

The Most Common Detected Bacteria in Sputum of Patients with the Acute Exacerbation of COPD

Vesna Cukic

Clinic for Pulmonary Diseases and TB "Podhrastovi", Clinical center of Sarajevo University, Bosnia and Herzegovina

Corresponding author: Vesna Cukic, MD. Clinic for Pulmonary Diseases and TB "Podhrastovi", Clinical center of Sarajevo University, Bosnia and Herzegovina. Phone: 00387 61 480 228; E-mail: vesna-cukic@hotmail.com

ABSTRACT

Introduction: Acute exacerbation of COPD (AECOPD) may be triggered by infection with bacteria or viruses or by environmental pollutants; the cause of about one-third of exacerbations cannot be identified. **Objective:** to determine the most common bacteria in sputum culture of patients with AECOPD hospitalized in Intensive care unit of Clinic for pulmonary disease and TB "Podhrastovi" in the 2012. **Material and methods:** This is a retrospective analysis of sputum bacterial cultures of patients with AECOPD treated in the Intensive care unit of Clinic for pulmonary disease and TB "Podhrastovi" during 2012 .year. Each patient was required to give two sputum for bacterial examination. Each patient was treated with antibiotics prior to admission in Clinic "Podhrastovi". The results of sputum bacterial culture findings are expressed in absolute number and percentage of examined patients. **Results:** In 2012, 75 patients with AECOPD were treated in Intensive care unit of Clinic for pulmonary disease and TB "Podhrastovi". 44 (58.66%) of patients had normal –nonpathogenic – usual bacterial flora isolated in sputum cultures, 31 (41.34%) had a pathogen bacteria in sputum culture as follows: 7 had *Streptococcus pneumoniae*, 8 had *Klebsiella pneumoniae* (2 with *Streptococcus pneumoniae*, one with *Acinetobacter baumannii*), 4 *Escherichia coli*, others are one or two cases with other bacteria. **Conclusion:** Bacterial airway infections play a great role in many, but not in all, of cases of AECOPD. So there is the need to do a sputum bacterial culture examination in each patient with AECOPD and with appropriate antibiotics to contribute to curing of them.

Key words: AECOPD, bacteria, sputum, bacterial culture.

1. INTRODUCTION

COPD is one of the major causes of chronic morbidity and mortality worldwide. It is the fourth leading cause of death in the world (1, 2, 3). COPD is a pulmonary disease with significant extrapulmonary effects. Its pulmonary component is characterized by airflow limitation that is not fully reversible (4) and usually is progressive (1).

The chronic airflow limitation of COPD is caused by a mixture of small airway disease (obstructive bronchiolitis) and parenchymal destruction (emphysema), the relative contributions of which vary from person to person (1). Chronic inflammation causes structural changes and narrowing of small airways. Destruction of the lung parenchyma leads to the loss of alveolar attachments to the small airways and decreases lung elastic recoil (5, 6, 7, 8, 9).

Although COPD is progressive illness it has periods of remission and exacerbations. An exacerbation of COPD is defined as an event in the common course of the disease characterized by a change in the patient's baseline dyspnoea, cough, and/or sputum production that is beyond common day-to-day variations, that

is acute in onset, and may warrant a change in regular medication (1). In severe exacerbations the patient may be unable to maintain normal blood gases that can lead to respiratory failure. Hospital mortality of patients admitted for a hypercarbic COPD exacerbation is approximately 10%, and the long-term outcome is poor (10).

Exacerbations of COPD have serious negative impacts on patients' quality of life, lung function (11, 12, 13), and socioeconomic costs (11). Thus, prevention, early detection, and prompt treatment of exacerbations may impact their clinical progression by ameliorating the effects on quality of life and minimizing the risk of hospitalization (14). Exacerbations represent a further amplification of the inflammatory response in the airways of COPD patients, and may be triggered by infection with bacteria or viruses or by environmental pollutants (15) but the cause of about one-third of severe exacerbations cannot be identified (1). The role of bacterial infections is controversial, but recent investigations with newer research techniques have begun to provide important information. Bronchoscopic studies have shown that at least 50% of patients have bacteria in high con-

centrations in their lower airways during exacerbations (16, 17, 18). However, a significant proportion of these patients also have bacteria colonizing their lower airways in the stable phase of the disease, but the bacterial burden increases during exacerbations (16), and strains of the bacteria that are new to the patient is associated (18). Development of specific immune responses to the infecting bacterial strains, and the association of neutrophil inflammation support the bacterial causation of a proportion of exacerbations (19, 20, 21).

Clinical features of acute infection in COPD include increased dyspnea, productive cough and sputum production. There may be fevers, chills, malaise, pleural chest pain and hemoptysis. The sputum's color or thickness may change. It is difficult to diagnose a respiratory infection in a patient with AECOPD because many of the symptoms and signs are present at baseline or can be seen in noninfectious exacerbations. This emphasizes the need to pursue laboratory confirmation of infection (22).

Despite several decades of study, the prevalence of bacterial infection and therefore the importance of antibacterial therapy in AECOPD have been controversial (22). This debate is largely based upon data suggesting that up to 50% of exacerbations are either viral or noninfectious i.e. nonbacterial (23, 24, 25, 26). Among the more common noninfectious causes are allergies, incomplete compliance to therapy and congestive heart failure (22, 23).

Microbiologic data is important in the diagnosis and management of bacterial infection complicating COPD. Unfortunately, colonizing, non-pathogenic bacteria are readily cultured from 30-50% of patients with COPD, making data interpretation difficult (27).

Sputum Gram's stain may be the most helpful of the available microbiologic tests for following reasons: the presence of neutrophils in the Gram's stain indicates that bacteria inducing an inflammatory response, rather than colonizing the airway, the type of bacteria may influence antimicrobial choice; the quantity of bacteria can help distinguish an infectious from a noninfectious exacerbation of COPD (22). Results never be used as a lone factor in making management decisions (27).

Sputum cultures do not always correlate with clinical parameters and Gram's stain results (22, 23).

AECOPD are caused by respiratory viruses or bacteria: typically 25% are caused by viruses, 26% by bacteria; 27% by a combination of the two; 22% have no ascertainable cause (28). Therefore bacterial infections are the predominant cause of acute exacerbation of COPD (28). A Gram stain of sputum and purulence of sputum, are used as the evidence for the presence of bacteria (28). A strong correlation has been shown between failure to eradicate bacterial infection and clinical failure rate, demonstrating that treatment of bacterial infection plays a key role in the clinical outcome (29).

The most common bacterial pathogens isolated in AECOPD are *Haemophilus influenzae*, *Haemophilus parainfluenzae*, *Streptococcus pneumoniae* and *Moraxella catharralis* (1, 28, 29). The presence of bacteria can depend on the severity of airway disease; more virulent organisms such as *Staphylococcus aureus* and *Pseudomonas aeruginosa* has been found in patients with more severe AECOPD (28). Nonpathogenic bacteria also appear to play a role in the etiology of AECOPD (28, 29).

The majority of studies available on the use of antibiotics

for treatment of AECOPD are very old. A large proportion of these studies show some benefit for the use of antibiotics for exacerbations of COPD, some showed no benefit (30). Most of the more recent positive information available for antibiotics in AECOPD comes from a study in 2001 (31). This study states that antibiotics are a vital therapy for patients with severe exacerbations on mechanical ventilation; patients with mild-to-moderate exacerbations have a high spontaneous remission rate.

Isolated microorganisms can be divided into three categories according to FEV1 severity (32): FEV1 <100% predicted (*Streptococcus pneumoniae*, *Streptococcus species*), FEV1 <50% predicted (*Haemophilus influenzae*, *Moraxella catharralis*, *Haemophilus parainfluenzae*), FEV1 <30% predicted (*Staphylococcus aureus* *Enterobacteriaceae*, *Pseudomonas aeruginosa*).

It is not yet known whether this system will be useful in clinical practice, because, to date, no studies have addressed this issue (28).

The ERS (European Respiratory Society) has divided patients into three groups according to their COPD severity (28, 33):

- Group A: mild with co-morbidities;
- Group B: moderate to severe without the risk factors for *Pseudomonas aeruginosa*;
- Group C: moderate to severe with the risk factors for *Pseudomonas aeruginosa*.

Each group has been assigned different microorganisms that could be involved in the infection, for example group A are most commonly infected with the *Haemophilus influenzae*, *Streptococcus pneumoniae*, *Moraxella catharralis*, *Mycoplasma pneumoniae* and *Chlamidophila pneumoniae* and group B with all in group A plus *Enterobacteriaceae*, *Klebsiella pneumoniae*, *Escherichia coli*, *Proteus* and *Enterobacter*.

Different organization gives different recommendations for use of antibiotics in AECOPD: antibiotics should be only considered for use in patients with purulent exacerbations (34), antibiotics are only effective with worsening dyspnea and cough, also increased sputum volume and purulence (35), antibiotics may be initiated in patients with altered sputum characteristics (36), antibiotics should be used to treat exacerbations of COPD associated with history of more purulent sputum (37).

All cited guidelines (34, 35, 36, 37) suggest that COPD exacerbations and purulence of sputum are the most important factors for the presence of bacterial infection which calls for the use of antibiotics. In recent study, sputum purulence was defined as a change in sputum color from uncolored to yellow-green monitored by the patient (38).

Sputum samples from all patients with COPD who need hospitalization would be required to monitor antibiotic therapy (28).

2. OBJECTIVE OF THE STUDY

Objective of this study is to determine the most common bacteria in sputum culture of patients with AECOPD hospitalized in Intensive care unit of Clinic for pulmonary disease and TB "Podhrastovi" in the 2012.

3. MATERIAL AND METHODS

This is a retrospective analysis of sputum bacterial cultures of patients with AECOPD treated in the Intensive care unit of Clinic for pulmonary disease and TB "Podhrastovi" during 2012 .year. During that year 75 patients with AECOPD were

treated. Each of them had a FEV1 less than 50% of normal values of FEV1 for that patient (according to sex, age, weight, height), and each of them had a respiratory failure (I or II type).

Each patient was required to give two sputum for bacterial sputum examination. Some of them were so weak and they were obliged to give more sputum until they give the sputum of quality enough for examination. Sputum was examined for identification of bacteria and for their sensitivity to antibiotics. The examinations were done in Laboratory for microbiology of Clinical Center of Sarajevo University. We did not do a tracheobronchial bronchoscopic aspiration for getting a material of better quality for bacterial cultures. Each patient was treated with antibiotics prior to admission in Clinic "Podhrastovi". The results of sputum bacterial culture findings are expressed in absolute number and percentage of examined patients.

4. RESULTS

From 75 treated patients we got sputum of good quality for bacterial cultures in all of them. Results are shown in the Table 1 and Figure 1 and 2.

Isolated bacteria	Number of patients	Per cent (%)
a Normal bacterial flora of airways	44	58.67
b Streptococcus pneumoniae	7	9.33
c Klebsiella pneumoniae	5	6.67
d Escherichia coli	4	5.33
e Acinetobacter baumannii	2	2.67
f Enterobacter cloacae	2	2.67
g Staphylococcus aureus	2	2.67
h Pseudomonas aeruginosa	2	2.67
i Klebsiella pneumoniae + Streptococcus pneumoniae	2	2.67
j Enterobacter freundii	1	1.33
k Proteus mirabilis	1	1.33
l Haemophilus influenzae	1	1.33
m Klebsiella oxytoca	1	1.33
n Klebsiella pneumoniae + Acinetobacter baumannii	1	1.33
Total	75	100

Table 1. The isolated bacteria in sputum bacterial culture in patients with AECOPD

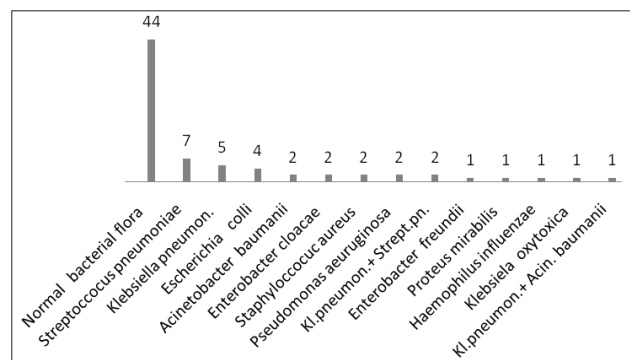


Figure 1. The isolated bacteria in sputum of seventy-five patients with AECOPD expressed in absolute number of examined patients

In 44 or 58.57% patients normal nonpathogenic bacterial flora was isolated. In 44 patients normal airway bacterial flora was isolated, in 31 pathogen bacteria were isolated in sputum

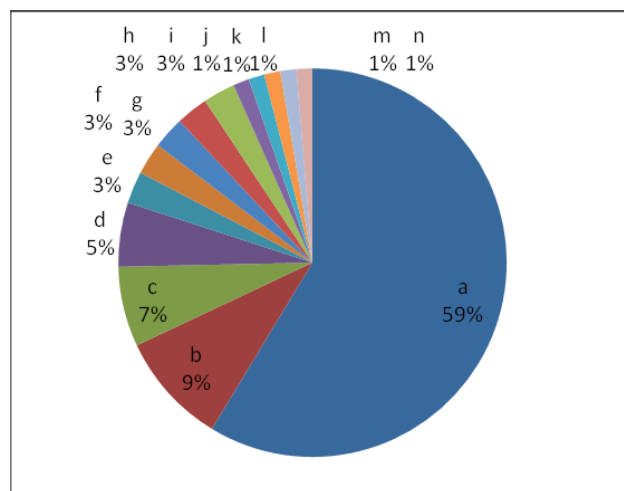


Figure 2. The isolated bacteria in sputum of seventy-five patients with AECOPD expressed in per-cents of examined patients

bacterial culture. In 59% patients normal airway bacterial flora was isolated, in 41% pathogen bacteria were isolated in sputum bacterial culture

5. DISCUSSION

Although COPD is progressive illness it has periods of remission and exacerbations. The impact of exacerbations is significant and a patient's symptoms and lung function may both take several weeks to recover to the baseline values (1, 10, 12).

The most common causes of an exacerbation are infection of the tracheobronchial tree and air pollution (15), but the cause of about one-third of severe exacerbations cannot be identified (1, 15). Acute exacerbations of COPD are caused according to some authors by respiratory viruses or bacteria: typically -25% are caused by viruses, 26% by bacteria and 27% by a combination of the two; 22% have no ascertainable cause (28). Up to 50 percent of exacerbations are either viral or noninfectious (i.e. nonbacterial) in origin (23-26). The prevalence of bacterial infection and therefore the importance of antibacterial therapy in AECOPD have been controversial (22).

According to literature the most common bacterial pathogens isolated in AECOPD are Haemophilus influenzae, Haemophilus parainfluezae, Streptococcus pneumoniae and Moraxella catharralis (1, 28, 29, 32, 33). The presence of these bacteria can depend on the severity of airway disease; more virulent organisms such as Staphylococcus aureus and Pseudomonas aeruginosa has been found in patients with more severe AECOPD (28,29). Nonpathogenic bacteria also appear to play a role in the etiology of COPD (28). Sputum samples from all patients with COPD who need hospitalization would be required.

Our study was done on 75 patients with AECOPD hospitalized in Intensive care unit of Clinic "Podharstovi" during 2012 .year and they gave high-quality sputum for bacterial examination in form of sputum culture. It shows the different types of bacteria isolated in patients with COPD. Most previous studies indicate that up to the 50% of COPD exacerbations are caused by bacteria, alone or in combination with viruses and that the most common identified bacteria in sputum culture are Haemophilus influenzae, Haemophilus parainfluezae, Streptococcus pneumoniae and Moraxella catharralis according to GOLD (1) and Mycoplasma pneumoniae and Chlamidophilia pneumoniae plus Enterobacteriaceae, Klebsiella pneumoniae

, *Escherichia coli*, *Proteus* and *Enterobacter* depending to severity of exacerbation according to ERS (28). In our study 44 (58.66%) of patients had normal bacterial flora isolated in sputum cultures in AECOPD, 31 of them (41,34%) had isolated pathogen bacteria: 7 had *Streptococcus pneumoniae*, 8 had *Klebsiella pneumoniae* (two associated with *Streptococcus*, one with *Acinetobacter baumani*), 4 *Escherichia coli*, others are one or two cases of other bacteria. The type of isolated bacteria (less of *Haemophilus influenzae* and *parainfluenzae*, and relative big proportion of *Klebsiella pneumoniae*) in our study is may be the consequence of the fact that our patients suffered from severe AECOPD with FEV1 less of 50% per cent of predicted, that they were in respiratory failure and that they were treated with antibiotics before admission in hospital.

There are not many studies about isolated bacteria in sputum culture in AECOPD but all of them indicate the importance of doing bacterial sputum culture in AECOPD because the great number, up to the 50% per cent, of exacerbation is caused by bacterial infection. So it is important to isolate bacteria and use appropriate antibiotic to accelerate the healing of each COPD exacerbation.

6. CONCLUSION

Exacerbations of COPD have serious negative impacts on patients' quality of life, lung function and socioeconomic costs. Exacerbations of COPD may be triggered by infection with bacteria or viruses or by environmental pollutants.

The role of bacterial infections is controversial because a significant proportion of these patients also have bacteria colonizing their lower airways in the stable phase of the disease. But the bacterial burden increases during exacerbations, and new strains of the bacteria are associated.

It is difficult to conclusively diagnose a respiratory infection in a patient with COPD exacerbation because many of the symptoms and signs are present at baseline or can also be seen with noninfectious exacerbations. This emphasizes the need to pursue laboratory confirmation of infection.

It is needed to obtain the routine sputum bacterial culture in each patient with COPD exacerbation because great number of COPD exacerbations is caused by bacterial airway infection, and with appropriate antibiotics we contribute to healing them.

REFERENCES

1. GOLD (Global Initiative for Chronic Obstructive Lung Disease) - global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease-revised 2006. <http://www.goldcopd.org>: 1-100.
2. World Health Report. Geneva: World Health Organization. Available from URL: <http://www.who.int/whr/2000/en/statistics.htm>; 2000.
3. Lopez AD, Shibuya K, Rao C, Mathers CD, Hansell AL, et al. Chronic obstructive pulmonary disease: current burden and future projections. *Eur Respir J*. 2006; 27(2): 397-412.
4. Soriano JB, Visick GT, Muellerova H, Payvandi N, Hansell AL. Patterns of comorbidities in newly diagnosed COPD and asthma in primary care. *Chest*. 2005; 128(4): 2099-2107.
5. Barnes PJ, Shapiro SD, Pauwels RA. Chronic obstructive pulmonary disease: molecular and cellular mechanisms. *Eur Respir J*. 2003; 22(4): 672-688.
6. Hogg JC. Pathophysiology of airflow limitation in chronic obstructive pulmonary disease. *Lancet*. 2004; 364(9435): 709-721.
7. Saetta M, Turato G, Maestrelli P, Mapp CE, Fabbri LM. Cellular and structural bases of chronic obstructive pulmonary disease. *Am J Respir Crit Care Med*. 2001; 163(6): 1304-1309.
8. Hogg JC, Chu F, Utokaparch S, Woods R, Elliott WM, et al. The nature of small-airway obstruction in chronic obstructive pulmonary disease. *N Engl J Med*. 2004; 350(26): 2645-2653.
9. Cosio MG, Majo J. Inflammation of the airways and lung parenchyma in COPD: role of T cells. *Chest*. 2002; 121(5, Suppl):160S-165S.
10. Connors AF, Jr., Dawson NV, Thomas C, Harrell FE, Jr., Desbiens N, Fulkerson

WJ, et al. Outcomes following acute exacerbation of severe chronic obstructive lung disease. The SUPPORT investigators (Study to Understand Prognoses and Preferences for Outcomes and Risks of Treatments). *Am J Respir Crit Care Med*. 1996; 154(4 Pt 1): 959-967.

11. Wouters EF. The burden of COPD in The Netherlands: results from the Confronting COPD survey. *Respir Med*. 2003; 97 Suppl C: S51-9.
12. Donaldson GC, Seemungal TA, Bhowmik A, Wedzicha JA. Relationship between exacerbation frequency and lung function decline in chronic obstructive pulmonary disease. *Thorax*. 2002; 57(10): 847-852.
13. Kanner RE, Anthonisen NR, Connett JE. Lower respiratory illnesses promote FEV1 decline in current smokers but not ex-smokers with mild chronic obstructive pulmonary disease: results from the lung health study. *Am J Respir Crit Care Med*. 2001; 164(3): 358-364.
14. Wilkinson TM, Donaldson GC, Hurst JR, Seemungal TA, Wedzicha JA. Early therapy improves outcomes of exacerbations of chronic obstructive pulmonary disease. *Am J Respir Crit Care Med*. 2004; 169(12): 1298-1303.
15. White AJ, Gompertz S, Stockley RA. Chronic obstructive pulmonary disease. 6: The etiology of exacerbations of chronic obstructive pulmonary disease. *Thorax*. 2003; 58(1): 73-80.
16. Monso E, Ruiz J, Rosell A, Manterola J, Fiz J, Morera J, et al. Bacterial infection in chronic obstructive pulmonary disease. A study of stable and exacerbated outpatients using the protected specimen brush. *Am J Respir Crit Care Med*. 1995; 152(4 Pt 1): 1316-1320.
17. Pela R, Marchesani F, Agostinelli C, Staccioli D, Cecarini L, Bassotti C, et al. Airways microbial flora in COPD patients instable clinical conditions and during exacerbations: a bronchoscopic investigation. *Monaldi Arch Chest Dis*. 1998; 53(3): 262-267.
18. Sethi S, Evans N, Grant BJ, Murphy TF. New strains of bacteria and exacerbations of chronic obstructive pulmonary disease. *N Engl J Med*. 2002; 347(7): 465-471.
19. Sethi S, Wrona C, Grant BJ, Murphy TF. Strain-specific immune response to *Haemophilus influenzae* in chronic obstructive pulmonary disease. *Am J Respir Crit Care Med*. 2004; 169(4): 448-453.
20. Sethi S, Muscarella K, Evans N, Klingman KL, Grant BJ, Murphy TF. Airway inflammation and etiology of acute exacerbations of chronic bronchitis. *Chest*. 2000; 118(6): 1557-1565.
21. Murphy TF, Brauer AL, Grant BJ, Sethi S. *Moraxella catarrhalis* in Chronic Obstructive Pulmonary Disease: Burden of Disease and Immune Response. *Am J Respir Crit Care Med*. 2005; 172(2): 195-199.
22. Isada CM. Pro antibiotics for chronic bronchitis with exacerbations. *Semin Respir Infect*. 1993; 8: 243.
23. Gump DW, Philips CA, Forsyth BR. Role of infection in chronic bronchitis. *Am Rev Respir Dis*. 1976; 113: 465.
24. Eadie MB, Scott EJ, Grist NR. Virological studies in chronic bronchitis. *Br Med J*. 1966; 2: 671.
25. Stenhouse S. Viral antibody levels and clinical status in acute exacerbations of chronic bronchitis: A controlled prospective study. *Br Med J*. 1968; 3: 287.
26. Chodos S. Treatment of acute exacerbations of chronic bronchitis. *State of the art. Am J Med*. 1991; 91(Suppl 6A): 87S.
27. Baileman W. Quantitative sputum Gram strains in chronic bronchial disease. *Lung*. 1979; 156: 265.
28. ATS/ ERS task Force. Standards for the diagnosis and treatment of patients with COPD: a summary of the ATS/ERS position paper. *Eur Respir J*. 2004; 23: 923-946.
29. Pechere JC. Modeling and predicting clinical outcomes of antibiotics therapy. *Infections in Medicine*. 1988; 15: Suppl. E 46-54.
30. Ram FSF, Rodriguez-Roisin R, Granados-Navarete A. Antibiotics for exacerbations of chronic obstructive pulmonary disease. *Cochrane Database Syst Rev*. 2006; 2: CDOO4403.
31. Nouria S, Marghi S, Belgith M, Basbes L. Once daily oral ofloxacin in chronic obstructive pulmonary disease exacerbation requiring ventilation; a randomized placebo-controlled trial. *Lancet*. 2001; 358: 2020-2025.
32. Eller J, Ede A, Schraberg T. Infective exacerbations of obstructive bronchitis. *Chest*. 1988; 113: 1442-1548.
33. Woodhead M, Blasi F, Ewig S. Guidelines for the management of adult lower respiratory tract infections. *Eur Respir J*. 2005; 26: 1138-1180.
34. O'Donnell DE, Aron S, Bourbau J. Canadian Thoracic society recommendations for management of chronic obstructive pulmonary disease-2007 update. *Can Respir J*. 2007; 14: Suppl. B.
35. Powels RA, Buist AC, Carveley PM. Global strategy for the diagnosis, management and prevention of chronic obstructive pulmonary disease. *Am J Respir Crit Care Med*. 2001; 163: 1256-1276.
36. Celi BR, MacNee. Standards for the diagnosis and treatment of patients with COPD: a summary of the ATS/ERS position paper. *Eur Respir J*. 2004; 23: 932-946.
37. National Institute for Clinical Excellence. Management of chronic obstructive pulmonary disease in adults in primary and secondary care. www.nice.org.uk/nicemedia/pdf/CGO12_nice_guidelines.pfd. Date last accessed: April 30, 2009, date created: February 2004.
38. Soler N, Agusti C. Bronchoscopic validation of the significance of sputum purulence in severe exacerbations of chronic obstructive pulmonary disease. *Thorax*. 2007; 62: 29-35.