Chronic lung sepsis in a sample of Egyptian patients with type II diabetes mellitus

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Background/aim
Chronic lung sepsis is one of the major causes of chronic respiratory symptoms such as chronic cough and pus formation. It has received very little attention over recent decades. In addition, failure of its characterization in immunocompromised patients such as diabetics has led to under-recognition and lack of early management.
Patients and methods
In this study, 61 patients with symptoms and signs of chronic lung disease were enrolled from Ahmed Maher Teaching Hospital in Egypt. Of them, 32 fulfilling the criteria of chronic lung sepsis were classified into two groups: diabetic (17 patients) and nondiabetic (15 patients). All of the patients were subjected to detailed medical history, thorough clinical examination, laboratory investigations, sputum culture and sensitivity, and high-resolution computed tomography of the chest.
Results
A total of 23 cases were diagnosed as bronchiectasis, four cases were diagnosed as lung abscess, two cases were pyopneumothorax, whereas there was one case each of infected cyst, empyema, and infected emphysematous bullous. Sputum culture showed that gram-negative organisms were more evident in the diabetic group. The management of cases of chronic lung sepsis showed the use of double or triple antimicrobial therapy in the diabetic group.
Conclusion
Targeting good control of pneumonia in patients with type II diabetes mellitus using double or triple antimicrobial therapy is essential to inhibit the progression of pulmonary infections to chronic lung sepsis.

Keywords:
bronchiectasis, diabetes mellitus, lung abscess, pneumonia, sepsis

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Introduction

Chronic lung sepsis is a group of diseases that include the foremost common clinical suppurative lung diseases empyema, lung abscess, bronchiectasis, infected cyst or bullous, and others. Till recently, bronchiectasis was the foremost common assortment of them all [1]. The common characteristics of this group are recurrent infection, severe neutrophilic inflammation, and poor clearance of infected material. Classic forms of them are characterized by pus in expectorated sputum, sampled with drainage procedures through pleural catheters or with bronchoalveolar lavage [2].

Chronic lung sepsis stays a serious medical problem despite the provision of antimicrobial medications. However, these pulmonary infections can occur in persons with structural lung diseases, genetic abnormalities, and disorders of innate or acquired immunity [3].

Diabetes is the seventh main cause of death globally. It is a chronic disease with an estimated number of 463 million individuals all over the world in 2019, representing 8.8% of the adult population; type 2 diabetes represented about 90% of the cases. In 2019, diabetes resulted in nearly 4.2 million deaths [4]. The International Diabetes Federation ranked Egypt ninth worldwide in the number of diabetes cases, with a prevalence of 15.56% among adults [4].

Intense efforts are required for better identification and quantification of pulmonary risks in patients with diabetes mellitus (DM). These are carried out by exploring the mechanisms and examining the relation of these comorbidities [5].

Certain types of pulmonary infections are more prevalent among diabetics than nondiabetics. The clinical spectrum and radiological presentation of such infections differ from those of nondiabetics [6].

Worldwide, *Streptococcus pneumoniae* and *Haemophilus influenzae* are the leading causes of bacterial pneumonia. The most common pathogens identified in the most recent population-based active surveillance were human rhinovirus, influenza virus, and *S. pneumoniae* [7].

Computed tomography (CT) has altered medical imaging dramatically since seventies. Its ability to produce detailed pictures of the lungs and thorax has made it the imaging modality of choice in respiratory medicine. It has the prospective to provide necessary insights into the underlying pathophysiological changes of chronic lung sepsis [8].

The aim of this work was to verify the relation of pneumonia and chronic lung sepsis, including bronchiectasis, lung abscess, empyema, and infected lung cyst or bullous, in patients with type II DM in a sample of adult Egyptian patients.

Patients and methods

Patients and study design

This cross-sectional study included 61 inpatients or patients visiting chest clinics of Ahmed Maher Teaching Hospital with age range between 30 and 71 years. All patients had symptoms and signs of chronic pulmonary diseases. Only 32 patients who fulfilled the inclusion criteria of chronic lung sepsis were involved in our study.

Of them, 23 were males and only nine patients were females. The inclusion criteria included documented clinical records by a respiratory physician, persistent and recurrent infections, intense neutrophilic inflammation, and poor clearance of the infected material. The classic form of these diseases is characterized by pus determined in expectorated sputum or sampled with drainage procedures through pleural catheters. In addition, 29 patients diagnosed with an alternate disease were excluded from the study.

The patients enrolled in this study were classified into two groups according to the presence or absence of DM. The diabetic group included 17 patients, whereas nondiabetic included 15 patients.

Ethical approval

The present study was conducted with the Code of Ethics of the World Medical Association, according to the principles expressed in the Declaration of Helsinki. This study has been approved by the local Ethics Committee of General Organization for Teaching Hospitals and Institutes (GOTHI), with approval number HAM00129. A written informed consent was provided by each participant before their inclusion in the study.

Methods

All of the patients were subjected to detailed medical history, thorough clinical examination, laboratory investigations, sputum culture and sensitivity, and high-resolution CT of the chest.

Laboratory investigations

A 5-ml sample of venous blood was obtained from each patient after 12 h of fasting for laboratory assessment. The blood samples were centrifuged, and the serum was separated and kept at −8°C for batch assessment. Fasting blood glucose was assessed using a kit of Biodiagnostic Co. (Dokki, Giza, Egypt), according to the method of Tietz [9].

Diagnosis of DM was carried out by past history of DM or treatment with oral antidiabetic drugs or insulin. As an alternative, diagnosis could be established when the fasting plasma glucose concentration was more than or equal to 126 mg/dl and/or 2-h postprandial blood sugar was more than or equal to 200 mg/dl on two or more separate occasions or could be supported by an glycated hemoglobin level more than 6.4 [10].

Complete blood picture was done by a Sysmex XS 500 (Sysemix Corporation, Japan) to assess red blood cells, white blood cells, and platelets. C-reactive protein, albumin, and kidney function (urea and creatinine) were done using a Cobas c 311 Analyzer of Roche Diagnostics International AG, (Rotkreuz, Switzerland). Arterial blood gases were done on a Gem Premier 3000 system of Diamond Diagnostics Inc. (Holliston, Massachusetts, USA).

Sputum culture and sensitivity

The sample was taken on a clean container. Macroscopic examination was done to describe the sample, and then gram-stained smear is prepared to detect pus cells and bacteria. Cultures of the sputum were done on the following media: blood agar with an Optochin disc placed in the middle of the secondary streaking; chocolate agar; MacConkey agar; and Sabouraud dextrose agar. Susceptibility testing was done using a standardized disc-diffusion method by different antibiotic discs [9].

Chest computed tomography examination

Chest CT examination was performed using a GE64 row 128-slice CT scanning equipment (GE Hangwei

Medical System, Beijing, China), from the level of the thoracic entrance to the level of the diaphragm, and completed at the end of inspiration. The scanning parameters were as follows: tube voltage 120 kV, tube current 250–450 mA, layer thickness 10 mm, and layer spacing 5 mm. At the end of scanning, a thin layer image with a layer thickness of 1.25 mm and a layer distance of 1.25 mm is automatically reconstructed and recorded as DICOM image data. Images of the lungs (window width 1600 HU, window level 500) and the mediastinum (window width 350 HU, window level 50) were observed.

Statistical analysis

Data were analyzed using the Statistical Package for the Social Sciences (SPSS/Windows, version 18, SPSS Inc., Chicago, Illinois, USA). Normality of data was tested using the Kolmogorov–Smirnov test. The data were normally distributed. The parametric data were expressed as mean±SD, where the qualitative ones were expressed as number and percentage (%). Student's *t* test was used to compare between two parametric groups, and χ^2 test was used to compare between groups with qualitative data. Standards of probability were set to *P* value less than 0.01, which were considered highly significant, and *P* value less than 0.05 was considered statistically significant.

Results

This study included 61 patients with symptoms and signs of chronic pulmonary diseases. Of them, 32 patients fulfilled the inclusion criteria of chronic lung sepsis, comprising 23 males and only nine females, with no significant difference detected between the two groups. The patients enrolled in this study were then classified into two groups according to presence or absence of DM. The diabetic group included 17 patients, whereas nondiabetic included 15 patients.

The age of the selected sample ranged between 30 and 71 years, with the mean age of the male patients being 53±9.81 years and that of female patients being 55.6 ±12.7 years. Three cases were aged between 30 and 40 years, seven cases between 40 and 50 years, nine cases between 50 and 60 years, and 13 cases were more than 60 years old. The diabetic group included ten cases aged more than 60 years, four cases between 40 and 50 years, and only three cases between 50 and 60 years.

Among the diabetic group, 64.7% of patients were smokers and 35.3% were nonsmokers, whereas in nondiabetic group, 66.7% were smokers and 33.3% were nonsmokers, with no significant difference detected between the two groups, as shown in Table 1.

In this study, 100% of patients were complaining of cough, whereas other symptoms such as expectoration, dyspnea, fever, chest pain, and wheezes had different percentages, with insignificant difference between diabetic and nondiabetic groups, as shown in Table 2.

In this study, the comparison between laboratory findings among diabetic and nondiabetic groups showed no significant difference between diabetic and nondiabetic groups, as shown in Table 3.

According to sputum culture, gram-negative organisms were more incident in the diabetic group, but gram-

Table 1 Characteristics of studied patients with chronic lung sepsis

	Diabetic (*N*=17) [*n* (%)]	Nondiabetic (*N*=15) [*n* (%)]	Total (*N*=32) [*n* (%)]	*P* value
Male	12 (70.6)	11 (73.3)	23 (71.9)	0.900
Female	5 (29.4)	4 (26.7)	9 (28.1)	
Nonsmoker	6 (35.3)	5 (33.3)	11 (34.4)	0.907
Smoker	11 (64.7)	10 (66.7)	21 (65.6)	
Total	100%	100%	100%	

No significant difference detected between the two groups using χ^2 test at *P* value less than 0.05.

Table 2 Symptoms among diabetic and nondiabetic cases of chronic lung sepsis

Symptoms	Diabetic (*N*=17) [*n* (%)]	Nondiabetic (*N*=15) [*n* (%)]	*P* value	Total (*N*=32) [*n* (%)]
Expectoration	16 (94.1)	15 (100)	0.900	31 (96.9)
Dyspnea	16 (94.1)	14 (93.3)	0.800	30 (93.8)
Fever	6 (35.3)	3 (20)	0.456	9 (28.1)
Pain	12 (70.6)	10 (66.7)	0.811	22 (68.8)
Wheezes	15 (88.2)	11 (73.3)	0.383	26 (81.3)

No significant difference detected between the two groups using χ^2 test at *P* value less than 0.05.

Table 3 Comparison between laboratory findings among diabetic and nondiabetic cases of chronic lung sepsis

	Diabetic group (*N*=17)	Nondiabetic group (*N*=15)	*P*
TLC (thousands/cmm)	3±0.4	4±0.5	0.400
Hemoglobin (g/dl)	13.44±0.86	13.15±1.14	0.427
PLT (thousands/cmm)	242.20±51.93	284.60±52.80	0.626
ESR (2nd h) (mm)	22.29±8.7	14.27±8.59	0.216
CRP (mg/l)	0.44±0.2	0.35±0.13	0.130
PCO_2 (mmHg)	50.06±9.85	48.07±11.35	0.604
PO_2 (mmHg)	75.94±11.12	74.21±15.55	0.742
SaO_2%	91.35±5.52	91.35±5.42	0.926
Serum albumin (g/dl)	4.2±0.68	3.7±0.58	0.094

CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; PLT, platelet count; TLC, total leukocytic count. No significant difference detected between the two groups using *t* test at *P* value less than 0.05.

Table 4 Sputum culture of both groups of chronic lung sepsis among diabetic and nondiabetic groups

Sputum culture	Diabetic group (*N*=17) [*n* (%)]	Nondiabetic group (*N*=15) [*n* (%)]	Total (*N*=32) [*n* (%)]
Normal flora	5 (29.4)	5 (33.3)	10 (31.2)
Gram +ve streptococci	2 (11.8)	0	2 (6.3)
Gram +ve staphylococci	3 (17.6)	9 (60)	12 (37.5)
Gram –ve klebsiella	7 (41.2)	1 (6.7)	8 (25)

Table 5 Sputum culture comparing gram-positive versus gram-negative organisms among diabetics and nondiabetics of both groups of chronic lung sepsis (diabetic and nondiabetic groups)

	Diabetic group (*N*=17) [*n* (%)]	Nondiabetic group (*N*=15) [*n* (%)]	*P* value
Gram +ve	5 (29.4)	9 (60)	0.031*
Gram –ve	7 (41.7)	1 (6.7)	

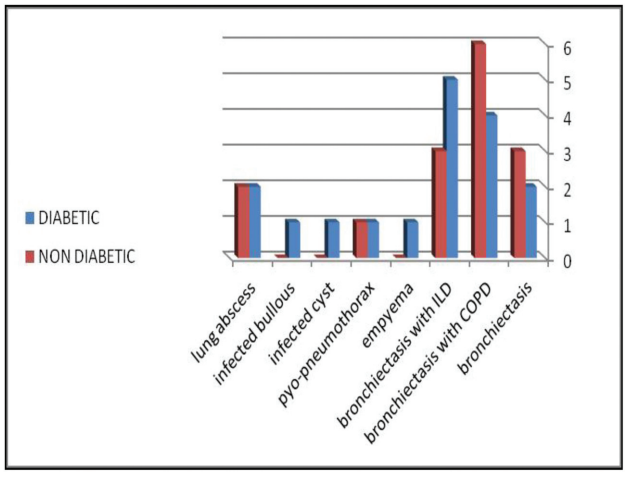
*Significant difference between gram-positive and gram-negative organisms among diabetics and nondiabetics at *P* value less than 0.05, using Fisher exact test.

positive organisms were more in the nondiabetic group, as shown in Table 4. Gram-negative organisms were present in seven diabetic cases and in only one nondiabetic case, but gram-positive organisms were present in five cases of the diabetic group and nine cases in the nondiabetic group. Further analysis of sputum culture comparing positive versus negative organisms among diabetics and nondiabetics showed a significant difference, as shown in Table 5.

CT of patients with chronic lung sepsis revealed a high incidence of bronchiectasis in both diabetic and nondiabetic groups mostly secondary to chronic obstructive lung disease followed by that caused by interstitial lung diseases, as shown in Fig. 1. Lung abscess showed no difference between diabetic and nondiabetic patients. Empyema and infected cyst were present in the diabetic group only.

Pneumonia was present in six patients with chronic lung sepsis, which was more incident in the diabetic group, as shown in Fig. 2. There were five cases with pneumonia in the diabetic group, whereas only one case in the nondiabetic group.

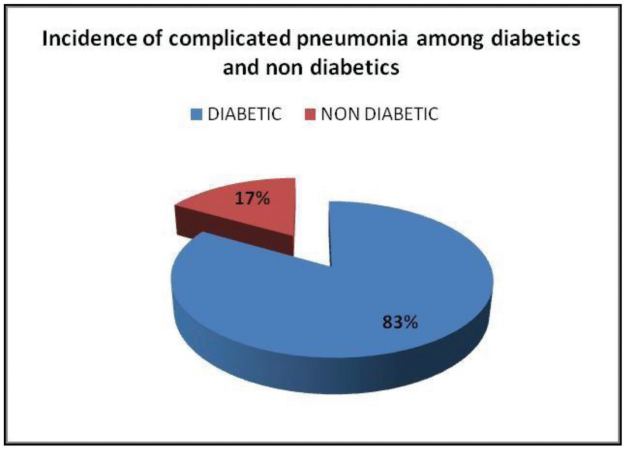
Figure 1



CT findings in cases of chronic lung sepsis. CT, computed tomography.

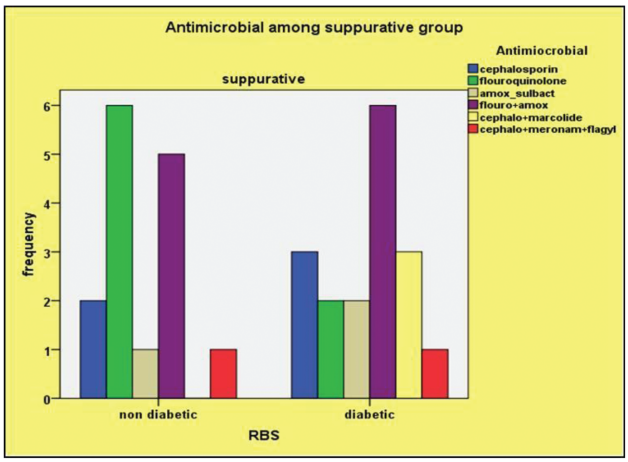
Heterogeneity in clinical patterns of chronic lung sepsis was revealed by the fact that 23 cases were diagnosed as bronchiectasis, four cases were diagnosed as lung abscess, two cases were pyopneumothorax, whereas there was one case each for infected cyst, empyema,

Figure 2



Incidence of complicated pneumonia among diabetics and nondiabetics.

Figure 3



Antimicrobial management among cases of chronic lung sepsis.

and infect emphysematous bullous, as shown in Table 6.

Management of cases of chronic lung sepsis showed the use of double or triple antimicrobial therapy in the diabetic group, as shown in Fig. 3. A total of nine diabetic cases were treated with double antimicrobial and one case with triple therapy, whereas in the nondiabetic group, only five cases were treated with double therapy and one cases with triple therapy.

Discussion

It was believed that healthy lung is a sterile environment; however, during the past decade, researchers have discovered that the lung has its own microbiome [11].

Table 6 Differential diagnosis of chronic lung sepsis among diabetic and nondiabetic groups

Diagnosis	Diabetic group (*N*=17) [*n* (%)]	Nondiabetic group (*N*=15) [*n* (%)]	Total (*N*=32) [*n* (%)]
Lung abscess	2 (11.8)	2 (13.3)	4 (12.5)
Bronchiectasis	11 (64.7)	12 (80)	23 (71.9)
Empyema	1 (5.9)	0	1 (3.1)
Pyopneumothorax	1 (5.9)	1 (6.7)	2 (6.3)
Infected emphysematous bulla	1 (5.9)	0	1 (3.1)
Lung cyst	1 (5.9)	0	1 (3.1)

Recent studies highlight the role of the commensals of the respiratory tract in the development of infections such as chronic lung sepsis [12].

In a healthy lung, this microbiome is balanced by the rate of bacterial reproduction and its elimination, but in chronic lung sepsis, changes occur in this balance [13]. This can decrease microbial elimination and provide areas of lower oxygen and rich in nutrients, allowing bacterial proliferation in the lung. Furthermore, many of the antibiotics that are administered during hospitalization for pneumonia can affect the composition of the microbiome [14].

Respiratory infections are the leading cause of death in developing countries and are associated with more than four million deaths annually. All over the world, lower respiratory infections result in the loss of 103 000 disability-adjusted life years, which means that lung infections are the largest cause of disease burden [15].

The common clinical chronic lung sepsis conditions are bronchiectasis, empyema, lung abscess, and to less often infected cyst or bullous, whereas bronchiectasis was the most common form [2].

This study included 32 patients fulfilling the criteria of chronic lung sepsis, with 21 being smokers and 11 being nonsmokers. The aforementioned finding could be explained by the fact that smoking-related chronic pulmonary infections have very thick mucus that builds up, permitting bacteria, viruses, and fungi to thrive, causing lung injury, particularly when mucociliary escalator cannot maintain lung health [16]. This finding was in line with the study by Kumar *et al.* [17], which documented that smoking was the most important risk factor for lung abscess (65.9% of the patients being smokers).

DM is a chronic metabolic disorder with an increasing prevalence all over the world. Very little attention has been paid to its association with lung disorders. In case of diabetes, the higher rate of lung infections is mainly owing to hyperglycemia, which adversely affects the immune system [5].

In health, the glucose concentration of airway surface liquid (ASL) is about 12 times lower than blood glucose level. Airway glucose homeostasis comprises processes that maintain low ASL glucose, which has an important role in airway defense against infections. Both airway inflammation, which increases glucose permeability, and hyperglycemia increase ASL glucose concentrations, with the greatest effect seen when both coexist. Elevated ASL glucose leads to proliferation of bacteria, including *Staphylococcus aureus*, *Pseudomonas aeruginosa*, and other gram-negative bacteria. This is important in driving exacerbations of chronic lung sepsis, especially in patients with comorbid DM [18].

In the current study, 17 (53.1%) patients were in the diabetic group and 15 (46.9%) patients in the nondiabetic group. No significant difference was elicited between diabetic and nondiabetic groups regarding clinical and laboratory findings. Two cases had low serum albumin despite being nondiabetic. The first case was diagnosed as bronchiectasis with expectoration of excess amount of secretions. The second one was complaining of pyopneumothorax with proteins lost in the huge amount of pus collected by an intercostal tube.

Prentice *et al.* [19] found that hyperglycemia results in an ineffective and frustrated pulmonary inflammatory response. A wide range of cellular functions are impaired in DM such as neutrophil and macrophage functions, including chemotaxis, adherence, phagocytosis, and ability to kill phagocytosed microorganisms with free radicals [20]. Pulmonary autonomic neuropathy, which reduces mucociliary clearance, might also explain it [21].

In the present study, sputum culture revealed gram-negative organisms were more incident in the diabetic group, but gram-positive organisms were more in the nondiabetic group. As in our study, Tan *et al.* [22] found that among diabetics, 72.1% of patients were diagnosed with pneumonia without a definite microbiological etiology. The most common etiologies for pneumonia in patients with DM were *Klebsiella pneumoniae* (6.3%), *S. aureus* (3.8%), and *Mycoplasma pneumoniae* (3.4%) [22].

In this study, normal flora was detected in 15% of cases. This finding was in line with Kumar *et al.* [17], who postulated that blood cultures were found to be the least sensitive; 80.5% of the cases revealed no growth of any organisms. In a study done by Woo *et al.* [23], *P. aeruginosa* and *H. influenzae* remain the most common causative microorganisms of bronchiectasis, and chronic infection with them persists over time unrelated to antibiotic treatment. However, Zhou *et al.* [24] found that the numbers of gram-positive bacteria, gram-negative bacteria, and fungal infections were 19 (24.1%), 49 (62.0%), and 11 (13.9%), respectively. Thirty (38.0%) patients of severe lung infections had DM.

CT is the best imaging modality in assessment and management of patients with lung diseases. It provides precise data on size, shape, and location of lesions [8].

In this study, heterogeneity in clinical patterns of chronic lung sepsis was determined. A total of 23 cases were diagnosed as bronchiectasis, four cases were diagnosed as lung abscess, two cases were pyopneumothorax, whereas there was one case each of infected cyst, empyema, and infected emphysematous bullous. However, Vishwakarma *et al.* [6] found that the radiological presentations of pulmonary infections in patients with DM were categorized as exudative consolidation, pleural effusion, cavitation, pneumothorax, or hydropneumothorax.

There was no significant difference between diabetic and nondiabetic patients in the bronchiectasis group. Most of them were associated with chronic obstructive pulmonary disease and others are associated with interstitial lung disease, which was detected by high-resolution CT. The previous findings were confirmed by Poh *et al.* [25] who stated that bronchiectasis and chronic obstructive pulmonary disease commonly coexist, and this clinical state is associated with greater disease severity.In this ongoing study, only four (12.5%) cases were diagnosed as lung abscesses with no difference between diabetic and nondiabetic groups. Kumar *et al.* [17] documented that the occurrence of lung abscess in the target population has shown the greatest association with cases with DM.

In the current study, suppurative complications of pneumonia showed more incidences in the diabetic group. There were seven patients associated with pneumonia; six (83%) cases of them were diabetic, whereas only one case (17%) was non-diabetic, which agreed with Korbel and Spencer [26], who postulated that pneumonia was the major infection associated with diabetes.

With evidence that support the role of DM on growth of respiratory pathogens detected by culture, it is therefore expected to find the altered pulmonary microbiome [27]. So, management requires an accurate microbiological diagnosis and prolonged antimicrobial therapy [28].

In this study, management of cases of chronic lung sepsis showed the use of double or triple antimicrobial therapy in the diabetic group. This was in keeping with the study by Duncan *et al.* [29], which used empiric combinations, such as clindamycin, beta-lactam/beta-lactamase combinations, beta-lactams with metronidazole, or carbapenems. Targeted therapy directed at a single organism without coverage of anaerobes should only be considered when no oral flora is isolated.

Conclusion

Chronic lung sepsis is one of the debilitating and life-threatening medical complications, especially when coexisting with type II DM. Suppurative complications of pneumonia are more frequent in diabetics with no significant difference between diabetics and nondiabetics in age, sex, or smoking. Targeting good control of infections in patients with type II DM using double or triple antimicrobial therapy is essential to inhibit progression to chronic lung sepsis.

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Conflicts of interest

There are no conflicts of interest.

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