# Pattern of sputum bacteriology in acute exacerbations of chronic obstructive pulmonary disease

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**Background** Chronic obstructive pulmonary disease (COPD) is a major cause of chronic morbidity and mortality worldwide.

Acute exacerbation of COPD is 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.
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## Introduction

Chronic obstructive pulmonary disease (COPD) is a major cause of 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. Exacerbations are also associated with considerable physiologic deterioration and increased airway inflammatory changes that are caused by various factors such as viruses, bacteria, and possibly common pollutants [3].

Many studies have been conducted on the role of bacterial infection in COPD and have isolated bacteria in significant numbers from patients with clinically stable COPD, indicating the presence of lower airway 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 [4].

## 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 ($FEV_1 \geq 50$).
Group 2: patients with severe to very severe COPD ($FEV_1 < 50$).
(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, $PaO_2$, $PaCO_2$, $HCO_3$, and $SO_2$%.
　(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 breath 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,

**Table 1 Number (%) of patients in relation to their sex**

| Sex | Number of patients (%) |
|---|---|
| Females | 10 (9.2) |
| Males | 100 (90.8) |

**Table 2 Mean age of patients with AE-chronic obstructive pulmonary disease**

| | Mean | SD | Minimum | Maximum |
|---|---|---|---|---|
| Age (years) | 54.88 | 8.82 | 40 | 78 |

**Table 3 Comparison of the incidence of different microorganisms isolated from sputum cultures of patients admitted to the ward, the ICU, and in the whole study**

| Isolated microorganisms | N (%) | | | P value |
|---|---|---|---|---|
| | ICU (n = 23) | Ward (n = 87) | Total (n = 110) | |
| *Klebsiella pneumoniae* | 5 (15.15) | 13 (14.9) | 18 (15) | 0.961 (NS) |
| *Acinetobacter* spp. | 5 (15.15) | 7 (8.04) | 12 (10) | 0.140 (NS) |
| *Pseudomonas aerugenosa* | 3 (9.1) | 6 (6.9) | 9 (7.5) | 0.582 (NS) |
| *Escherichia coli* | 2 (6.1) | 3 (3.4) | 5 (4.2) | 0.381 (NS) |
| *Streptococci* spp. | 2 (6.1) | 2 (2.3) | 4 (3.3) | 0.190 (NS) |
| *Haemophilus influenzae* | 1 (3.03) | 1 (1.1) | 2 (1.7) | 0.342 (NS) |
| *Staphylococcus aureus* | 1 (3.03) | 2 (2.3) | 3 (2.5) | 0.752 (NS) |
| *Moraxella catarrhalis* | 1 (3.03) | 1 (1.1) | 2 (1.7) | 0.342 (NS) |
| *Morganella morgagni* | 1 (3.03) | 1 (1.1) | 2 (1.7) | 0.342 (NS) |
| *Proteus* spp. | 0 (0) | 4 (4.6) | 4 (3.3) | 0.032 (S) |
| *Citrobacter* spp. | 0 (0) | 2 (2.3) | 2 (1.7) | 0.129 (NS) |
| *Enterobacter* spp. | 0 (0 | 5 (5.7) | 5 (4.2) | 0.017 (S) |
| Nonpathogenic organisms | 12 (36.4) | 40 (46 | 52 (43.3) | 0.154 (NS) |

The number of isolates in ICU patients is 33, whereas the number of isolates in the ward is 87; S, significant.

**Table 4 Comparison of sensitivity rates of all antibiotics regardless of type of organism in the ICU and ward, and total number**

| Antibiotics | N (%) | | | P value |
|---|---|---|---|---|
| | ICU (n = 23) | Ward (n = 87) | Total (n = 110) | |
| Imipenem | 14 (60.9) | 29 (33.3) | 43 (39.1) | 0.004 (S) |
| Meropenem | 10 (43.5) | 20 (23) | 30 (27.3) | 0.012 (S) |
| Levofloxacin | 9 (39.1) | 28 (32.2) | 37 (33.6) | 0.414 (NS) |
| Doxycycline | 8 (34.8) | 27 (31) | 35 (31.8) | 0.088 (NS) |
| Amikacin | 8 (34.8) | 27 (31) | 35 (31.8) | 0.088 (NS) |
| Cefotaxime | 7 (30.4) | 17 (19.5) | 24 (21.8) | 0.12 (NS) |
| Ampicillin–sulbactam | 6 (26.1) | 17 (19.5) | 23 (21) | 0.328 (NS) |
| Cefoperazone | 5 (21.7) | 18 (20.7) | 23 (21) | 0.878 (NS) |
| Ceftazidime | 5 (21.7) | 18 (20.7) | 23 (21) | 0.878 (NS) |
| Gentamicin | 5 (21.7) | 11 (12.6) | 16 (14.5) | 0.120 (NS) |
| Ceftriaxone | 5 (21.7) | 17 (19.5) | 22 (20) | 0.732 (NS) |
| Piperacillin | 3 (13) | 18 (20.7) | 21 (19.1) | 0.185 (NS) |
| Ofloxacin | 3 (13) | 17 (19.5) | 20 (18.2) | 0.254 (NS) |
| Sxt | 3 (13) | 21 (24.1) | 21 (19.1) | 0.068 (NS) |
| Cefepime | 3 (13) | 14 (16.1) | 17 (15.5) | 0.566 (NS) |
| Amoxicillin–clavulinic acid | 2 (8.7) | 4 (4.6) | 6 (5.5) | 0.261 (NS) |
| Tetracycline | 2 (8.7) | 1 (1.15) | 3 (2.75) | 0.016 (S) |
| Vancomycin | 2 (8.7) | 0 (0) | 2 (1.8) | 0.003 (S) |
| Erythromycin | 1 (4.3) | 3 (3.4) | 4 (3.6) | 0.746 (NS) |
| Azithromycin | 1 (4.3) | 2 (2.3) | 3 (2.75) | 0.436 (NS) |
| Penicillin | 1 (4.3) | 1 (1.15) | 2 (1.8) | 0.177 (NS) |
| Kanamycin | 0 (0) | 6 (6.8) | 6 (5.5) | 0.009 (S) |
| Cefadroxil | 0 (0) | 5 (5.8) | 5 (4.5) | 0.016 (S) |
| Ciprofloxacin | 0 (0) | 4 (4.6) | 4 (3.6) | 0.032 (S) |
| Cephradine | 0 (0) | 2 (2.3) | 2 (1.8) | 0.129 (NS) |
| Ampicillin | 0 (0) | 1 (1.15) | 1 (0.9) | 0.284 (NS) |
| Tazocin | 0 (0) | 1 (1.15) | 1 (0.9) | 0.284 (NS) |
| Azactam | 0 (0) | 1 (1.15) | 1 (0.9) | 0.284 (NS) |
| Cefoxitin | 0 (0) | 1 (1.15) | 1 (0.9) | 0.284 (NS) |

S, significant.

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 (28 cases, 32.2%) 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 acidotic 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 acidotic 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 meropenem (10 cases, 43.5%).

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, 11.11%).

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, 83.33%); those for *Enterobacter* spp. were amikacin and doxycycline (five isolates, 100%); the most sensitive antibiotic for *Acinetobacter* spp. was doxycycline (eight

**Table 5 Comparison of the incidence of most prevalent organisms according to severity of chronic obstructive pulmonary disease**

| | Severity groups [*N* (%)] | | Total (*n* = 110) [*N* (%)] | *P* value |
|---|---|---|---|---|
| | Mild to moderate COPD (*n* = 87) | Severe to very severe COPD (*n* = 23) | | |
| *Klebsiella* spp. | 14 (15.22) | 4 (14.3) | 18 (15) | 0.866 (NS) |
| *Acinetobacter* spp. | 7 (7.61) | 5 (17.9 | 12 (10) | 0.042 (S) |
| *Pseudomonas* spp. | 5 (5.43) | 4 (14.3) | 9 (7.5) | 0.046 (S) |
| *Escherichia coli* | 3 (3.2) | 2 (7.14) | 5 (4.2) | 0.220 (NS) |
| *Enterobacter* spp. | 2 (2.17) | 3 (10.7) | 5 (4.2) | 0.017 (S) |

The number of isolates in mild to moderate COPD is 92, whereas the number of isolates in severe to very severe COPD is 28; COPD, chronic obstructive pulmonary disease; S, significant.

**Table 6 Comparison of sensitivity rates of highly effective antibiotics among severity groups**

| | Severity groups [*N* (%)] | | Total (*n* = 110) [*N* (%)] | *P* value |
|---|---|---|---|---|
| | Severe to very severe COPD (*n* = 23) | Mild to moderate COPD (*n* = 87) | | |
| Imipenem | 14 (60.9) | 29 (33.3) | 43 (39.1) | 0.0001 (HS) |
| Meropenem | 10 (43.5) | 20 (23) | 30 (27.3) | 0.002 (S) |
| Levofloxacin | 9 (39.1) | 28 (32.2) | 37 (33.6) | 0.308 (NS) |
| Amikacin | 8 (34.8) | 27 (31) | 35 (31.8) | 0.567 (NS) |
| Doxycycline | 8 (34.8) | 27 (31) | 35 (31.8) | 0.567 (NS) |
| Cefotaxime | 7 (30.4) | 17 (19.5) | 24 (21.8) | 0.075 (NS) |

COPD, chronic obstructive pulmonary disease; S, significant.

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**

| | pH groups [N (%)] | | Total (n = 110) [N (%)] | P value |
|---|---|---|---|---|
| | With acidosis (n = 23) | Without acidosis (n = 87) | | |
| *Acinetobacter* spp. | 6 (16.22) | 6 (7.23) | 12 (10) | 0.063 (NS) |
| *Klebsiella* | 5 (13.51) | 13 (15.66) | 18 (16.4) | 0.691 (NS) |
| *Pseudomonas* spp. | 4 (10.81) | 5 (6.02) | 9 (8.2) | 0.243 (NS) |
| *Escherichia coli* | 2 (5.4) | 3 (3.6) | 5 (4.2) | 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**

| | pH groups [N (%)] | | Total (n = 110) [N (%)] | P value |
|---|---|---|---|---|
| | With acidosis (n = 23) | Without acidosis (n = 87) | | |
| Imipenem | 18 (78.3) | 25 (28.7) | 43 (39.1) | 0.0001 (HS) |
| Levofloxacin | 11 (47.8) | 26 (29.9) | 37 (33.6) | 0.009 (S) |
| Meropenem | 10 (43.5) | 20 (23) | 30 (27.3) | 0.002 (S) |
| Amikacin | 8 (34.8) | 27 (31) | 35 (31.8) | 0.567 (NS) |
| Doxycycline | 8 (34.8) | 27 (31) | 35 (31.8) | 0.567 (NS) |
| Cefotaxime | 6 (26.1) | 18 (20.7) | 24 (21.8) | 0.367 (NS) |

HS, highly significant; S, significant.

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

| | Smoking groups [N (%)] | | Total (n = 110) [N (%)] | P value |
|---|---|---|---|---|
| | Ex-smoker (n = 93) | Smoker (n = 17) | | |
| *Klebsiella* spp. | 18 (17.6) | 0 (0) | 18 (16.4) | 0.0001 (HS) |
| *Acinetobacter* spp. | 12 (11.8) | 0 (0) | 12 (10) | 0.001 (S) |
| *Pseudomonas* spp. | 9 (8.8) | 0 (0) | 9 (8.2) | 0.003 (S) |
| *Enterobacter* spp. | 5 (4.9) | 0 (0) | 5 (4.2) | 0.027 (S) |
| *Proteus* spp. | 2 (2) | 2 (11.11) | 4 (3.3) | 0.012 (S) |
| *Streptococcus* spp. | 1 (0.9) | 3 (16.6) | 4 (3.3) | 0.0001 (HS) |

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**

| | Smoking groups [N (%)] | | Total (n = 110) [N (%)] | P value |
|---|---|---|---|---|
| | Ex-smoker (n = 93) | Smoker (n = 17) | | |
| Imipenem | 41 (44.1) | 2 (11.8) | 43 (39.1) | 0.0001 (HS) |
| Levofloxacin | 35 (37.6) | 2 (11.8) | 37 (33.6) | 0.0001 (HS) |
| Amikacin | 33 (35.5) | 2 (11.8) | 35 (31.8) | 0.0001 (HS) |
| Doxycycline | 33 (35.5) | 2 (11.8) | 35 (31.8) | 0.0001 (HS) |
| Meropenem | 28 (30.1) | 2 (11.8) | 30 (27.3) | 0.001 (S) |
| Cefotaxime | 22 (23.7) | 2 (11.8) | 24 (21.8) | 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 aerugenosa* (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 Cukic [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**

| | N (%) | | | | | P value |
|---|---|---|---|---|---|---|
| | *Pseudomonas* spp. (*n* = 9) | *Klebsiella* spp. (*n* = 18) | *Enterobacter* spp. (*n* = 5) | *Acinetobacter* spp. (*n* = 12) | *Proteus* spp. (*n* = 4) | |
| 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) | 0.0001 (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) |
| Levofloxacin | 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 in mild to moderate COPD vs. four (14.3%) isolates in severe to very severe COPD] (Table 5).

Lin *et al.* [9] and Li *et al.* [10] observed that *K. pneumoniae* was more frequently isolated in stage I COPD than in stages II, III, and IV.

Our results agree with those of Li *et al.* [10], Miravittles *et al.* [13], and Brunton *et al.* [14], who concluded that *P. aeruginosa* was associated with poor clinical outcome. In addition, Noweta *et al.* [15] found that the most prevalent microorganism in acute exacerbation of severe and very severe COPD was *A. baumannii* (21%).

However, these results disagree with those of Lior *et al.* [16], who found in 468 patients with moderate COPD that the most prevalent microorganism was *S. pneumoniae* (34.8%), followed by *M. catarrhalis* (23.9%) and *H. influenzae* (12.6%). This disagreement may be due to the large difference in the number of cases.

The previous results disagree with those of Lode *et al.* [17], Rosell *et al.* [18], and Miravittles *et al.* [13], who found that the most prevalent microorganism in acute exacerbation of severe COPD was *H. influenzae*, followed by *S. pneumoniae* and *P. aeruginosa*. The disparity may be due to the difference in environment.

As regards the presence or absence of respiratory acidosis, it was found that there was statistically significant difference in the incidence of *Acinetobacter* spp. among pH groups, with a higher incidence in acidotic pH than in patients 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, 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. aerugenosa* (five isolates, 6.02%). The most prevalent organism in patients with acidotic 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 $CO_2$ 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, 11.11%) (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

*P. aerugenosa* and other Gram-negative virulent strains in patients with acute exacerbation of COPD.

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–clavulinic 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–clavulinic 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–clavulinic 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–clavulinic acid, and 2.75% for azithromycin.

Erkan *et al*. [23] noted the poor efficacy of penicillin, ampicillin, amoxicillin–clavulinic 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–clavulinic 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 levofloxacin (nine isolates, 100%), followed by imipenem (eight isolates, 88.89%) and amikacin (seven isolates, 77.78%). The most sensitive antibiotics for *Klebsiella* spp. were imipenem and meropenem (15 isolates each, 83.33%), followed by amikacin (13 isolates, 72.22%) and cefotaxime, levofloxacin, and doxycycline (eight isolates, 44.44%). The most sensitive antibiotics for *Enterobacter* spp. were amikacin and

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).
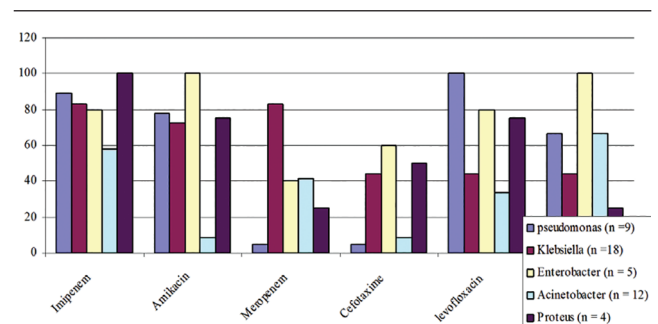
As regards the sensitivity rates of antibiotics in relation to severity, it was found that there was statistically significant difference in the sensitivity rates of imipenem and meropenem among severity groups, with higher sensitivity rates of both antibiotics in severe to very severe COPD than in mild 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,

**Fig. 1**



Comparison of sensitivity rates of highly effective antibiotics in relation to most prevalent organisms.

levofloxacin, and meropenem among pH groups, with higher sensitivity of these antibiotics in patients with acidotic 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 acidotic 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

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