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# Microbiological analysis of nosocomial pneumonia at Tanta University Chest Hospital

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## Abstract

**Background** Hospital-acquired pneumonia (HAP) and ventilator-associated pneumonia (VAP) represent a major health problem among hospitalized patients leading to consequent morbidity and mortality specially after Covid-19 era and spread of multidrug-resistance organisms (MDRO) in hospitals.

**Aim** This study aimed to analyze the commonest microorganisms responsible for HAP and VAP at Tanta University Chest Hospital.

**Methods** This prospective observational study was done at Chest Department, Faculty of Medicine, started from June 2022 to February 2023. Fifty HAP patients' sputum samples and 50 VAP patients (25 endotracheal aspirates and 25 bronchoalveolar lavages) were included. All collected samples were submitted to standard microbiological tests at Microbiology Department, Tanta Faculty of Medicine.

**Results** A total number of 50 HAP and 50 VAP cases were included. Microbial isolates were relatively the same in both groups, where *Klebsiella pneumoniae* was the predominant isolates (56) followed by *Staphylococcus aureus* (25), *Escherichia coli* (14), *Pseudomonas aeruginosa* (13), *Acinetobacter baumannii* (5), *Streptococcus pneumoniae* (4), *Enterococci* (3), *Stenotrophomonas maltophilia* (2), *Citrobacter freundii* (2), *Streptococcus pyogenes* (2), *Providencia stuartii* (1), and 7 isolates of *Candida*. Antimicrobial susceptibility showed predominance of drug-resistance organisms in VAP (78%) versus HAP (28%), *P*-value: < 0.001. *Klebsiella pneumoniae* showed higher rates of resistance (37 out of 56 isolates, *P*-value = 0.020). Four out of 5 *Acinetobacter baumannii* isolates were multidrug resistant, and 2 isolates of *Stenotrophomonas maltophilia* were polydrug resistant. Multivariate logistic regression analysis showed that intravenous antibiotic administration within last 3 months was associated with risk for MDR-HAP, while univariate regression analysis showed that intravenous antibiotic administration within the last 3 months was the strongest predictor for MDR-VAP. A higher mortality rate was recorded in VAP group (66%), versus (14%) in HAP group (*P*-value: < 0.001).

**Conclusion** Microbial isolates were relatively the same in both HAP and VAP, but VAP showed significant predominance of drug-resistant organisms. The most significant predictor for risk of MDRO infection in HAP and VAP was intravenous antibiotic administration within last 3 months; so, raising attention towards antibiotic choice may improve the outcome. Finally, VAP was associated with higher mortality compared to HAP.

**Keywords** Hospital-acquired pneumonia, Ventilator-associated pneumonia, Multidrug-resistant organisms, MDR-HAP, MDR-VAP, MDR *Klebsiella*

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## Introduction

Nosocomial pneumonia is a major health concern that represents about 22% of hospital infections worldwide [1]. Nosocomial pneumonia is a term that describes hospital-acquired pneumonia (HAP) and ventilator-acquired pneumonia (VAP). HAP is defined as pneumonia which is developed at least 48 h after hospital admission either in intensive care unit or in hospital wards, while VAP describes pneumonia which is developed after 48 h on mechanical ventilation [2]. Diagnosis of nosocomial pneumonia includes different approaches including clinical examination, laboratory investigations, and radiological assessment. Furthermore, microbiological assessment of nosocomial pneumonia is essential for proper management. It is known that early treatment of nosocomial pneumonia utilizing empirical antibiotics is advised to improve the clinical outcome until cultures of the causative organisms become available [3]. Hence, microbiological analysis in different healthcare facilities is mandatory for recognition of the commonest pathogens and targeting those pathogens with empirical antibiotic regimen according to the collected data [4].

## Patients and methods

### Patient selection

Study protocol was approved from Ethical Committee of Faculty of Medicine, Tanta University, with approval code (22/5/35500), and informed consents for procedure were obtained from the patients or their relatives. This prospective observational study was carried out at Chest Department, Tanta Faculty of Medicine, within 9 months: from June 2022 to February 2023. This study included 50 patients diagnosed as hospital-acquired pneumonia defined as follows: pneumonia developing 48 h after hospital admission and not incubating at admission time, classified as early-onset HAP which developed 2–4 days after admission, and late-onset HAP which developed  $\geq 5$  days after hospitalization. Also, this study included 50 cases diagnosed as ventilator-associated pneumonia, defined as pneumonia developing in a patient who has received mechanical ventilation for  $\geq 48$  h, classified as early-onset VAP which developed 2–4 days after intubation, and late-onset VAP which developed  $\geq 5$  days after intubation. Criteria for diagnosis of both HAP and VAP depend on the presence of new pulmonary infiltrates acquired in hospital with two or more of the following: temperature  $> 38.3^\circ\text{C}$  or  $< 36^\circ\text{C}$ , leukocytic count  $> 10 \times 10^9/\text{L}$  or  $< 4 \times 10^9/\text{L}$ , and the presence of purulent respiratory tract secretions [3]. Patients with community-acquired pneumonia (CAP) and severe immunocompromised patients including chemotherapy, HIV, and organ transplant were excluded as well as patients who refused to participate in the study.

All included patients were subjected to history taking, physical examination, laboratory investigations including complete blood count (CBC), C-reactive protein (CRP), D-dimer, liver function tests, blood urea and serum creatinine, INR as well as radiological investigations, and chest X-ray (CXR) done for all cases, while computerized tomography (CT) chest scan was requested for some HAP patients when CXR was apparently normal in the presence of suggestive clinical and laboratory findings of nosocomial pneumonia. Regarding 50 included HAP patients, sputum samples were taken, while 50 included VAP cases; 25 patients who were unfit for bronchoscopy were sampled by endotracheal aspirate (ETA), and another 25 patients who were fit for bronchoscopy were sampled by bronchoalveolar lavage (BAL). All collected samples (sputum, BAL, ETA) were sent to Medical Microbiology and Immunology Department, for subsequent standard microbiological cultures and examination.

### Technique of the procedure

#### Collection of sputum samples

The patients were provided with sterile specimen container with instructing the patient not to touch the inside of the container; they were asked to take a slow deep breath and to cough after a full inspiration and then expectorate sputum directly into the sterile container. This maneuver was repeated until a sufficient amount at least 5 mL of sputum was collected. The top of the specimen container was secured tightly and lastly; any sputum present on the outside of the container was removed with a disinfectant wipe. Saliva samples were excluded [5].

#### Collection ETA samples

ETA was performed for mechanically ventilated patients who were unfit for bronchoscopy by intensive care unit (ICU) residents with assistance of nursing staff. First, the patient was hyperoxygenated with 100% FIO<sub>2</sub> (fraction of inspired oxygen) for 1 min, then a 50-cm suction catheter (16 French) was inserted through the endotracheal tube (ETT) or tracheostomy tube without suctioning until resistance was met and then was withdrawn, and suction was done in an interrupted manner with 1-min interval between performed 5 insertions according to the recommendations of the latest endotracheal suctioning directives of the American Association for Respiratory Care (AARC) [6]. Finally, aspirates were collected in a sterile container to be sent for microbiological analysis as quickly as possible.

#### Collection of BAL samples

For mechanically ventilated patients who were fit for bronchoscopy, BAL was performed by pulmonology

consultant with assistance of nursing staff. First, the patient was hyperoxygenated with FIO<sub>2</sub> 100% for 1 min, and then a fiber-optic bronchoscope (KARL STORZ, Germany; model 11004BC1, SN 2252850) was introduced through ETT (8 mm) or tracheostomy tube (8 mm) and then wedged into the targeted segmental bronchi. Sterile saline (0.9% NaCl at room temperature) was instilled in four aliquots of 50 mL and then rapidly aspirated, and recovered BAL fluid samples were collected and transported as quickly as possible for microbiological studies [7].

#### **Handling of the specimens**

The collected samples were transferred within 1 to 2 h to Medical Microbiology and Immunology Department, Faculty of Medicine, Tanta University. A full microbiological examination was done to identify the isolated pathogens from different sample types and then stored at 4 °C. Sputum was considered microbiologically adequate only if it contained > 10 white blood cells for each epithelial cell at a magnification of  $\times 400$  [8]. The purulent ETA secretions were defined as lower respiratory tract samples that contained  $\geq 25$  neutrophils and  $\leq 10$  squamous epithelial cells per lower power field  $100\times$ . The threshold values of  $10^5$  colony-forming units (CFU/mL) for ETA and  $10^6$  for sputum cultures were taken as positive cultures, and values below the threshold were considered as colonization [9, 10]. For BAL fluid, if BAL recovered volume was less than 20 mL, total cell count was less than 60,000 cells/mL; if prepared samples showed excessive amounts of intracellular debris or damaged nucleated cells or more than 1% squamous epithelial cell, BAL was rejected [7]. The threshold values of  $10^4$  CFU/mL for BAL were taken as a positive BAL culture [11].

#### **Samples processing and culture**

Samples were vortexed for 1 min and cultured on MacConkey's blood agar, chocolate agar, and Sabaraud dextrose agar. Blood and chocolate agars were incubated in candle jar overnight at 37 °C incubator. Identification of isolated colonies was done by gram staining and different biochemical tests such as catalase test, coagulase test, oxidase test, urease test, triple sugar iron agar, citrate, and indole tests [12].

Antimicrobial susceptibility tests were done on Muller-Hinton agar plates by Kirby-Bauer disc diffusion plate method. The antibiotic disc used was amikacin (30 µg), amoxicillin/clavulanic acid (30 µg), aztreonam (30 µg), ceftriaxone (30 µg), ceftazidime (30 µg), cefoxitin (30 µg), cefepime (30 µg), cefoperazone (75 µg), clindamycin (2 µg), erythromycin (15 µg), imipenem (10 µg), meropenem (10 µg), gentamicin (10 µg), nitrofurantoin (300 µg), colistin (10 µg), tetracycline (30 µg), tigecycline (15 µg),

teicoplanin (30 µg), levofloxacin (5 µg), ciprofloxacin (5 µg), linezolid (30 µg), penicillin G (10 units), piperacillin/tazobactam (110 µg), trimethoprim/sulfamethoxazole (1.25/23.75 µg), and vancomycin (30 µg) (Oxoid, UK). Extended-spectrum beta-lactamase (ESBL) production was tested by phenotypic confirmatory tests, and the interpretation of the results was done according to the CLSI (Clinical and Laboratory Standards Institute, 2022) [13]. The pattern of antibiotic resistance of organisms was defined according to the guidelines suggested by the European Center for Disease Control and Prevention (ECDC). Multidrug resistant (MDR) was defined as acquired nonsusceptibility to at least one agent in three or more antimicrobial categories. Extensively drug resistant (XDR) was defined as nonsusceptibility to at least one agent in all but two or fewer antimicrobial categories (i.e., bacterial isolates remain susceptible to only one or two antimicrobial categories). Pan-drug resistant (PDR) was defined as nonsusceptibility to all agents in all antimicrobial categories [14].

#### **Statistical analysis**

##### **Statistical analysis**

Statistical analysis was conducted using (SPSS version 20). Descriptive statistics for quantitative data were done using mean, standard deviation, and minimum and maximum of the range, while qualitative data were represented as number and percentage. Continuous variables were compared using Student's *t*-test, and categorical variables were compared using Pearson's chi-square. *P*-value < 0.05 is considered significant. Simple logistic regression analysis was performed to determine the predictors for risk of multidrug-resistant organisms in nosocomial pneumonia. These were reported as the *P*-value (level of significance, *P*-value  $\leq 0.05$ ) and odds ratio (OR).

#### **Results**

Demographic data of the patients were listed in Table 1 where mean  $\pm$  SD age in HAP and VAP groups was  $54.520 \pm 13.762$  with median 55 years and  $58.940 \pm 18.008$  with median 64 years respectively, number of males in HAP was 27 versus 26 in VAP, while females were 23 versus 24 patients in VAP group with no statistically significant difference between both groups regarding age and gender.

Among laboratory investigations, CRP and D-dimer showed higher values in VAP than HAP group with significant difference between both groups (*P*-value: < 0.001 for both). Regarding the cause of hospital admission, variable causes showed a significant difference between both groups (*P*-value: 0.009, listed in Table 2). Among those acute exacerbation of chronic obstructive pulmonary diseases (AE. COPD) was the

**Table 1** Demographic data of the patients

		Group						T-test	
		HAP N= 50			VAP N= 50			t	p-value
Age	Range	22	-	81	20	-	86	- 1.379	0.171
	Mean $\pm$ SD	54.520	$\pm$	13.762	58.940	$\pm$	18.008		
	Median (IQR)	55 (45–66)			64 (47–72)				
Chi-square		N		%	N		%	$\chi^2$	p-value
Gender	Male	27		54.00	26		52.00	0.040	0.841
	Female	23		46.00	24		48.00		
Occupation	Housewife	17		34.00	18		36.00	14.660	0.101
	Student	1		2.00	2		4.00		
	Farmer	9		18.00	6		12.00		
	Retired employee	4		8.00	13		26.00		
	Employee	8		16.00	2		4.00		
	Worker	6		12.00	6		12.00		
	Fruit seller	3		6.00	0		0.00		
	Retired nurse	1		2.00	2		4.00		
	Retired engineer	0		0.00	1		2.00		
	Driver	1		2.00	0		0.00		
Smoking status	Nonsmoker	35		70.00	28		56.00	4.585	0.101
	Smoker	7		14.00	16		32.00		
	Ex-smoker	8		16.00	6		12.00		
Comorbidities	Yes	35		70.00	28		56.00	2.102	0.147
	No	15		30.00	22		44.00		
Comorbidities	DM	20		40.00	15		30.00	1.099	0.295
	HTN	16		32.00	19		38.00	0.396	0.529
	IHD	5		10.00	4		8.00	0.122	0.727
	Epilepsy	1		2.00	0		0.00	1.010	0.315
	Liver disease	2		4.00	0		0.00	2.041	0.153
	Stroke	3		6.00	4		8.00	0.154	0.695
	Cor pulmonale	1		2.00	3		6.00	1.042	0.307
	Rheumatoid arthritis	1		2.00	0		0.00	1.010	0.315
	Obesity	0		0.00	2		4.00	2.041	0.153
	Bipolar disorder	1		2.00	0		0.00	1.010	0.315
	Hodgkin lymphoma	1		2.00	0		0.00	1.010	0.315
	Thyroid lymphoma	0		0.00	1		2.00	1.010	0.315
	AF	0		0.00	1		2.00	1.010	0.315
	Allergic rhinitis	3		6.00	0		0.00	3.093	0.079
	Chronic kidney disease	1		2.00	0		0.00	1.010	0.315

AF atrial fibrillation, DM diabetes mellitus, HAP hospital-acquired pneumonia, HTN hypertension, IHD ischemic heart disease, VAP ventilator-associated pneumonia. Data were presented by median (interquartile range, IQR), numbers (percentage) or mean  $\pm$  standard deviation ( $x \pm s$ ) (continuous). Continuous variables were compared using Student's *t*-test and categorical variables using Pearson's chi-square with consideration of *P*-value are significant if  $< 0.05$

predominant cause in both groups followed by AE. asthma and HP in HAP group versus acute exacerbation of idiopathic pulmonary fibrosis (AE. IPF) and bronchiectasis and obesity hypoventilation syndrome in VAP group. Furthermore, radiological findings showed significant difference between both groups (*P*-value:

0.037) with predominance of lobar pneumonia in HAP (40%), while bronchopneumonia was the predominant (52%) in VAP group, while onset of pneumonia did not show any significant difference between both groups (Table 2). All VAP patients were managed in ICU, while only 15 patients of HAP group were managed in ICU, and the remaining 35 patients were managed in wards.

**Table 2** Clinical data of patients in HAP and VAP groups

Laboratory investigations		Group						T-test	
		HAP N = 50			VAP N = 50			t	p-value
TLC at time of NP diagnosis	Range	4.8	-	33	5	-	34	-0.706	0.482
	Mean ± SD	17.812	±	6.879	18.748	±	6.359		
CRP at time of NP diagnosis	Range	12	-	210	60	-	200	-4.106	<0.001*
	Mean ± SD	80.180	±	45.947	114.300	±	36.628		
D-dimer at time of NP diagnosis	Range	0.1	-	1.84	0.4	-	2.5	-4.943	<0.001*
	Mean ± SD	0.662	±	0.376	1.134	±	0.561		
Chi-square		N		%	N		%	X <sup>2</sup>	P-value
Cause of admission	AE. COPD	18		36.00	18		36.00	25.083	0.009*
	AE. asthma	15		30.00	4		8.00		
	AE. IPF	1		2.00	6		12.00		
	AE. HP	4		8.00	3		6.00		
	AE bronchiectasis	3		6.00	6		12.00		
	AE. RA-ILD	1		2.00	0		0.00		
	Obesity hypoventilation syndrome	3		6.00	6		12.00		
	Organophosphorus poisoning	0		0.00	3		6.00		
	Pleural effusion	3		6.00	0		0.00		
	Pulmonary edema	0		0.00	3		6.00		
	Lung cancer	2		4.00	0		0.00		
	Acute upper airway obstruction	0		0.00	1		2.00		
Onset of nosocomial pneumonia	Early	21		42.00	22		44.00	0.041	0.840
	Late	29		58.00	28		56.00		
Radiological findings	Lobar pneumonia with pleural effusion	2		4.00	5		10.00	10.190	0.037*
	Lobar pneumonia	20		40.00	17		34.00		
	Bronchopneumonia	17		34.00	26		52.00		
	Lung abscess	7		14.00	2		4.00		
	Bilateral GGO	4		8.00	0		0.00		

AE. COPD acute exacerbation of chronic obstructive pulmonary diseases, AE. HP acute exacerbation of hypersensitivity pneumonitis, AE/IPF acute exacerbation of idiopathic pulmonary fibrosis, AE. RA-ILD acute exacerbation of rheumatoid arthritis-interstitial lung diseases, CRP C-reactive protein, GGO ground-glass opacities, NP nosocomial pneumonia, TLC total leukocytic count

\*P-value is significant if < 0.05

Regarding microbiological results, among HAP group, thirty-three patients (66%) had one organism in their cultures versus thirty-five patients (70%) in VAP group, and 17 patients (34%) had two organisms in their cultures in HAP versus 15 patients (30%) in VAP group with no significant difference between both groups. *Klebsiella pneumoniae* was the most predominant organism recorded in both groups: 20 isolates (40%) in HAP group versus 36 isolates (72%) in VAP group with a significant difference between both groups ( $P$ -value: 0.001). In HAP group, *Staph. aureus* was 16 isolates (32%) and *E. coli* 8 isolates (16%); meanwhile, in VAP group, *Staph. aureus* was 9 isolates (18%) and *pseudomonas aeruginosa* 7 isolates (14%). *Acinetobacter baumannii* was recorded only in VAP group: 5 patients (10%) with a significant difference between both groups ( $P$ -value: 0.022). On the other hand, *Candida* was recorded only in HAP group: 7 patients (14%) ( $P$ -value: 0.006) (Table 3).

Antimicrobial sensitivity tests showed a significant difference between both groups ( $P$ -value: < 0.001) with predominance of susceptible organisms in HAP group (72%), while resistance was evident in VAP group (78%). Furthermore, the distribution of antimicrobial susceptibility showed a significant difference between both groups ( $P$ -value: < 0.001) (Table 3).

The distribution of organisms according to antimicrobial susceptibility test was listed in Table 4. In gram-negative organisms, among 56 isolated *Klebsiella pneumoniae*, 19 isolates were sensitive to standard antibiotics regimens, while 26 isolates were MDR, 8 were XDR, and 3 were PDR isolates with a predominance of MDR *Klebsiella* among hospitalized patients ( $P$ -value: 0.020). Among 29 carbapenems-resistant *Klebsiella*, there were 9 isolates resistant to glycylicycline (tigecycline), and one isolate was resistant to polymyxin (colistin), and 3 were resistant to both colistin and tigecycline.

**Table 3** Microbiological results of the patients

Microbiological results		Group				Chi-square	
		HAP N= 50		VAP N= 50		X <sup>2</sup>	p-value
		N	%	N	%		
Number of organisms/patient	One	33	66.00	35	70.00	0.184	0.668
	Two	17	34.00	15	30.00		
Organism distribution	<i>Candida</i>	7	14.00	0	0.00	7.527	0.006*
	<i>Citrobacter freundii</i>	0	0.00	2	4.00	2.041	0.153
	<i>Escherichia coli</i>	8	16.00	6	12.00	0.332	0.564
	<i>Enterococci</i>	3	6.00	0	0.00	3.093	0.079
	<i>Staph. aureus</i>	16	32.00	9	18.00	2.613	0.106
	<i>Klebsiella pneumoniae</i>	20	40.00	36	72.00	10.390	0.001*
	<i>Stenotrophomonas maltophilia</i>	2	4.00	0	0.00	2.041	0.153
	<i>Pseudomonas aeruginosa</i>	6	12.00	7	14.00	0.088	0.766
	<i>Acinetobacter baumannii</i>	0	0.00	5	10.00	5.263	0.022*
	<i>Strep. pneumoniae</i>	2	4.00	2	4.00	0.000	1.000
	<i>Providencia stuartii</i>	1	2.00	0	0.00	1.010	0.315
	<i>Strep. pyogenes</i>	2	4.00	0	0.00	2.041	0.153
Antimicrobial susceptibility test	Sensitive	36	72.00	11	22.00	25.090	< 0.001*
	Resistant	14	28.00	39	78.00		
Antimicrobial susceptibility test	Sensitive	36	72.00	11	22.00	32.833	< 0.001*
	MDR isolates	5	10.00	31	62.00		
	PDR isolates	4	8.00	2	4.00		
	XDR isolates	5	10.00	6	12.00		

MDR multidrug resistant, PDR pan-drug resistant, XDR extensively drug resistant

\*P-value is significant if &lt; 0.05

**Table 4** Organisms distribution according to antimicrobial susceptibility test

Organism distribution	Antimicrobial susceptibility test										Chi-square	
	Sensitive		MDR		PDR		XDR		Total		X <sup>2</sup>	p-value
	N	%	N	%	N	%	N	%	N	%		
<i>Candida</i>	7	14.89	0	0.00	0	0.00	0	0.00	7	7.00	8.488	0.037*
<i>Citrobacter freundii</i>	0	0.00	2	5.56	0	0.00	0	0.00	2	2.00	3.628	0.305
<i>Escherichia coli</i>	8	17.02	4	11.11	0	0.00	2	18.18	14	14.00	1.742	0.628
<i>Enterococci</i>	3	6.38	0	0.00	0	0.00	0	0.00	3	3.00	3.488	0.322
<i>Staph. aureus</i>	16	34.04	5	13.89	1	16.67	3	27.27	25	25.00	4.673	0.197
<i>Klebsiella pneumoniae</i>	19	40.43	26	72.22	3	50.00	8	72.73	56	56.00	9.808	0.020*
<i>Stenotrophomonas maltophilia</i>	0	0.00	0	0.00	2	33.33	0	0.00	2	2.00	31.973	< 0.001*
<i>Pseudomonas aeruginosa</i>	6	12.77	5	13.89	1	16.67	1	9.09	13	13.00	0.247	0.970
<i>Acinetobacter baumannii</i>	1	2.13	4	11.11	0	0.00	0	0.00	5	5.00	4.541	0.209
<i>Strep. pneumoniae</i>	3	6.38	1	2.78	0	0.00	0	0.00	4	4.00	1.543	0.672
<i>Providencia stuartii</i>	1	2.13	0	0.00	0	0.00	0	0.00	1	1.00	1.139	0.768
<i>Strep. pyogenes</i>	2	4.26	0	0.00	0	0.00	0	0.00	2	2.00	2.301	0.512

\*P-value is significant if &lt; 0.05

Two isolates of *Stenotrophomonas maltophilia* were recorded, and both were PDR (*P* value: < 0.001). Among 14 isolates of *E. coli*, 8 were sensitive, while 4 isolates were MDR and 2 XDR. Among 4 carbapenems-resistant

*E. coli*, 2 isolates were resistant to tigecycline, while no resistance was recorded to colistin. *Pseudomonas aeruginosa* sensitive isolates were 6, while 5 isolates were MDR, one was XDR, and another isolate was PDR. Among 6



carbapenems-resistant *Pseudomonas aeruginosa*, one isolate was resistant to tigecycline, and one isolate was resistant to both tigecycline and colistin. Regarding *Acinetobacter baumannii*, one isolate was sensitive to standard antibiotics, and 4 isolates were MDR which all were susceptible to tigecycline and colistin.

Among gram-positive organisms, *Staph. aureus* was the predominant organism, 16 isolates were methicillin-sensitive *Staphylococcus aureus* (MSSA), and 9 methicillin-resistant *Staphylococcus aureus* (MRSA) isolates were recorded; 2 isolates were resistant to linezolid and vancomycin; 2 isolates were resistant to teicoplanin; 2 isolates were resistant to linezolid, vancomycin, and teicoplanin; and one isolate was PDR including tigecycline and sulfamethoxazole-trimethoprim. Moreover, *Candida albicans* was recorded in this study; only in HAP group, 7 cases (14%) and all isolates were susceptible to fluconazole ( $P$ -value: 0.037).

Among various risk factors for infection with antibiotic-resistant organisms in HAP group, hospitalization of >2 days in the last month and intravenous antibiotic use within the last 3 months showed statistical significance ( $P$ -value 0.025 and 0.001, respectively), as shown in Table 5. Logistic regression analysis was done for detection of the strongest predictors for infection by MDR

organisms HAP; in univariate regression analysis, hospitalization of >2 days in last month (OR: 6.800, 95.0% confidence interval (CI): 1.082–42.730,  $P$ -value 0.041) and intravenous antibiotic use within last 3 months (OR: 8.750, 95.0% confidence interval (CI): 2.156–35.507,  $P$ -value 0.002) were the strongest predictors associated with risk for MDR-HAP. In multivariate analysis, intravenous antibiotic use within last 3 months (OR 7000, 95.0% confidence interval (CI): 1.498–32.720,  $P$ -value 0.013) was the strongest predictor associated with risk for MDR-HAP (Table 6).

Among various risk factors for infection with antibiotic-resistant organisms in VAP group, intravenous antibiotic use within last 3 months showed statistical significance with  $P$ -value, 0.001 (Table 7). Logistic regression analysis was done for detection of the strongest predictors of infection by MDR organisms-VAP; in univariate regression analysis, intravenous antibiotic use within last 3 months (OR 10.333, 95.0% confidence interval (CI): 2.220–48.092,  $P$ -value 0.003) was the strongest predictor associated with risk for MDR-VAP (Table 8).

Regarding duration of mechanical ventilation for VAP group, it ranged between 7 and 48 days with mean  $\pm$  SD 15.160  $\pm$  9.153, while total duration of hospital admission ranged between 10 and 34 days

**Table 5** Risk factors for infection by antibiotic-resistant organisms in HAP group

Variable in HAP (N = 50)	Antimicrobial susceptibility test				Chi-square	
	Sensitive		Resistant		$\chi^2$	$p$ -value
	N	%	N	%		
Immunosuppressive drugs	1	2.78	2	14.29	2.367	0.124
Systemic steroid therapy	9	25.00	6	42.86	1.531	0.216
Inhaled steroid therapy	29	80.56	11	78.57	0.025	0.875
Hospitalization of > 2 days in last month	2	5.56	4	28.57	5.057	0.025*
Hospitalization of $\geq$ 5 days prior NP occurrence	18	50.00	11	78.57	3.378	0.066
Intravenous antibiotic use within last 3 months	8	22.22	10	71.43	10.593	0.001*

\* $P$ -value is significant if < 0.05

**Table 6** Logistic regression analysis for the most important predictors of MDR HAP

Variable in HAP (N = 50)	Univariate				Multivariate			
	Odd ratio	95.0% CI for odd ratio		p-value	Odd ratio	95.0% CI for odd ratio		p-value
Immunosuppressive drugs	5.833	0.484	20.244	0.165				
Systemic steroid therapy	2.250	0.613	8.254	0.221				
Inhaled steroid therapy	0.885	0.194	4.047	0.875				
Hospitalization of > 2 days in last month	6.800	1.082	42.730	0.041*	2.000	0.260	15.381	0.505
Hospitalization of ≥ 5 days prior NP occurrence	3.665	0.874	15.373	0.076				
Intravenous antibiotic use within last 3 months	8.750	2.156	35.507	0.002*	7.000	1.498	32.720	0.013*

CI confidence interval, MDR-HAP multidrug-resistant-hospital-acquired pneumonia, NP nosocomial pneumonia

\*  $P$ -value is significant if < 0.05

with mean  $\pm$  SD  $21.340 \pm 6.026$  in HAP group versus range of 7 to 50 days with mean  $\pm$  SD  $19.960 \pm 10.654$  in VAP group with no significant difference between both groups (Table 9). On the other hand, outcomes of the patients showed significant difference between both groups ( $P$ -value:  $< 0.001$ ) where mortality was the predominant outcome in VAP group, 33 patients (66%) versus 7 patients (14%) in HAP group in which most of the patients were cured, and discharged 43 patients (86%) versus 17 patients (34%) in VAP group (Table 9).

## Discussion

In comparison to our data, Farhadi et al. (2021) reported in their study which aimed to screen frequency of MDR. In *Klebsiella pneumoniae*, mean age of studied patients was 51.7 years (ranged from 15 to 91 years), where 58% of the patients were females and 42% were males [15]. Also, Maurici et al. (2022) informed that among 329 patients with hospital-acquired respiratory infection, age ranged from 18 to 93 years, 96 (29.2%) were females, while 233 (70.8%) were male individuals; there were no significant differences in the average age compared to gender despite

**Table 7** Risk factors for infection with antibiotic-resistant organisms–VAP

Variable in VAP (N = 50)	Antimicrobial susceptibility test				Chi-square	
	Sensitive		Resistant		$\chi^2$	$p$ -value
	N	%	N	%		
Immunosuppressive drugs	0	0.00	4	10.26	1.226	0.268
Systemic steroid therapy	3	27.27	14	35.90	0.284	0.594
Inhaled steroid therapy	4	36.36	26	66.67	3.283	0.070
Hospitalization of $> 2$ days in last months	1	9.09	7	17.95	0.501	0.479
Hospitalization of $\geq 5$ days prior NP occurrence	6	54.55	22	56.41	0.012	0.912
Intravenous antibiotic use within last 3 months	3	27.27	31	79.49	10.750	0.001*

\* $P$ -value is significant if  $< 0.05$

**Table 8** Logistic regression analysis for the most important predictors of MDR-VAP

Variable in VAP (N = 50)	Univariate			
	Odd ratio	95.0% CI for odd ratio		p-value
Immunosuppressive drugs	0.343	0.017	6.865	0.484
Systemic steroid	1.493	0.340	6.556	0.595
Inhaled steroid	3.500	0.865	14.155	0.079
Hospitalization of > 2 days in last months	2.185	0.239	19.940	0.489
Hospitalization of ≥ 5 days prior NP occurrence	1.078	0.281	4.139	0.912
Intravenous antibiotic use within last 3 months	10.333	2.220	48.092	0.003*

CI confidence interval, MDR-VAP multidrug-resistant-ventilator-associated pneumonia, NP nosocomial pneumonia

\*  $P$ -value is significant if  $< 0.05$

**Table 9** Duration of mechanical ventilation, hospital admission, and outcome in HAP and VAP groups

		Group						T-test	
		HAP N = 50			VAP N = 50			t	p-value
Duration of mechanical ventilation (days)	Range	-	-	-	7	-	48	-	-
	Mean $\pm$ SD	-	$\pm$	-	15.160	$\pm$	9.153		
Duration of hospital admission (days)	Range	10	-	34	7	-	50	0.797	0.427
	Mean $\pm$ SD	21.340	$\pm$	6.026	19.960	$\pm$	10.654		
Chi-square		N		%	N		%	$\chi^2$	P-value
Outcome	Discharge	43		86.00	17		34.00	28.167	$< 0.001^*$
	Death	7		14.00	33		66.00		

\* $P$ -value is significant if  $< 0.05$



males were more than females. One-hundred forty (42.6%) patients were suffering from chronic diseases, lung disease ( $n=46$ , 14.0%), heart failure ( $n=45$ , 13.7%), kidney failure (51, 15.5%), and onco-hematological (24, 7.3%) diseases [16]. Kumar et al. (2018) showed that among 318 included patients for criteria of HCAP and HAP, 90 cases were diagnosed as HAP and 63 were diagnosed as VAP, whereas a total category (153 patients) age ranged from 16 to 85 years, mean  $\pm$  SD  $45.15 \pm 20.6$  and median 45 years, and 92 were males, regarding associated diseases, hypertension (71; 46.4), diabetes (11; 7.2%), coronary artery disease (13; 8.5%), chronic kidney diseases (5; 3.3%), neurological (34; 22.2%), and malignancy (13; 8.5%) [17]. In this study, diagnosis of suspected HAP and VAP was depending on clinical findings, regarding fever, deterioration of respiratory manifestation in the context of impaired oxygenation, purulent respiratory secretions, elevated inflammatory markers, and TLC, CRP, and D-dimer beside progressive or new radiological findings. In agreement with this study, Fagon et al. (1993) reported that standard diagnostic clinical criteria for HAP and VAP, beside abnormal chest radiographic findings, are composed of at least two of the three findings: fever, leukocytosis, and purulent tracheal secretions. When those occur, the possibility of VAP is high [18]. Also, the presence of radiographic infiltrates in a patient with fever, leukocytosis, or purulent tracheobronchial secretions has a high diagnostic sensitivity but low specificity. When all four criteria are present, specificity improves, but sensitivity drops to below 50% [19].

C-reactive protein is rapidly upregulated in the liver in response to cytokines originating at pathology site (particularly IL-6, which induces CRP mRNA) [20] and its synthesis rate depending on response to the inflammation intensity. Therefore, CRP is a superior biomarker for complex acute-phase characteristics, e.g., leukocytosis and fever. CRP secretion begins in 4–6 h and peaks at 36–50 h, potentially limiting its efficacy in predicting early treatment failure [21]. A single elevated plasma CRP concentration is not highly informative; so, CRP is not specific enough for diagnosis of nosocomial pneumonia [22], but continuous monitoring of CRP levels appears to be useful in the early prediction of VAP and the response to antibiotics [23]. Another challenge seems to be the differentiation of inflammation and infection using CRP [24]. This study agrees with the previous reports at the point of continuous monitoring, and not only CRP was already repeated for all patients suspecting nosocomial pneumonia but also total leucocytic count was repeated. We use D-dimer as another biomarker for inflammation and diagnosis of nosocomial pneumonia. D-dimer has a significant role not only in evaluation of venous thromboembolism

but also in inflammatory diseases. With emergence of Covid-19 and associated hypercoagulable state, significance of D-dimer has increased not only as a predictor for venous thromboembolism but also as an inflammatory marker correlated with other inflammatory markers such as CRP and ferritin for predicted morbidity and mortality. Rueda-Camino et al. (2022) also documented through their study that estimating a corrected value of plasma D-dimer as a linear function of ferritin, CRP, and fibrinogen, establishing a cutoff point of high probability of VTE that high CRP and elevated levels of D-dimer levels among COVID-19 patients predict higher odds of mortality, and by using this predictive model based on levels, CRP and D-dimer can help the clinicians to make timely clinical decisions, improve patients' treatment, and optimize use of limited clinical resources, but also, they recommended large-scale and longer-term studies to validate their results [25].

Borowiec et al. (2020) concluded that elevated levels of D-dimer in patients with granulomatosis with polyangiitis are associated with disease activity and inflammation rather than with the risk of venous thromboembolism, and value of d-dimer as a biomarker of venous thromboembolism in patients with small vessel vasculitis is low [26]. Also, Bao et al. (2017) documented in their study that correlated D-dimer level with the inflammatory conditions in patients with gastrointestinal diseases, and overall analysis showed positive correlation of D-dimer with white blood cell, percentage of neutrophils, neutrophil count, CRP, high sensitive CRP, procalcitonin, and blood culture results but negative correlation with lymphocyte percentage and count [27]. Higher values of CRP and D-dimer in VAP versus HAP may be explained with amplified inflammatory response and cytokine release in VAP patients [28].

Regarding admission cause, as this study was conducted at chest hospital, all patients were complaining of respiratory illness whatever it is acute or chronic, so most predominant causes were exacerbation of chronic respiratory diseases. Also, in Kumar et al. (2018) who conducted their study in a tertiary care hospital, among 153 recruited patients diagnosed with HAP and VAP, chronic lung disease was diagnosed in 15 patients, COPD was diagnosed in 14, and one cases for both asthma and bronchiectasis [17]. Maurici et al. (2022) conducted a study on 329 patients admitted at Italian teaching hospital diagnosed with hospital-acquired respiratory infections, and lung diseases were recorded in 46 (14%) patients [16]. Also, Chung et al. (2011) reported that among 2554 cases (1577 HAP and 977 VAP), chronic lung disease was determined in 472 (18.5%) patients, 288 in HAP group, and 184 patients in VAP group; also, there were 67 lung cancer cases in HAP versus 14 cases in VAP group [29].

Regarding radiological findings, CXR was done for all patients, and in some cases of HAP group, CT chest was requested when CXR was normal in the presence of clinical findings suggesting nosocomial pneumonia. Wunderink et al. (1992) and Winer-Muram et al. (1993) informed that diagnosis of HAP or VAP based on the presence of alveolar infiltrates on chest radiography has a sensitivity of 58 to 83% when using air bronchogram signs and is 50 to 78% for new or worsening infiltrates when compared with invasive techniques or histological studies [30, 31]. Also, Pugin et al. (1991) combined body temperature, white blood cell count, volume and appearance of tracheobronchial secretions, oxygenation, chest radiographic findings, and tracheal aspirate cultures into a Clinical Pulmonary Infection Score (CPIS) for VAP with a total score greater than six out of a maximum of 12 correlated with high bacterial counts isolated from the lower respiratory tract and a sensitivity and specificity of 93% and 100%, respectively [32]. More recently, Fartoukh et al. (2003) found that clinical prediction alone was inaccurate, but a modified CPIS score, incorporating a gram stain of respiratory tract secretions, improved diagnostic accuracy [33]. In this study, 3 sampling types (sputum, BAL, and ETA) yielded positive culture results. Also, Corrêa Rde, Luna, Anjos, Barbosa, Rezende, Rezende, Pereira, and Rocha (2014) concluded that management of VAP patients, based on the results of quantitative endotracheal aspirate cultures and BAL fluid cultures, had similar clinical outcomes [34].

Regarding microbiological findings in our study, gram-negative organisms were more predominant than gram-positive ones. *K. pneumoniae*, *Staph. aureus*, *E. coli*, and *Pseudomonas* were the predominant organisms with uniqueness of *A. baumannii* in VAP versus *Candida albicans* in HAP. Feng et al. (2019), agreed with our results in that, a predominance of gram-negative than gram-positive bacteria with significant predominance of *A. baumannii* in VAP, also, in our results *K. pneumoniae* showed significant predominance in VAP group and *Candida albicans* showed significant predominance in HAP group [35]. Also, Maurici et al. (2022) reported that respiratory samples including bronchoalveolar lavage fluid, bronchial aspirate, sputum specimen, and tracheal swab were examined, and microbiological analysis revealed that 332 (57.1%) organisms were gram-negative bacteria, 140 (24.1%) gram-positive bacteria, 2 (0.3%) mycobacterium tuberculosis, and 107 (18.4%) were fungal isolates; regarding gram-positive isolates, *S. aureus* (69.8%) and *Enterococcus* spp. (19.4%) were the prevalent bacteria, followed by *Streptococcus pneumoniae* (5.8%), *Streptococcus pyogenes* (4.3%), and *Rothia* (0.7%). In the gram-negative group, *Klebsiella* spp. (23.1%), *Pseudomonas* spp. (21.6%), and *A. baumannii* (18.6%) were

the most prevalent microorganisms, followed by *Enterobacter* spp. (9.3%), *E. coli* (9.0%), *Stenotrophomonas maltophilia* (4.5%), *Proteus* spp. (3.9%), and others. *Candida* spp. represented the majority of fungal isolates (87.0%), followed by *Aspergillus* spp. (12.1%) [16].

On the other hand, Chung et al. (2011) reported in their study that *P. aeruginosa* (15.6%) and *S. aureus* (15.5%) were the most frequent isolates in HAP followed by *Acinetobacter* spp. (13.6%) and *K. pneumoniae* (12%), while in VAP, *Acinetobacter* spp. was the most frequently isolated (36.5%) followed by *P. aeruginosa* (25.9%), *K. pneumoniae* (16.8%), and *S. aureus* (12.2%) [29], and Kumar et al. (2018) reported that *Acinetobacter baumannii* (62; 41%), *Pseudomonas aeruginosa* (21; 14%), and *E. coli* (17; 11%) were the most common organisms among HAP and VAP patients [17]. In this study, *Providencia stuartii* was recorded only in one female HAP case. In concordance with our findings, Abdallah et al. (2018) reported their first case of HAP caused by carbapenem-resistant *Providencia stuartii* in a 31-year-old man, and the patient responded well to the regimen, targeting carbapenem-resistant *P. stuartii* which was extended infusion of double-dose meropenem [36].

Although *Providencia* species have been isolated in humans from urine (most common), stool, blood, and from sputum, skin, and wound cultures, *P. stuartii* septicemia is primarily of urinary origin. One case study has informed *P. stuartii* as the etiology of infective endocarditis [37]. Also, an Italian study found that the prevalence of extended spectrum  $\beta$ -lactamases (ESBL)-producing *P. stuartii* in the general patient population increased from 31% in 1999 to 62% in 2002. Over a 4-year span, *P. stuartii* was isolated in 0.08% of patients. A total of 87% of isolates were found in urine, 10% in blood, and 3% in respiratory tract secretions [38].

Rahav et al. (1994) reported frequent isolation of *P. stuartii* from patients with indwelling urinary catheters and more persistence of organism in females. They explained that persistence may be due to different receptor characteristics in male and female urinary tracts and a bacterial predilection for Foley catheters over condom catheters, which are used more commonly in males [39].

Regarding organisms' distribution according to antimicrobial susceptibility test, in agreement with our results, Ferreira et al. (2019) reported in their study high prevalence of MDR *K. pneumoniae* (21/25; 84%) with high resistance rate to the common antibiotics used either alone or in association with one another, such as  $\beta$ -lactams (including carbapenems), aminoglycosides, quinolones, glycylicycline, and polymyxin E [40]. Also, Chung et al. (2011) found in their study in Asian countries on HAP and VAP cases common bacterial isolates which were *Acinetobacter*, *P. aeruginosa*,

*S. aureus*, and *K. pneumoniae*; all those isolates were highly resistant to major antimicrobial agents. Eighty-two percent of *S. aureus* isolates were MRSA, and most of those were MDR. ESBL production rate was high in *K. pneumoniae*. A significant proportion of *P. aeruginosa* were MDR and resistant to imipenem as well. *Pseudomonas* isolates from China were especially highly resistant to imipenem, and three strains showed PDR. *Acinetobacter* spp. showed high resistance rates to imipenem in Malaysia, Thailand, India, and China, and XDR rate was remarkably high [29]. Also, Maurici et al. (2022) recorded 82 out of the 581 isolated microorganisms were antibiotic resistant. *A. baumannii*, *K. pneumoniae*, and *S. aureus* represented the majority (62.2%) of antibiotic-resistant organisms: 22 MDR and 2 PDR *A. baumannii*, 9 PDR and 5 MDR *K. pneumoniae*, and 13 MDR *S. aureus*. No *Pseudomonas* spp. isolates exhibited antibiotic resistance. Six *Aspergillus* spp. isolates were found to be azole resistant, whereas all *Candida* spp. isolates were non-resistant [16]. Kumar et al. (2018) also reported among 153 cases of HAP and VAP, microbial isolates were 33 MDR, 110 XDR, and 3 PDR with 53 isolates were sensitive only to colistin. In *Acinetobacter* species, 7 MDR, 60 XDR, zero PDR isolates, and 33 isolates were sensitive only to colistin. In *E. coli*, 7 MDR, 7 XDR, zero PDR, and 3 isolates were sensitive only to colistin. In *Pseudomonas*, 1 MDR, 20 XDR, 1 PDR, and 13 were sensitive only to colistin. In *K. pneumoniae*, 2 MDR, 13 XDR, zero PDR, and 7 isolates were sensitive only to colistin. There were 5 isolates of MRSA, 4 MDR, and 1 XDR [17].

In our study, uniqueness of *Candida albicans* in HAP (5 ICU cases and 2 ward cases) is explained with several factors, among 7 cases; 4 patients were diabetic (poorly controlled) while other 3 cases; one case had ischemic heart disease and malnourished with late HAP, remaining 2 cases had late HAP, chronic inhaled corticosteroid use with past history of intravenous antibiotic use in last 3 months, and all 7 cases received broad-spectrum antibiotic at early management which predisposed to fungal infection as well as abundance of organism with the absence of another pathogenic organisms at microbiological examination and response to antifungal therapy which encouraged diagnosis of *Candida* pneumonia. On the other hand, Schnabel et al. (2014) reported that among included 701 BAL specimens, only 5 patients (0.7%) diagnosed with *Candida* pneumonia (malnutrition, malignancy, steroid therapy, and aspiration were risk factors for *Candida pneumonia* and informed that most *Candida pneumonia* reports are based on isolation of *Candida* from sputum aspirates or BAL in the absence of other causative pathogens with conclusion of *Candida pneumonia* as a rare clinical issue [41].

Regarding risk factors for infection by MDRO, in agreement with this study, Feng et al. (2019) reported antibiotic therapy in the preceding 90 days was an important risk factor for MDRO-HAP in their study [35]. Also, this finding is similar to that of the previous studies of Nseir et al. (2008) and Raman et al. (2015) that suggested the impact of virulence and antibiotic tolerance [42, 43]. Regarding VAP, Thom et al. (2017) suggested that patients who required mechanical ventilation or have undergone tracheotomy can easily be colonized by MDRO [44]. ICU admission or broad-spectrum antibiotic use also contributes to MDRO infection [45].

On the other hand, Kalil et al. (2016) and Ekren et al. (2018) reported risk factor for MDRO with HAP or VAP was  $\geq 5$  days of hospitalization [3, 46]. Kumar et al. (2018) documented in their study that among risk factors for antibiotic-resistant organisms, length of hospital stay  $\geq 5$  days was seen in 68 cases of HCAP and 81 cases of HAP ( $P$ -value=0.036), and by using multivariate regression analysis, chronic lung diseases were the strongest predictor of MDR bacteria ( $OR$  2.73, 95%  $CI$  1.26–5.915,  $P$ -value=0.011). Detection of *A. baumannii* ( $OR$  35.503, 95%  $CI$  14.688–85.817,  $P$ =0.000), *Pseudomonas* spp. ( $OR$  8.913, 95%  $CI$  2.762–28.76,  $P$ -value=0.000), and bacteria belonging to family of Enterobacteriaceae ( $OR$  9.533, 95%  $CI$  2.62–34.688,  $P$ -value=0.001) as well as immunocompromised condition ( $OR$  4.050, 95%  $CI$  1.39–11.796,  $P$ -value=0.010) were the strongest predictors for XDR organisms [17].

Regarding outcomes of the patients, in agreement with these results, Feng et al. (2019) reported the 30-day mortality rates in their study of HAP and VAP were 18.5% and 42.5%, respectively, [35], in consistence with previous reports of Ewan et al. (2015) and Ding et al. (2017) [47, 48]. Also, Da Silveira et al. (2019) and Siniscalchi et al. (2016) referred the higher mortality rates in VAP group to higher incidence of severe infection or comorbid conditions in those category [49, 50]. On the other hand, Chung et al. (2011) reported mortality rates of HAP and VAP in their study were 34.4% and 45.7%, respectively [29], and also, Kumar et al. (2018) reported death rate in HAP patients was 35.6% (32/90) while in VAP patients was 28/63, 44% [17].

There were some limitations in this study; this study was a single-center one conducted at University Chest Hospital and included only medical patients with certain indications for admission for respiratory diseases and mechanical ventilation. Small sample size leads to sparse data bias. No scoring system was used to evaluate severity of pneumonia and associated complications, lack of testing for viruses and atypical organisms and lack of invasive sampling procedure, and bronchoalveolar lavage (BAL) and endotracheal aspirate (ETA) for HAP group.

## Conclusion

In this study, the etiological organisms for HAP and VAP were relatively the same with predominance of antimicrobial-resistant organisms in VAP group, especially *Klebsiella pneumoniae*, *Acinetobacter baumannii*, and *Stenotrophomonas maltophilia*. Intravenous antibiotic use within the last 3 months was the strongest predictor for risk of MDRO infection in both HAP and VAP group. VAP was associated with higher death rates compared with HAP. Our results should be considered as an alarm for raising attention towards prevention and control of the MDR organisms specially *K. pneumoniae* in hospitals which showed resistance to drugs commonly used for these organisms as well as antimicrobial agents such as polymyxin E and glycylicycline which are lastly resorted for life-threatening infections in ICU patients.

## Abbreviations

<i>A. baumannii</i>	<i>Acinetobacter baumannii</i>
BAL	Bronchoalveolar lavage
Cm	Centimeter
CXR	Chest X-ray
COPD	Chronic obstructive pulmonary disease
CPIs	Clinical Pulmonary Infection Score
CFU	Colony-forming units
CI	Confidence interval
Covid-19	Coronavirus disease 2019
CRP	C-reactive protein
CT	Computerized tomography
ETA	Endotracheal aspirate
ETT	Endotracheal tube
<i>E. coli</i>	<i>Escherichia coli</i>
ESBL	Extended spectrum $\beta$ -lactamases
FIO <sub>2</sub>	Fraction of inspired oxygen
HCAP	Healthcare-associated pneumonia
HAP	Hospital-acquired pneumonia
HIV	Human immunodeficiency virus
ICU	Intensive care unit
INR	International normalized ratio
<i>K. pneumoniae</i>	<i>Klebsiella pneumoniae</i>
L	Liter
MRSA	Methicillin-resistant <i>Staphylococcus aureus</i>
mL	Milliliter
mm	Millimeter
MDR	Multidrug resistant
MDRO	Multidrug-resistance organisms
mRNA	Messenger ribonucleic acid
OR	Odds ratio
PDR	Pan-drug resistant
<i>P. stuartii</i>	<i>Providencia stuartii</i>
<i>P. aeruginosa</i>	<i>Pseudomonas aeruginosa</i>
SN	Serial number
Spp.	Species
<i>S. aureus</i>	<i>Staph. aureus</i>
SPSS	Statistical Package for the Social Sciences
$\mu$ g	Microgram
VTE	Venous thromboembolism
VAP	Ventilator-associated pneumonia
XDR	Extensively drug-resistant XDR

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## Authors' contributions

AAE, collection, analysis, and interpretation of data, performing some cases of BAL, and writing, reviewing, and editing manuscript. MT, conception, design, and sharing in collection of data, performing some cases of BAL, and writing, reviewing, and editing manuscript. MMM, did cultures and microbiological analysis, writing methodology, and reviewing and editing the manuscript. AST and MAE, adjust therapeutic doses of antimicrobial agents and follow up drugs interactions. MSH and AHAEZ supervised manuscript. All authors read and approved the final manuscript.

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## Availability of data and materials

All are available from the corresponding author on request.

## Declarations

## Ethics approval and consent to participate

Ethical Committee approval was taken from Faculty of Medicine, Tanta University, approval code (22/5/35500), and written consents were obtained from all patients and their families.

## Consent for publication

Not applicable. Neither identifying images nor personal data were included in the manuscript.

## Competing interests

The authors declare that they have no competing interests.

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