Pattern of sputum bacteriology in acute exacerbations of chronic obstructive pulmonary disease
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Introduction
Chronic obstructive pulmonary disease (COPD) is a major cause of chronic morbidity and mortality worldwide [1]. COPD is characterized by progressive airflow limitation caused by chronic inflammation of the airways and lung parenchyma [2].

The definition of acute exacerbation of COPD is a major point of criticism in many of the studies dealing with that issue. Recently, acute exacerbation of COPD was redefined as a sustained worsening of a patient’s condition from a stable state (beyond normal day-to-day variations) that is acute in onset and that may warrant additional treatment in a patient with underlying COPD.

Aim
This study aimed at searching for a pattern of sputum bacteriology and antibiotic sensitivity for acute exacerbation of COPD in patients admitted to Abbassia Chest Diseases Hospital.

Patients and methods
This study included 110 patients who presented with acute exacerbation of COPD. The patients were classified into several groups according to different variables, such as severity, respiratory acidosis, and smoking habits. Bacteriological investigations were performed for all patients including Gram stain examination together with culture and sensitivity testing after proper processing of sputum or endotracheal samples.

Results and conclusion
Klebsiella pneumoniae and Acinetobacter spp. were the most common isolates in patients with mild to moderate COPD admitted to the respiratory ICU and to the ward. Each had an incidence of five (15.15%) isolates in the ICU, whereas in the ward there were 13 (14.9%) isolates of Klebsiella spp. and seven (8.04%) isolates of Acinetobacter spp. Acinetobacter spp., however, was the most common isolate in patients with severe to very severe COPD, with an incidence of five (17.9%) isolates. Imipenem was the most sensitive antibiotic in all patient groups in the ICU and ward.

Keywords: chronic obstructive pulmonary disease, exacerbation, sputum

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Received 2 December 2014 Accepted 12 December 2014

Bacterial colonization. The presence of bacteria in the lower airway can result in a range of important effects on the lungs, including activation of host defenses with release of inflammatory cytokines and subsequent neutrophil recruitment, mucus hypersecretion, impaired mucociliary clearance, and respiratory epithelial cell damage [3].

Aim
The study aimed at searching for a pattern of sputum bacteriology and antibiotic sensitivity for acute exacerbation of COPD in patients admitted to Abbassia Chest Diseases Hospital as a representation of the Egyptian population. A correlation was also determined between sputum bacteriology with severity, respiratory acidosis, and smoking pattern.

Patients and methods
This study included 110 patients admitted to Abbassia Chest Diseases Hospital who presented with acute exacerbation of COPD between September 2010 and July 2013. The patients were classified into several groups according to different variables.
(1) According to severity, the patients were classified as follows:
   Group 1: patients with mild to moderate COPD (FEV1 ≥50).
   Group 2: patients with severe to very severe COPD (FEV1 <50).
(2) According to the presence or absence of respiratory acidosis, patients were classified as follows:
   Group 1: pH <7.35 (acidosis).
   Group 2: pH = 7.35–7.45.
(3) According to smoking habits, patients were classified as follows:
   Group 1: ex-smokers.
   Group 2: smokers.

All patients were subjected to the following:
(1) Thorough history taking.
(2) Thorough clinical examination.
(3) Other investigations including:
   (a) Plain chest radiograph.
   (b) Flow volume loop (if possible).
   (c) Arterial blood gases with estimation of pH, PaO2, PaCO2, HCO3, and SO2%.
   (d) Bacteriological investigations including the following.

Sputum
The specimen for culture was collected before antibiotic therapy was initiated. The patient was instructed to rinse his or her mouth with water to decrease mouth bacteria and dilute saliva. Patients were instructed to take a deep breath, hold it momentarily, and then cough vigorously into a cup. Specimens were transported to the laboratory within minutes of collection. Sputum was collected in sterile sputum cups. If coughing up sputum was difficult, the patient was instructed to breathe in a sterile hypertonic saline produced by a nebulizer.

Endotracheal suctioning
Endotracheal aspirates were performed using a sterile catheter. The suction tube was blindly introduced through intubation. The patient received hyperoxygenation by delivery of 100% oxygen for more than 30 s before the suctioning event. The procedure was performed by placement of a suction catheter through the artificial airway into the trachea and the application of negative pressure as the catheter was being withdrawn. The duration of each suctioning event was ∼10–15 s and the suction pressure was set as low as possible.

Gram stain
A Gram stain of the sputum was examined for polymorphonuclear leukocytes and epithelial cells. Leukocytes and squamous epithelial cells were counted. Only sputa showing fewer than 10 squamous epithelial cells and more than 25 leukocytes per low-power field (×100) were accepted for culture examination.

Sputum culture
Sputa were cultured on blood agar, MacConkey’s medium, and chocolate agar. On the second day films stained by Gram’s stain were made from different types of colonies. On the third day, sensitivity was evaluated from the suspected pathological colonies [5]. All these steps were performed inside a biological safety cabinet. Identification of isolated bacteria was carried out through:
   (1) Microscopic examination.
   (2) Culture appearance.
   (3) Antibiotic sensitivity tests.
   (4) Disc-diffusion method.

Statistical analysis
(1) All data were collected, summarized, presented, and analyzed by using an appropriate statistical package for the social sciences program (SPSS, version 10; SPSS Inc., Chicago, Illinois, USA).
(2) Quantitative data were summarized as mean and SD.
(3) Qualitative data were summarized as number and percentage.
(4) The test of significance used for qualitative data was the \( \chi^2 \)-test.
The test of significance used for quantitative data for two groups was the \( T \)-test and that for more than two groups was the \( F \)-test, whereas the post-hoc test (least significant difference) was used for within-group comparisons.

Level of significance
\( P \) value more than 0.05 was considered nonsignificant (NS); \( P \) value less than 0.05 was considered significant (S); and \( P \) value less than 0.01 was considered highly significant (HS) [6].

Results
Table 1 shows that the patients with AE-COPD included 110 patients: 100 (90.8%) were male and 10 (9.2%) were female.

Table 2 shows that the age of these patients ranged from 40 to 78 years, with a mean of 54.88 ± 8.82 years.

Table 3 shows that the most prevalent organisms in both the ICU and the ward were *Klebsiella pneumoniae* and *Acinetobacter* spp. [five (15.15%) isolates each in the ICU], whereas their incidence in the ward was 13 (14.9%) isolates of *Klebsiella* spp. and seven
(8.04%) isolates of Acinetobacter spp. Although there was no statistically significant difference between the incidence of Acinetobacter spp. in the ward and that in the ICU, it was higher in the ICU than in the ward. There was a statistically significant difference between the incidence of Enterobacter spp. and Proteus spp. in the ICU and their incidence in the ward, with higher incidence of both in the ward.

Table 4 shows that there was a statistically significant difference in the sensitivity rates of imipenem, meropenem, tetracycline, vancomycin, kanamycin, cefadroxil, and ciprofloxacin between the ICU and the ward, with higher sensitivity rates of imipenem, meropenem, tetracycline, and vancomycin in the ICU and higher sensitivity rates of kanamycin, cefadroxil, and ciprofloxacin in the ward. The most sensitive antibiotics in the ICU were imipenem (14 cases, 60.9%), followed by meropenem (10 cases, 43.5%), levofloxacin (nine cases, 39.1%), doxycycline, and amikacin (eight cases each, 34.8%), and cefotaxime (seven cases, 30.4%).

The most sensitive antibiotic in the ward was imipenem (29 cases, 33.3%), followed by levofloxacin (28 cases, 32.2%) and doxycycline and amikacin (27 cases each, 31%).

Table 5 shows that there was a statistically significant difference in the incidence of Acinetobacter spp., Pseudomonas spp., and Enterobacter spp. between mild to moderate COPD and severe to very severe COPD, with higher incidence in severe to very severe COPD. Klebsiella spp. is common in both groups [14 (15.22%) isolates in mild to moderate COPD vs. four (14.3%) isolates in severe to very severe COPD].
Table 6 shows that there was a statistically significant difference in the sensitivity rates of imipenem and meropenem among severity groups, with higher sensitivity rates of both antibiotics in severe to very severe COPD than in mild to moderate COPD. The most sensitive antibiotic in severe to very severe COPD was imipenem (14 cases, 60.9%), followed by meropenem (10 cases, 43.5%) and levofloxacin (nine cases, 39.1%). The most sensitive antibiotic in mild to moderate COPD was imipenem (29 cases, 33.3%), followed by levofloxacin (26 cases, 29.9%) and amikacin and doxycycline (27 cases, 31%).

Table 7 shows that there was a statistically significant difference in the incidence of Acinetobacter infection among pH groups, with higher incidence in acidic patients than in those without acidosis [six (16.22%) isolates vs. six (7.23%) isolates, respectively]. Klebsiella spp. is common in both groups [five (13.51%) isolates vs. 13 (15.66%) isolates].

Table 8 shows that there was a statistically significant difference in the sensitivity rates of imipenem, levofloxacin, and meropenem among pH groups, with higher sensitivity rates of these antibiotics in acidic patients than in patients without acidosis. The most sensitive antibiotics in patients without acidosis were amikacin and doxycycline (27 cases, 31%), followed by levofloxacin (26 cases, 29.9%) and imipenem (25 cases, 28.7%). The most sensitive antibiotic in patients with acidosis was imipenem (18 cases, 78.3%), followed by levofloxacin (11 cases, 47.8%) and amikacin and doxycycline (27 cases, 31%).

Table 9 shows that there was a statistically significant difference in the incidences of Klebsiella spp., Acinetobacter spp., Pseudomonas spp., Enterobacter spp., Proteus spp., and Streptococci spp. between ex-smokers and smokers, with a higher incidence of Klebsiella spp., Acinetobacter spp., Pseudomonas spp., and Enterobacter spp. in ex-smokers and a higher incidence of Proteus spp. and Streptococci spp. in smokers. The most prevalent organism in ex-smokers was K. pneumoniae (18 isolates, 17.6%), followed by Acinetobacter spp. (12 isolates, 11.8%). The most prevalent organism in smokers was Streptococcus pneumoniae (three isolates, 16.6%), followed by Proteus spp. (two isolates, 11.1%).

Table 10 shows that there was a statistically significant difference in the sensitivity rates of imipenem, levofloxacin, amikacin, doxycycline, meropenem, and cefotaxime, with higher sensitivity rates of these antibiotics in ex-smokers than in smokers. The most sensitive antibiotic in ex-smokers was imipenem (41 cases, 44.1%), followed by levofloxacin (35 cases, 37.6%) and amikacin and doxycycline (33 cases, 35.5%). The most sensitive antibiotics in smokers were imipenem, levofloxacin, amikacin, doxycycline, meropenem, and cefotaxime (each two cases, 11.8%).

Table 11 shows that the most sensitive antibiotic for Pseudomonas spp. was levofloxacin (nine isolates, 100%); the most sensitive antibiotics for Klebsiella spp. were imipenem and meropenem (each 15 isolates, 16.6%); those for Enterobacter spp. were amikacin and doxycycline (five isolates, 100%); the most sensitive antibiotic for Acinetobacter spp. was doxycycline (eight isolates, 16.6%); those for Proteus spp. were amikacin and doxycycline (12 isolates, 11.8%).
isolates, 66.7%); and that for *Proteus* spp. was imipenem (four isolates, 100%).

**Table 7 Comparison of the incidence of most prevalent organisms according to presence or absence of acidosis**

| Organism          | With acidosis | Without acidosis | Total [N (%)] | P value |
|-------------------|---------------|------------------|---------------|---------|
| *Acinetobacter*   | 6 (16.22)     | 12 (10)          | 18 (16.4)     | 0.063 (NS) |
| *Klebsiella*      | 5 (15.15)     | 18 (16.4)        | 23 (20.9)     | 0.691 (NS) |
| *Pseudomonas*     | 4 (10.81)     | 9 (8.2)          | 13 (11.8)     | 0.243 (NS) |
| *Escherichia coli*| 2 (5.4)       | 5 (4.2)          | 7 (6.3)       | 0.549 (NS) |

The number of isolates in acidotic patients was 37, whereas the number of isolates in nonacidotic patients was 83.

**Table 8 Comparison of sensitivity rates of highly effective antibiotics among patients with acidosis**

| Antibiotic        | With acidosis | Without acidosis | Total [N (%)] | P value |
|-------------------|---------------|------------------|---------------|---------|
| Imipenem          | 18 (78.3)     | 43 (39.1)        | 61 (55.4)     | 0.0001 (HS) |
| Levofloxacin      | 11 (47.8)     | 37 (33.6)        | 58 (52.7)     | 0.009 (S) |
| Meropenem         | 10 (43.5)     | 30 (27.3)        | 40 (36.4)     | 0.002 (S) |
| Amikacin          | 8 (34.8)      | 35 (31.8)        | 43 (38.9)     | 0.567 (NS) |
| Doxycycline       | 8 (34.8)      | 35 (31.8)        | 43 (38.9)     | 0.567 (NS) |
| Cefotaxime        | 6 (26.1)      | 24 (21.8)        | 30 (27.3)     | 0.367 (NS) |

HS, highly significant; S, significant.

**Table 9 Comparison of the incidence of most prevalent organisms among smoking groups**

| Smoking groups     | Total [N (%)] | P value |
|--------------------|---------------|---------|
| Ex-smoker          | 18 (16.4)     | 0.0001 (HS) |
| Smoker             | 18 (16.4)     |         |

The number of isolates in ex-smokers was 102, whereas the number of isolates in smokers was 18; HS, highly significant; S, significant.

**Table 10 Comparison of sensitivity rates of highly effective antibiotics among smoking groups**

| Antibiotic        | Ex-smoker [N (%)] | Smoker [N (%)] | P value |
|-------------------|-------------------|----------------|---------|
| Imipenem          | 41 (44.1)         | 2 (11.8)       | 0.0001 (HS) |
| Levofloxacin      | 35 (37.6)         | 2 (11.8)       | 0.0001 (HS) |
| Amikacin          | 33 (35.5)         | 35 (31.8)      | 0.0001 (HS) |
| Doxycycline       | 33 (35.5)         | 35 (31.8)      | 0.0001 (HS) |
| Meropenem         | 28 (30.1)         | 21 (11.8)      | 0.001 (S) |
| Cefotaxime        | 22 (22.7)         | 22 (11.8)      | 0.028 (S) |

HS, highly significant; S, significant.

**Discussion**

COPD is a major cause of chronic morbidity and mortality throughout the world. Many people suffer from this disease for years and die prematurely from the disease or from its complications [1].

This study was conducted to search for the pattern of sputum bacteriology and antibiotic sensitivity for acute exacerbation of COPD in patients admitted to Abbassia Chest Diseases Hospital as a representation of the Egyptian population between September 2010 and July 2013 in order to correlate sputum bacteriology with severity, respiratory acidosis, and smoking pattern.

In our study, it was found that the most prevalent organisms in both the ICU and the ward were *K. pneumoniae* and *Acinetobacter* spp. [five (15.15%) isolates each in the ICU, and 13 (14.9%) isolates of *Klebsiella* spp. and seven (8.04%) isolates of *Acinetobacter* spp. in the ward]. Although there was no statistically significant difference between the incidence of *Acinetobacter* spp. in the ward and that in the ICU, it was higher in the ICU than in the ward. The most prevalent organism in the whole study was *K. pneumoniae* (18 isolates, 15%), followed by *Acinetobacter* spp. (12 isolates, 10%), *Pseudomonas aeruginosa* (nine isolates, 7.5%), and *Enterobacter* spp. and *Escherichia coli* (five isolates each, 4.2%) (Table 3).

*K. pneumoniae* was also the predominant organism in a study performed by Cucic [7]. They assessed 75 patients with AE-COPD who were treated in the ICU of the Clinic for Pulmonary Disease. In their study 44 (58.66%) patients had normal, nonpathogenic, usual bacterial flora isolated in sputum cultures and 31 (41.34%) had pathogenic bacteria in their sputum culture as follows: eight had *K. pneumoniae*, seven had *S. pneumoniae*, four had *E. coli*, and the others had other bacteria.

These results also agree with those of Hui et al. [8], who found that *Klebsiella* spp., *P. aeruginosa*, and *Acinetobacter* spp. constitute a large proportion of pathogens identified in patients with AECB. These results also coincide with those of Lin et al. [9], who found that the most prevalent microorganism in the sputum culture of patients with acute exacerbation of COPD was *K. pneumoniae* (19.6%), followed by *P. aeruginosa* (16.8%), *Haemophilus influenzae* (7.5%), and *Acinetobacter baumannii* (6.9%), of *Enterobacter* spp. In accordance with these results, Li et al. [10] concluded that *K. pneumoniae* and *P. aeruginosa* are the most common sputum pathogens in hospitalized patients with AE-COPD.
Table 11 Comparison of sensitivity rates of highly effective antibiotics in relation to most prevalent organisms

|                  | Pseudomonas spp. (n = 9) | Klebsiella spp. (n = 18) | Enterobacter spp. (n = 5) | Acinetobacter spp. (n = 12) | Proteus spp. (n = 4) | P value |
|------------------|--------------------------|--------------------------|--------------------------|-----------------------------|---------------------|---------|
| Imipenem         | 8 (88.89)                | 15 (83.33)               | 4 (80)                   | 7 (58.33)                   | 4 (100)             | 0.0001 (HS) |
| Amikacin         | 7 (77.78)                | 13 (72.22)               | 5 (100)                  | 1 (8.33)                    | 3 (75)              | 0.001 (HS) |
| Meropenem        | 4 (44.4)                 | 15 (83.33)               | 2 (40)                   | 5 (41.67)                   | 1 (25)              | 0.0001 (HS) |
| Cefotaxime       | 4 (44.4)                 | 8 (44.44)                | 3 (60)                   | 1 (8.33)                    | 2 (50)              | 0.0001 (HS) |
| Levofloxacine    | 9 (100)                  | 8 (44.44)                | 4 (80)                   | 4 (33.3)                    | 3 (75)              | 0.0001 (HS) |
| Doxycycline      | 6 (66.7)                 | 8 (44.44)                | 5 (100)                  | 8 (66.7)                    | 1 (25)              | 0.0001 (HS) |

HS, highly significant.

However, these results disagree with those of Fagon et al. [11], who found that the most prevalent microorganism in COPD patients was H. influenzae (39%), followed by S. pneumoniae (16%) and Moraxella catarrhalis (7%). This disagreement may be due to the difference in environment, timing of the study, number of cases, and the method of sample collection, such as bronchoalveolar lavage and use of a protective brush.

These results also disagree with those of Monsó et al. [12], who found that the most prevalent microorganism was H. influenzae (58%), followed by M. catarrhalis and S. pneumoniae (each 10%).

As regards severity in relation to organisms, it was found that there was a statistically significant difference in the incidence of Acinetobacter spp., Pseudomonas spp., and Enterobacter spp. between mild to moderate COPD and severe to very severe COPD, with a higher incidence of these organisms in severe to very severe COPD compared with mild to moderate COPD. Klebsiella spp. is common in both groups [14 (15.22%) isolates vs. six (7.23%) isolates, respectively]. Klebsiella spp. is common in both groups [five (13.51%) isolates vs. 13 (15.66%) isolates, respectively] and the most prevalent organism in patients without acidosis was Klebsiella spp. (13 isolates, 15.66%), followed by Acinetobacter spp. (six isolates, 7.23%) and P. aeruginosa (five isolates, 6.02%). The most prevalent organism in patients with acidic pH was Acinetobacter spp. (six isolates, 16.22%), followed by Klebsiella spp. (five isolates, 13.51%) (Table 7). Hypercapnia, an elevation of the level of CO₂ in blood and tissues, is a marker of poor prognosis in COPD and other pulmonary disorders. Hypercapnia inhibits the expression of tumor necrosis factor and interleukin 6 and phagocytosis in macrophages in vitro [19].

As regards smoking habits, it was found that there was statistically significant difference in the incidence of Klebsiella spp., Acinetobacter spp., Pseudomonas spp., Enterobacter spp., Proteus spp., and Streptococci spp. between ex-smokers and smokers, with higher incidence of Klebsiella spp., Acinetobacter spp., Pseudomonas spp., Enterobacter spp. in ex-smokers and higher incidence of Proteus spp. and Streptococci spp. in smokers. The most prevalent organism in ex-smokers was K. pneumoniae (18 isolates, 17.6%). The most prevalent organism in smokers was Streptococci spp. (three isolates, 16.6%), followed by Proteus spp. (two isolates, 11.1%) (Table 9).

These results agree with those of Monsó et al. [20], who found that excessive smoking and duration of smoking are associated with progressive deterioration in lung function and associated with infection with
As regards the sensitivity rates of antibiotics regardless of the type of organism, it was found that the most sensitive antibiotic in the whole study was imipenem (43 cases, 39.1%), followed by levofloxacin (37 cases, 33.6%), doxycycline and amikacin (35 cases each, 31.8%), meropenem (30 cases, 27.3%), and cefotaxime (24 cases, 21.8%). It was also found that the most sensitive antibiotic in the ICU was imipenem (14 cases, 60.9%), followed by meropenem (10 cases, 43.5%) and levofloxacin (nine cases, 39.1%). The most sensitive antibiotic in the ward was imipenem (29 cases, 33.3%), followed by levofloxacin (28 cases, 32.2%) (Table 4).

Destache et al. [21] found that the efficacy of trimethoprim–sulfamethoxazole, tetracycline, and Erythromycin was 81%, whereas the efficacy of azithromycin, ciprofloxacin, and amoxicillin–clavulanic acid was 93%. These findings disagree with the results of this study, in which the sensitivity rate was 19.1% for trimethoprim–sulfamethoxazole, 5.5% for amoxicillin–clavulanic acid, 3.6% for each of erythromycin and ciprofloxacin, and 2.75% for each of azithromycin and tetracycline.

Wilson et al. [22] found that the rate of bacterial eradication after treatment with amoxicillin–clavulanic acid was 76.7%, that after treatment with levofloxacin was 96.3%, and that after treatment with azithromycin was 87.4%. These figures mismatch with the ours, in which the sensitivity rate was 33.6% for levofloxacin, 5.5% for amoxicillin–clavulanic acid, and 2.75% for azithromycin.

Erkan et al. [23] noted the poor efficacy of penicillin, ampicillin, amoxicillin–clavulanic acid, tetracycline, and Erythromycin against most prevalent respiratory pathogens in acute exacerbation of COPD. Their results agree with the low sensitivity rates of these antibiotics in this study (5.5% for amoxicillin–clavulanic acid, 3.6% for erythromycin, 2.75% for tetracycline, 1.8% for penicillin, and 0.9% for ampicillin).

As regards the sensitivity rates of antibiotics in relation to most prevalent organisms, it was found that the most sensitive antibiotic for *Pseudomonas* spp. was doxycycline (five isolates, 100%). The most sensitive antibiotic for *Acinetobacter* spp. was doxycycline (eight isolates, 66.7%), followed by imipenem (seven isolates, 58.33%). The most sensitive antibiotic for *Proteus* spp. was imipenem (four isolates, 100%), followed by amikacin and levofloxacin (three isolates each, 75%) (Table 11 and Fig. 1).

As regards the sensitivity rates of antibiotics in relation to severity, it was found that there was statistically significant difference in the sensitivity rates of imipenem and meropenem among severity groups, with higher sensitivity rates of both antibiotics in severe to very severe COPD than in mild to moderate COPD. The most sensitive antibiotic in severe to very severe COPD was imipenem (14 cases, 60.9%), followed by meropenem (10 cases, 43.5%), levofloxacin (nine cases, 39.1%), amikacin (eight cases, 34.8%), and cefotaxime (seven cases, 30.4%). The most sensitive antibiotic in mild to moderate COPD was imipenem (29 cases, 33.3%), followed by levofloxacin (28 cases, 32.2%) and amikacin and doxycycline (27 cases, 31%) (Table 6).

Fein and Fein [24] recommended doxycycline, levofloxacin, and other drugs as a treatment strategy for mild acute exacerbation of COPD and recommended cefotaxime, levofloxacin, and other drugs for severe acute exacerbation of COPD. This agrees with the previously mentioned susceptibility rates in our study.

GOLD guidelines [1] recommended β-lactam and other drugs as a treatment strategy for mild and moderate acute exacerbation of COPD and recommended imipenem, meropenem, and high dose of levofloxacin for severe acute exacerbation of COPD. This agrees with the previously mentioned susceptibility rates in our study.

As regards the sensitivity rates of antibiotics in relation to pH, it was found that there was statistically significant difference in sensitivity rates of imipenem, doxycycline, and other antibiotics (Table 7).
levofloxacin, and meropenem among pH groups, with higher sensitivity of these antibiotics in patients with acidic pH than in those without acidosis. The most sensitive antibiotics in patients without acidosis were amikacin and doxycycline (27 cases, 31%). The most sensitive antibiotic in patients with acidic pH was imipenem (18 cases, 78.3%), followed by levofloxacin (11 cases, 47.8%) (Table 8).

As regards the sensitivity rates of antibiotics in relation to smoking, it was found that there was statistically significant difference in sensitivity rates of imipenem, levofloxacin, amikacin, doxycycline, meropenem, and cefotaxime, with higher sensitivity rates of these antibiotics in ex-smokers than in smokers. The most sensitive antibiotic in ex-smokers was imipenem (41 cases, 44.1%), followed by levofloxacin (35 cases, 37.6%). The most sensitive antibiotics in smokers were imipenem, levofloxacin, amikacin, doxycycline, meropenem, and cefotaxime (two cases each, 11.8%) (Table 10). To our knowledge, there are no studies with results comparable to our results.

Acknowledgements
Conflicts of interest
There are no conflicts of interest.

References
1. Global Initiative for Chronic Obstructive Lung Disease (GOLD). Workshop report, global strategy for diagnosis, management, and prevention of COPD. Bethesda, MD: National Institutes of Health, National Heart, Lung, and Blood Institute. 2006.
2. Barnes PJ. Chronic obstructive pulmonary disease. N Engl J Med 2000; 343:269–280.
3. Burge S, Wedzicha JA. COPD exacerbations: definitions and classifications. Eur Respir J Suppl 2003; 41:48s–53s.
4. Wilkinson TM, Patel IS, Wilks M, Donaldson GC, Wedzicha JA. Airway bacterial load and FEV1 decline in patients with chronic obstructive pulmonary disease. Am J Respir Crit Care Med 2003; 167:1090–1095.
5. Chemeky CC, Brown SE, Light TIW. Culture techniques and results. Infect Immun 2001; 122:341–349.
6. Altman DG, Schulz KF, Moher D, Egger M, Davidoff F, Elbourne D, et al. The revised CONSORT statement for reporting randomized trials: explanation and elaboration. Ann Intern Med 2001; 134:663–694.
7. Cukic V. The most common detected bacteria in sputum of patients with the acute exacerbation of COPD. Mater Sociomed 2013; 25:226–229.
8. Hui DS, Ip M, Ling T, Chang SC, Liao CH, Yoo CG, et al. A multicentre surveillance study on the characteristics, bacterial aetiologies and in vitro antibiotic susceptibilities in patients with acute exacerbations of chronic bronchitis. Respirology 2011; 16:532–539.
9. Lin SH, Kuo PH, Hsueh PR, Yang PC, Kuo SH. Sputum bacteriology in hospitalized patients with acute exacerbation of chronic obstructive pulmonary disease in Taiwan with an emphasis on Klebsiella pneumoniae and Pseudomonas aeruginosa. Respirology 2007; 12:81–87.
10. Li H, Kuo S-H, Yang P-C. Bacteria in acute exacerbations of chronic bronchitis. Chest 2006; 363:600–607.
11. Fagon JY, Chastre J, Trouillet JL, Domart Y, Dombret MC, Bomet M, Gibert C. Characterization of distal bronchial microflora during acute exacerbation of chronic bronchitis. Use of the protected specimen brush technique in 54 mechanically ventilated patients. Am Rev Respir Dis 1990; 142:1004–1008.
12. Monsó E, Ruiz J, Rosell A, Manterola J, Fiz J, Morera J, Ausina V. 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(Pt 1):1316–1320.
13. Miravitlles M, Episnosa C, Fernandez-Laso E, Martos JA Maldonado JA, Gallego M. Relationship between bacterial flora in sputum and functional impairment in patients with acute exacerbations of COPD. Chest 1999; 116:40–46.
14. Brunton S, BP Carmichael, Colgan R. Acute exacerbation of chronic bronchitis. Am J Manag Care 2004; 10:689–696.
15. Noweta K, Frankowska M, Grzelewska-Rzymowska I. Exacerbations of chronic obstructive pulmonary disease and the role of sputum bacteriological examination. Pneumonol Alergol Pol 2006; 74:396–402.
16. Lior C, Cots JM, Herreras A. Bacterial etiology of chronic bronchitis exacerbations. Arch Bronconeumol 2006; 42:388–393.
17. Lode H, Allewelt M, Balk S, De Roux A, Mauch H, Niederman M, Schmid-loanas M. A prediction model for bacterial etiology in acute exacerbations of COPD. Infection 2007; 35:143–149.
18. Rosell A, Monsó E, Soler N, Torres F, Angrill J, Rlise G, et al. Microbiological determinants of exacerbations in chronic obstructive pulmonary disease. Arch Intern Med 2007; 167:891–897.
19. Gates KL, Howell HA, Nair A, Vohwinkel CW, Welch LC, Beitel GJ, et al. Hypercapnia impairs lung neutrophil function and increases mortality in murine Pseudomonas pneumonia. Am J Respir Cell Mol Biol 2013; 49:821–828.
20. Monsó E, Garcia-Aymerich J, Soler N, Farrero E, Felez MA, Antó JM, Torres A. EFRAm Investigators. Bacterial infection in exacerbated COPD with changes in sputum characteristics. Epidemiol Infect 2003; 131(1):799–804.
21. Destache CJ, Dewan N, O’Donohue WJ, Campbell JC, Angelillo VA. Clinical and economic considerations in the treatment of acute exacerbations of chronic bronchitis. J Antimicrob Chemother 1999; 43(Suppl A):107–113.
22. Wilson R, Anzueto A, Miravitlles M, Aris P, Faragó G, Haverstock D, et al. A novel study design for antibiotic trials in acute exacerbations of COPD: MAESTRAL methodology. Int J Chron Obstruct Pulmon Dis 2011; 6:373–383.
23. Erkan L, Uzun O, Findik S, Katar D, Sanic A, Atili AG. Role of bacteria in acute exacerbations of chronic obstructive pulmonary disease. Int J Chron Obstruct Pulmon Dis 2008; 3:463–467.
24. Fein A, Fein AM. Management of acute exacerbations in chronic obstructive pulmonary disease. Curr Opin Pulm Med 2000; 6:122–128.