Introduction
Chronic obstructive pulmonary disease (COPD) is ‘a common preventable and treatable disease characterized by persistent airflow limitation that is usually progressive and associated with an enhanced chronic inflammatory response in the airways and the lung to noxious particles or gases’ [1]. Acute exacerbation of chronic obstructive pulmonary disease (AECOPD) is defined as ‘an acute worsening of respiratory symptoms that result in additional therapy.’ It is classified into mild exacerbation, which is treated with short-acting bronchodilators only, moderate exacerbation treated with short-acting bronchodilators plus antibiotics and/or oral corticosteroids, or severe exacerbation (patient requires hospitalization or visits the emergency room), which may be associated with acute respiratory failure [2]. AECOPD may be caused by infectious and noninfectious causes. However, the cause of AECOPD is unknown in up to 30% of cases [3]. In ~40–60% of AECOPD, bacterial pathogens can be isolated from distal airways [4]. The aim of this study was to identify the causative bacteria, antibiotic sensitivity, and resistance in patients with AECOPD in respiratory ICU.

Patients and methods
This prospective cross-sectional study was done on 50 critically ill patients with COPD admitted to the respiratory ICU of Assiut university hospital with acute exacerbation in the period from July 2017 to June 2018. Patients were diagnosed as having COPD based on history of exposure to risk factors, clinical examination, and confirmation by spirometry. AECOPD was diagnosed depending upon the presence of two of the following symptoms: increased cough, increased purulence and/or volume of sputum, and increased severity of dyspnea [1]. Patients having interstitial lung disease, bronchial asthma, bronchiectasis, tuberculosis, pneumonia, malignancy, heart diseases, or another diagnosis in proportion of morbidity and antibiotic use. This study aimed to identify the causative bacteria, antimicrobial sensitivity, and resistance of hospitalized patients in respiratory ICU owing to AECOPD.

Results
Klebsiella pneumoniae was the most frequently detected organism in 29 (58%) patients followed by Pseudomonas aeruginosa in 14 (28%) patients, methicillin resistant Staphylococcus aureus (MRSA) in eight (16%) patients, Acinetobacter baumannii in seven (14%) patients, Proteus spp. and Staphylococcus aureus in five (10%) patients each, and Escherichia coli in three (6%) patients. No growth was reported in three (6%) patients. Among gram-positive organisms, linezolid had the upper hand of efficacy followed by vancomycin and teicoplanin. Gram-negative organisms had high rate or resistance to most tested antibiotics. Frequency of death was more (62.5%) in patients with MRSA.

Conclusion
K. pneumoniae was the most frequent organism followed by P. aeruginosa, MRSA, and A. baumannii. The isolated bacterial strains were characterized by high resistance rates to the most used antimicrobials. Mortality rate was more among patients with MRSA.

Keywords: acute exacerbation, bacteriological profile, chronic obstructive pulmonary disease

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chest radiography and/or computed tomography were excluded. Patients with previous hospital admission or antibiotic use in the past 3 months were excluded. The study was approved by the regional ethical committee of Assiut University Hospital, and a written consent was obtained from all enrolled patients or their close relatives.

**Specimen collection**

Universal precautions were followed [5]. Patients were instructed to rinse their mouth twice with plain water and then collect deep coughed sputum into a sterile wide-mouth container with a screw cap. The specimen was collected early in the morning, before breakfast, to obtain an overnight accumulation of secretions. In the intubated patients, the sample was collected by suction from endotracheal tube that was cut from both ends, and sample in its midportion was taken to avoid contaminated sample. Immediately after admission and before starting antibiotics, the specimen was labeled with the patient’s name, specimen type, and the date and time of collection. The samples were brought to microbiology laboratory immediately and were processed within 30 min of collection, and if a delay of more than 1–2 h was expected, the specimen was refrigerated [5]. Samples were processed at Assiut University Hospitals, Clinical Pathology Department, Microbiology Unit.

**Isolation and identification**

All specimens were cultured on blood agar and incubated at 37°C for 24 h. All samples were subjected to the following: (a) Gram’s stain of the colonies, (b) culture on MacConkey’s agar and blood agar (Becton, Dickinson and Company (BD), headquartered in Franklin Lakes, New Jersey, USA), (c) biochemical reactions, and (d) identification and antimicrobial sensitivity test by VITEK 2 Compact (BioMérieux, France).

The instructions of the manufacturer were followed during sample testing [5]. In brief, strains were cultured on MacConkey agar for 18–24 h at 37°C before the isolate was subjected to analysis. Strains that had been stored at −70°C were subcultured twice before analysis. A bacterial suspension was adjusted to a McFarland standard of 0.50. Identification cards were inoculated with microorganism suspensions using an integrated vacuum apparatus. Each test reaction was read every 15 min to measure either turbidity or colored products of substrate metabolism. The databases of the VITEK 2 identification products were constructed with large strain sets of well-characterized microorganisms tested under various culture conditions. Regarding sensitivity of the organisms to different antibiotics in this study, bacteria were classified into two groups. The first group included gram-negative bacteria, and the second group included gram-positive bacteria. The first group was tested for amoxicillin–clavulanic acid, piperacillin–tazobactam, cefaclor, ceftizidime, cefepime, meropenem, ciprofloxacin, levofloxacin, and amikacin. The second group was tested for amoxicillin–clavulanic acid, erythromycin, linezolid, teicoplanin, and vancomycin.

**Results**

Demographic data of the study group are shown in Table 1. Mean±SD age of patients was 65±8.06 years, 33 (66%) of patients were males, and 32 (64%) had previous history of ICU admission. Mean±SD of duration of the disease was 15.16±2.01 years. Results of sputum culture showed that the most frequent organism detected in those patients was *Klebsiella pneumoniae* in 29 (58%) patients followed by *Pseudomonas aeruginosa*, methicillin resistant *Staphylococcus aureus* (MRSA), and *Acinetobacter baumannii* in 14 (28%), eight (16%), and seven (14%) patients, respectively. No growth was reported in three (6%) patients. Culture showed more than one organism in 22 (44%) patients; the most frequent combination was *K. pneumonia* and *P. aeruginosa*, which occurred in six (12%) patients (Table 2). Regarding sensitivity of the organisms to different antibiotics, this study reported a

| Variables                  | Frequency (%) |
|----------------------------|---------------|
| Age (years)                | 65.02±8.06    |
| Sex                        |               |
| Male                       | 33 (66)       |
| Female                     | 17 (34)       |
| Smoking state              |               |
| Current smoker             | 18 (36)       |
| Nonsmoker                  | 18 (36)       |
| Ex-smoker                  | 10 (20)       |
| Passive smoker             | 4 (8)         |
| Comorbidities              |               |
| Diabetes mellitus          | 17 (34)       |
| Hypertension               | 17 (34)       |
| Chronic liver disease      | 6 (12)        |
| Chronic kidney disease     | 5 (10)        |
| Cardiac disease            | 4 (8)         |
| Hypothyroidism             | 2 (4)         |
| None                       | 20 (40)       |
| Residence                  |               |
| Urban                      | 11 (22)       |
| Rural                      | 39 (78)       |
high resistant rate of all organisms to most tested antibiotics except for reasonable sensitivity of *Streptococcus pneumoniae* and *Staphylococcus aureus* to linezolid, teicoplanin, and vancomycin (Tables 3 and 4). Median hospital stay had no statistical differences between types of organisms \((P=0.08)\), but the frequency of death was more \((62.5\%)\) in patients with MRSA \((P=0.04)\) (Table 5).

**Discussion**

COPD is a known cause of morbidity and mortality. AECOPD is defined as an acute worsening of respiratory symptoms that result in additional therapy [1]. By early introduction of empirical antibiotics, outcome is improved and mortality is reduce [6].

The present study reported high frequency of deaths, as death occurred in 25 \((50\%)\) patients, and 25 \((50\%)\) patients improved and were discharged. Connors *et al.* [7] reported mortality rates of 6–42%. Groenewegen *et al.* [8] and Soler-Cataluña *et al.* [9] reported similar results. The current study reported a higher mortality rate in contrast to previous studies, as we deal with patients with COPD with severe exacerbation who necessitate hospital admission and mechanical ventilation in many cases.

In this work, there is a high COPD percentage among women, which may be attributed to the fact that most women in Upper Egypt are exposed to indoor air pollution from using fuel in cooking in overcrowded living houses. This increases the incidence of COPD among women in our study.

This study found that sputum culture was positive for bacteria in 94% of the studied patient. This study was somewhat comparable with that of Patel *et al.* [10] who demonstrated a positive sputum culture in 82% of patients with AECOPD. Moreover, Aleemullah *et al.* [11] reported that growth of pathogenic bacteria was found in 73% of sputum samples. Moreover, in this study, positivity of sputum culture for bacteria was higher as compared with other studies, such as that of Chawla *et al.* [12], which estimated that sputum culture was positive in 60.1%. Madhavi *et al.* [13] estimated that sputum culture was positive in 53% of the patients. The study done by Groenewegen and Wouters [14] reported that the presence of bacterial pathogens was found in 50% of all admitted patients. The difference may be related to the type of studied patients, where our study was done on critically ill patients who needed ICU admission and the AECOPD mostly owing to infection in those patients, whereas most of other studies were done on patients with AECOPD who were admitted to the ward or outpatients.

**Table 2 Microbiological results of the 50 critically ill patients with chronic obstructive pulmonary disease admitted to respiratory intensive care unit**

| Organisms                     | Frequency (%) |
|-------------------------------|---------------|
| *Klebsiella pneumoniae*       | 29 (58)       |
| *Pseudomonas aeruginosa*      | 14 (28)       |
| MRSA                          | 8 (16)        |
| *Acinetobacter baumannii*     | 7 (14)        |
| *Proteus* spp.                | 5 (10)        |
| *Staphylococcus aureus*       | 5 (10)        |
| *Streptococcus pneumonia*     | 2 (4)         |
| *Escherichia coli*            | 3 (6)         |
| More than one organism        | 22 (44)       |
| No growth                     | 3 (6)         |

MRSA, methicillin resistant *Staphylococcus aureus.*

**Table 3 Sensitivity of the organisms to first group of antibiotics**

|                     | *Klebsiella pneumoniae* \((N=29)\) | *Pseudomonas aeruginosa* \((N=14)\) | *Proteus* spp. \((N=5)\) | *Acinetobacter baumannii* \((N=7)\) | *Escherichia coli* \((N=3)\) |
|---------------------|-----------------------------------|------------------------------------|--------------------------|-------------------------------------|---------------------------|
|                     | S       | I       | R       | S       | I       | R       | S       | I       | R       | S       | I       | R       |
| Amoxicillin–clavulanic | 0      | 1      | 25     | 0      | 0      | 14     | 0      | 0      | 5       | 0      | 0      | 7       | 0      | 0      | 3       |
| Piperacillin–tazobactam | 1      | 0      | 28     | 0      | 2      | 12     | 2      | 1      | 2       | 0      | 1      | 6       | 0      | 0      | 3       |
| Cefaclor            | 0      | 0      | 29     | 0      | 0      | 14     | 0      | 0      | 5       | 0      | 0      | 7       | 0      | 0      | 3       |
| Cefazidime          | 1      | 2      | 26     | 1      | 1      | 12     | 0      | 1      | 4       | 0      | 1      | 6       | 1      | 1      | 1       |
| Cefepime            | 2      | 1      | 26     | 1      | 2      | 11     | 1      | 1      | 3       | 1      | 1      | 5       | 0      | 1      | 2       |
| Ceftriaxone         | 0      | 0      | 29     | 0      | 0      | 14     | 0      | 0      | 5       | 0      | 0      | 7       | 0      | 0      | 3       |
| Meropenem           | 1      | 0      | 28     | 0      | 0      | 14     | 1      | 0      | 4       | 1      | 0      | 6       | 0      | 0      | 3       |
| Ciprofloxacin       | 0      | 0      | 28     | 2      | 0      | 12     | 0      | 0      | 5       | 0      | 0      | 7       | 0      | 0      | 3       |
| Levofloxacin        | 0      | 0      | 29     | 2      | 0      | 12     | 0      | 0      | 5       | 0      | 0      | 7       | 0      | 0      | 3       |
| Amikacin            | 3      | 4      | 22     | 0      | 0      | 14     | 2      | 0      | 3       | 0      | 0      | 7       | 1      | 0      | 2       |

Data were expressed in the form of frequency. I, intermediate resistance; R, resistance; S, sensitive.
Regarding the results of sputum culture, the current study showed that the most frequently detected organism was *K. pneumoniae* in 29 (58%) patients followed by *P. aeruginosa* in 14 (28%) patients, MRSA in eight (16%) patients, *A. baumannii* in seven (14%) patients, Proteus spp. and *S. aureus* in five (10%) patients each, and *Escherichia coli* in three (6%) patients. No growth was reported in three (6%) patients. This was comparable to the study of Lin et al. [15], which showed that *K. pneumoniae* is the most common organism, followed by *P. aeruginosa*, followed by *A. baumannii* and *S. aureus*. The incidence of *S. pneumoniae* was the least one. This finding was also in agreement with another study that found that *K. pneumoniae* was the most common organism [13].

A study from India conducted by Chawla et al. [12] had found that *P. aeruginosa* was the predominant isolate among the hospitalized patients followed by *S. pneumoniae* and *Acinetobacter* spp., *Klebsiella* spp., and *Moraxella catarrhalis*. Moreover, this study was in consistent with Chakraborty et al. [16] who demonstrated that *K. pneumonia*, *P. aeruginosa*, *A. baumannii*, and *E. coli* were the predominant organisms, and *S. aureus* and *S. pneumoniae* formed the rest.

On the contrary, the results of this study differ from that of Agmy et al. [17] that was done in Upper Egypt, which found that the predominant isolates in 376 patients with AECOPD were *Haemophilus influenzae* (30%), *S. pneumoniae* (25%), *M. catarrhalis* (18%), and *K. pneumoniae* (12%). The difference may be owing to different characteristics of the patients, as the current study was done on critically ill patients; however, the study of Agmy and colleagues was done on patients admitted to the ward. Moreover, this may be owing to different timing of both studies, as winter season and low humidity are confirmed triggers for AECOPD and hospital admissions.

Another study in Upper Egypt done by Hassan et al. [18] reported that the most predominantly encountered strains were *H. influenzae*, *S. pneumoniae*, and *K. pneumoniae* isolated in 31 (18%), 26 (15%), and 24 (14%), respectively. *H. influenzae* was the most common bacteria detected in their study. The difference may be owing to different timing and different characteristics of the patients, as the current study was done on critically ill patients who needed respiratory ICU admission.

On the contrary, the results of the current study disagree with those of Fagon et al. [19], who found that the most prevalent microorganism in patients with COPD was *H. influenzae* (39%), followed by *S. pneumoniae* (16%) and *M. catarrhalis* (7%). This disagreement may be owing to the difference in
In the analysis of the sensitivity of microorganisms to different antibiotics, among gram-positive organisms (MRSA, *S. aureus*, and *S. pneumoniae*), linezolid had the upper hand of efficacy followed by vancomycin and teicoplanin, whereas erythromycin and amoxicillin–clavulanic acid had the least effect. This is in agreement with Chakraborty et al. [16] who found that among the gram-positive organisms, linezolid was found to be sensitive in all the cases, followed by vancomycin.

The high efficacy of linezolid and vancomycin is owing to little use of them because of many causes, as these antibiotics are expensive and have frequent adverse effects. In contrary, Patel et al. [10] reported that linezolid showed high resistance against gram-positive bacteria. Among gram-negative organisms (*K. pneumoniae, P. aeruginosa, E. coli, A. baumannii*, and *Proteus* spp.), the current study noted especially no efficacy of cefaclor and ceftriaxone and poor efficacy of amikacin, piperacillin–tazobactam, meropenem, ceftazidime, cepfime, amoxicillin–clavulanic acid, ciprofloxacin, and levofloxacin. This agrees with a previous study done by Hassan et al. [18] that showed isolated bacterial strains were characterized by high resistance rates to most groups of antimicrobials. Sensitivity was high to linezolid and the carbapenem group. In a study done in India by Patel et al. [10], they found that the piperacillin–tazobactam was the most effective antibiotic in this area against gram-positive and gram-negative bacteria, and this disagree with our study, which may be owing to overuse of this antibiotic in our locality.

Agmy et al. [17] reported very high susceptibility rates for the respiratory quinolones (levofloxacin, ciprofloxacin, and moxifloxacin) and recommend the importance of using such agents for AECOPD in the locality. Moreover, the study conducted by Chawla et al. [12] in 2008 found that quinolones were the most effective. In contrary, our study reported a high resistance rate to levofloxacin and ciprofloxacin. This may be owing to the difference in environment, time of the study, number of cases, and the method of sample collection, such as bronchoalveolar lavage and use of protective brush. However, Patel et al. [10] showed that piperacillin–tazobactam was the most effective antibiotic in their region, and was more effective than quinolones. The high efficacy of piperacillin–tazobactam in that region may be owing to wise use of it. This is in contrary to high resistance in this study which may be owing to high frequency of description of this antibiotic.

**Conclusions**

*K. pneumoniae* was the most frequent organism followed by *P. aeruginosa*, MRSA, and *A. baumannii*. Our bacteriological profiles highlighted the role of other pathogen including *E. coli, S. aureus*, and *Proteus* spp. in AECOPD. The isolated bacterial strains were characterized by high resistance rates to most groups of antimicrobials. Sensitivity was high to linezolid and vancomycin. Mortality rate was more among patients with MRSA.

**Recommendations**

Antimicrobial sensitivity pattern must be checked for all the patients. Further studies should include large number of patients and different places and other methods to obtain samples, for example, bronchoalveolar lavage and protected specimen brush.

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Nil.

**Conflicts of interest**

There are conflicts of interest.

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