	32(64%)
Tuberculosis	12(24%)
Childhood whooping cough	2(4%)
Childhood pneumonia	2(4%)
Bronchial obstruction	1(2%)
Cystic fibrosis	1(2%)
Imaging	
Chest XR (only)	34(68%)
Chest CT	14(28%)
Chest MRI	2(4%)
Findings	
Cystic bronchiectasis	14(28%)
Pneumonia	14(28%)

The cause of the disease was not determined in 32 patients (64%). Among identified causes, tuberculosis was the commonest; followed by childhood whooping cough, childhood pneumonia, cystic fibrosis and bronchial obstruction (Table 2).

Radiological assessment showed that 14 patients (28%) have extensive cystic bronchiectasis (the severe form of the disease). Pneumonia was diagnosed by chest radiograph in 14 patients (28%) and thought to be responsible for the exacerbation (Table 2).

Sputum Gm stain and culture was positive in all but one patient (98%). There was a high concordance between the Gm stain and culture result. *Streptococcus*

pneumoniae was the commonest PPM detected in 18 patients (36%), followed by *Klebsiella pneumoniae*, *Pseudomonas aeruginosa* and *Haemophilus influenzae*. *Moraxella catarrhalis*, *Staphylococcus aureus*, other Gm negative bacilli and *Nocardia asteroides* were detected in 2 patients each (Table 3). Collectively Gm negative bacilli were responsible for the acute exacerbation in 18 patients (36%).

Considering patients with long standing disease (≥ 15years), Gm negative bacilli were detected in 9 patients (52.9%), compared to 9 patients (27.3%) in whom the disease was for less than 15 years (Table 4). The relationship was not statistically significant, $P = 0.073$ (>0.05).

Table (3): Potentially pathogenic microorganisms isolated and the frequency of detection.

PPMs	No. of patients (percent)
<i>Streptococcus pneumoniae</i>	18 (36%)
<i>Klebsiella pneumoniae</i>	9 (18%)
<i>Pseudomonas aeruginosa</i>	7 (14%)
<i>Haemophilus influenzae</i>	7 (14%)
<i>Moraxella catarrhalis</i>	2(4%)
<i>Staphylococcus aureus</i>	2 (4%)
Other Gm negative bacilli (<i>Enterobacter Spp</i> and <i>Escherichia coli</i>)	2 (4%)
<i>Nocardia asteroides</i>	2 (4%)
No significant growth	1 (2%)

Table (4): Difference in PPMs detection between patients of short duration of disease < 15 years and those of long duration >15 years.

PPMs	Patients of short disease duration <15y (33 patients)	Patients of long disease duration >15y (17 patients)
<i>Streptococcus pneumoniae</i>	16(48.5%)	2(11.8%)
<i>Klebsiella pneumoniae</i>	5(15.2%)	4(23.5%)
<i>Pseudomonas aeruginosa</i>	3(9.1%)	4(23.5%)
<i>Haemophilus influenzae</i>	5(15.2%)	2 (11.8%)
<i>Moraxella catarrhalis</i>	0(0)	2 (11.8%)
<i>Staphylococcus aureus</i>	1(3%)	1 (5.9%)
Other Gm negative bacilli	1(3%)	1 (5.9%)
<i>Nocardia asteroides</i>	2(6.1%)	0(0)
No significant growth	0(0)	1(5.9%)

Gm negative Bacilli	9(27.3%)	9(52.9%)
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$X^2 = 3.481$, P-value= 0.073 (>0.05 N.S)

Table (5): Difference in PPMs detection between patient with extensive cystic bronchiectasis and patients with less severe disease..

PPMs	Patients with extensive cystic bronchiectasis (14 patients)	Patients with less severe disease (36 patients)
<i>Streptococcus pneumoniae</i>	3(21.4%)	15(41.7%)
<i>Klebsiella pneumoniae</i>	2(14.3%)	7(19.4%)
<i>Pseudomonas aeruginosa</i>	4(28.6%)	3(8.3%)
<i>Haemophilus influenzae</i>	1(7.1%)	6(16.6%)
<i>Moraxella catarrhalis</i>	1(7.1%)	1(2.78%)
<i>Staphylococcus aureus</i>	1(7.1%)	1(2.78%)
Other Gm negative Bacilli	1(7.1%)	1(2.78%)
<i>Nocardia asteroides</i>	1(7.1%)	1(2.78%)
No significant growth	0(0)	1(2.78%)

Gm negative bacilli	7(50%)	11(30.6%)
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$X^2 = 3.43$, P-value= 0.064 (>0.05 N.S)

Patients with extensive cystic bronchiectasis were found to be more likely to yield *Pseudomonas aeruginosa* (PA) in their sputum during acute exacerbation; (28.6%) compared with (8.3%) in less severe disease (Table 5), but the association was not statistically significant (P = 0.064 (>0.05)).

Having pneumonic consolidation on chest radiograph did not affect the types of pathogens detected (compared with patients without pneumonia), nor was there any difference between patients with underlying tuberculosis if compared with other causes.

Table (6): Antibiotic sensitivity of the major bacterial isolates detected.

	Ciprofloxacin	Cefotaxime	Gentamicin	Amoxicillin	Cephalexin	chloramphenicol
<i>Streptococcus pneumoniae</i> (18 isolates)	13 (72.2%)	13 (72.2%)		3 (16.7%)	5 (27.3%)	
<i>Klebsiella pneumoniae</i> (9 isolates)	6 (66.7%)	5 (55.6%)	7 (77.8%)			5 (55.6%)
<i>Pseudomonas aeruginosa</i> (7 isolates)	6 (85.7%)	5 (71.4%)	4 (57.1%)			
<i>Haemophilus influenzae</i> (7 isolates)	4 (57.1%)	4 (57.1%)		4 (71.4%)	3 (42.1%)	

NB. The figures represent the number of isolates found sensitive to the antibiotic.

For the four major pathogens isolated, the sensitivity pattern was shown in Table 6. The majority of *Streptococcus pneumoniae* (SP) strains was resistant to amoxicillin and cephalexin, as only 16.7% and 27.2% of the strains were sensitive to these two antibiotics, respectively. Most of the bacterial isolates were sensitive to ciprofloxacin and cefotaxime.

DISCUSSION

More than two thirds of the study group were females suggesting that bronchiectasis is a predominantly female disease. Similar findings of female predominance were shown in other studies⁽¹⁰⁻¹³⁾. One study had concluded that non-cystic fibrosis bronchiectasis is even more aggressive in females⁽¹⁴⁾.

The majority of cases (64%) were of unknown cause. This is similar to other studies, which failed to identify a cause in a high percentage of patients^(15, 16), even after extensive investigation⁽¹²⁾. Tuberculosis was the most common identifiable cause, which was in agreement with studies performed in other developing countries^(17, 18), while tuberculosis was not an important cause of bronchiectasis in the more developed world^(13, 15), reflecting the prevalence of the disease in the former.

Sputum was used as a representative specimen for the bronchial microbiological status during exacerbation, as sputum was shown to be comparable to protected catheter specimen for that purpose⁽¹⁰⁾. These acutely ill patients may not tolerate the more invasive procedures of obtaining bronchoscopic bronchial wash or bronchoalveolar lavage.

The vast majority of sputum samples were positive for PPMs. Lower rates of positive culture (50-60%) were detected in other studies that included patients in stable condition without acute exacerbation^(10, 15, 17).

SP was the most common PPM detected, followed by *K. pneumoniae*; PA and *H. influenzae* came next. Many earlier studies in the western countries have noted that SP and *H. influenzae* are the major pathogens⁽¹⁹⁾, although in a recent study from USA (that included an aging cohort), PA was the most common⁽¹³⁾.

In other recently conducted studies from the Far East (Hong Kong⁽⁶⁾, Thailand⁽¹⁷⁾ and Taiwan⁽²⁰⁾) and from Saudi Arabia⁽¹⁸⁾, PA was the most important pathogen, followed by *H. influenzae*. While in Spain⁽¹⁰⁾, and UK⁽¹⁷⁾, *H. influenzae* was the most common followed by PA.

Our study draws attention to the importance of Gm negative bacilli in the exacerbation of bronchiectasis, where

these microorganisms contributed to 36% of cases. Interestingly, patients with long standing disease (≥ 15 years) were even more likely to harbor Gm negative bacilli, compared to those with shorter duration of symptoms (52.9% versus 27.3%). Such observation although did not reach statistical significance (probably because of small sample size) is explained by the frequent long standing exposure to antibiotic therapy, which had resulted in the emergence of the more resistant Gm negative bacilli. This finding which, to the best of our knowledge, had not been reported in other studies, can have an important therapeutic implication.

Many studies have shown that patients with bronchiectasis who have PA colonizing their airways are more likely to have a more severe disease, with lower FEV₁⁽²¹⁾, and more advanced radiological features of extensive disease and cystic changes⁽²²⁾. On the other hand, patients with cystic bronchiectasis as shown by CT scan were more likely than less severely affected patients to grow PA in their sputum culture⁽²³⁻²⁴⁾. PA infection of bronchiectatic airways contributes to more rapid decline in pulmonary function⁽²⁵⁾. The above observations are consistent with the findings of this study; where patients with radiological evidence of extensive cystic bronchiectasis were more likely to have PA colonizing their airways than other patients (28.6% vs 8.3%). Although this relation had not reached statistical significance, PA should be especially considered in these severely affected patients.

Nocardia asteroides, which has previously been shown to colonize bronchiectatic cavities⁽²⁶⁾, was isolated in 2 (4%) of our patients. There were rare reports of invasive nocardiosis in bronchiectatic patients⁽²⁷⁾.

For the four major pathogens, most of the isolates were sensitive to ciprofloxacin and cefotaxime. While the majority were resistant to amoxicillin and cephalexin indicating a high percentage of resistance to commonly used antibiotics. These findings are supported by clinical studies recently performed which suggest that ciprofloxacin (and other quinolones) are effective in the treatment of acute exacerbation of bronchiectasis and are equivalent to ceftazidime⁽²⁸⁾ and superior to amoxicillin⁽²⁹⁾ in this regard.

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