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Original article

Antibiotic resistance patterns in endotracheal aspirates of mechanically ventilated patients: A cross-sectional study

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ABSTRACT

Background: Major nosocomial infections in intensive care units (ICUs) that significantly increase morbidity, and lengthen hospital stays, and death are ventilator-associated pneumonia (VAP) and ventilator-associated tracheobronchitis (VAT). **Aim of work:** This study evaluated the bacterial profile and antibiotic resistance patterns in endotracheal aspirates collected from 96 mechanically ventilated patients at Kasr Al-Ainy Hospital, Cairo University. **Methods**: This is a cross-sectional study of a12 month duration including data from culture-proven VAP OR VAT patients admitted at the ICU, in Cairo University Hospital. **Results:** Out of 96 endotracheal aspirate samples, 73 (76%) were culture positive. Of these positive cultures, 46.9% demonstrated monomicrobial growth, while 29.2% were polymicrobial. The findings of testing for antibiotic susceptibility and microbiological cultures showed that multidrug-resistant organisms (MDROs) were highly prevalent, especially in Gram-negative bacteria. Notably, 3.5% of cases had extended-spectrum β-lactamase (ESBL) synthesis, AmpC production was noticed in 27.9% of isolates, while 45.3% of isolates had carbapenem resistance. **Conclusions:** our research offers vital epidemiological information that can help drive the creation of focused interventions and clinical decision-making to lessen the risk of antibiotic resistance in critical care settings. To guarantee efficient management of VAP/VAT and to enhance patient survival in the face of growing antibiotic resistance, these approaches must be included in standard clinical practice. Also highlights how urgently strong antimicrobial stewardship initiatives and focused infection control (IC) strategies are needed to direct empirical treatment for patients in critical condition.

Introduction

Nosocomial infections pose a significant threat to intensive care units (ICUs) around the world, especially ventilator-associated pneumonia (VAP) and ventilator-associated tracheobronchitis (VAT). While the widely accepted criteria to diagnose VAT are similar to those of VAP, but without radiological evidence of pneumonia, VAP is defined as pneumonia that manifests at least 48 hours after mechanical breathing and includes infiltrates on a chest radiograph with two of either fever, leukocytosis, or purulent sputum [1]. These disorders are associated with significant clinical and financial costs. VAP is thought to affect 10% to 40% of ventilated patients, and the associated mortality risk ranges from 3 to 17% [2]. Although less well-known, VAT can also happen before VAP and increase morbidity.

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-The critically ill nature of ICU patients with factors such as advanced age, multiple comorbidities (diabetes, hypertension, ischemic heart disease), and prolonged exposure to invasive devices renders them particularly vulnerable to such infections. Early diagnosis and appropriate antimicrobial management are crucial to improving outcomes [2].

Microbial Etiology and Emerging Resistance

Klebsiella pneumoniae, Acinetobacter baumannii, Pseudomonas aeruginosa, Enterobacter species, and Escherichia coli are among the Gram-negative bacteria that dominate the microbiological etiology of VAP/VAT [3]. Significant contributions are also made by gram-positive organisms, including methicillin-resistant *Staphylococcus aureus (MRSA)* [4]. In certain instances, fungal colonization specifically by *Candida spp*. is noted, particularly in patients on broad-spectrum antibiotics [5].

Antimicrobial resistance in ICU microorganisms has significantly increased over the last decade. *Acinetobacter baumannii* and *Klebsiella pneumoniae* bacteria that are resistant to carbapenem have become serious problems; in some environments, resistance rates have been reported to surpass 50% [6]. Furthermore, the spread of metallo-β-lactamases (MBL) and extended-spectrum β-lactamases (ESBL) significantly reduces the effectiveness of conventional treatment plans. The local difficulties in treating infections caused by multidrug-resistant (MDR) organisms have been highlighted in regional studies from Egypt, which have mirrored these worldwide trends [7, 8].

Since epidemiological studies for ventilated patients are desperately needed to understand the local microbial flora and their antibiotic profiles for the rational use of antibiotics, this study was a cross-sectional study of 12 months duration including prospectively collected data at the ICU, in Cairo University Hospitals (Chest ICU), carried out to determine the prevalence of pathogenic bacteria in respiratory secretions of ventilated patients from tracheal aspirate and their antibiotic susceptibility patterns.

Study Objectives

Because MDR organisms are becoming more common and there are fewer antimicrobial treatments available, the following goals guided the design of this study:

1. To identify the type of bacteria, present in endotracheal aspirates from patients on mechanical ventilation.

2. To evaluate the patterns of antibiotic resistance in the organisms that were isolated.

3. To determine clinical risk factors linked to the development of multidrug-resistant illnesses.

Methods

Study Design and Setting

The present study was a cross-sectional study of 12 months duration including collected data at the ICU, in Cairo University Hospitals (Chest ICU). The study included 96 mechanically ventilated patients suspected of having VAP or VAT. While the widely accepted criteria to diagnose VAT are similar to those of VAP, but without radiological evidence of pneumonia, VAP is defined as pneumonia that manifests at least 48 hours after mechanical breathing and includes infiltrates on a chest radiograph with two of either fever, leukocytosis, or purulent sputum. [1, 9, 10]. Inclusion criteria required patients to be 18 years or older and to have been on mechanical ventilation for at least 48 hours. The study was approved by the faculty of medicine, Cairo University Ethical Committee under the number (N 108/2023) on 24/6/2023.

The sample size was determined using ClinCalc software for a cross-sectional study, with 0.05 alpha error and power of the study 0.80, CI of 95%, which calculated the required number to be 64 tracheal aspirates from mechanically ventilated patients across the study [11].

Sample Collection and Processing

A thorough history, a clinical examination, a chest X-ray, and laboratory tests (CBC, CRP with titter, urea, creatinine, ALT, and AST) were performed on each participant in this study.

-Aseptic aspirate collection: A Nelton catheter 16FG suction catheter (Ultra-Med, Egypt) was carefully inserted into the endotracheal tube for approximately 25 cm to gather endotracheal aspirates. After a gentle aspiration without saline instillation, the catheter was taken out of the endotracheal tube. To flush the exudates into a sterile container for collection, a sterile syringe was used to inject two milliliters of 0.9% saline into the endotracheal tube. An hour was allotted for processing the samples to reduce contamination or overgrowth Specimens were refrigerated if

immediate processing was not possible for 6 hours maximum [12, 13].

-For the Gram staining, all aspirate specimens were ready within the first hour. Then identified by standard microbiological identification, inoculate 5% blood agar, chocolate agar, MacConkey agar, and Sabouraud agar (Oxoid, Ltd., UK), Media were reconstituted according to the manufacturer's instructions and then sterilized for 15 minutes at 121°C. At 37°C, the plates were incubated for 18 to 24 hours. The following day, the plates were read; however, the reading time would be extended to 48 hours if no bacterial growth was discovered in the first 24 hours. Moreover, some cultures after incubation for 48 hours give results either Inhibited normal flora mean complete absence of microbial growth on culture media plate or Normal flora growth of mixed growth of viridans streptococci, beta hemolytic streptococci, *CONS*, enterococci with no prevalence of any of them [14]. Biochemical testing and Gram staining were employed to identify the isolated colonies. Conventional biochemical testing was followed by the VITEK 2 automated system to verify the results [15]. The Kirby-Bauer disk diffusion method was used to test for antibiotic susceptibility, and the results were interpreted following the guidelines of the Clinical and Laboratory Standards Institute (CLSI) [16]. A microorganism that is resistant to a minimum of one antimicrobial in three or more antimicrobial classes is said to be multidrug-resistant (MDR). The antibiotic discs used in the testing were regularly provided by Oxoid. Methicillin resistance in *Staphylococcus* was identified through the use of a cefoxitin disc (30 μg). The screening for *vancomycin-resistant Staphylococcus* began with the use of Vancomycin screening agar (brain heart infusion agar (BHI) with 6 μg/ml vancomycin). Any suspected colonies underwent further confirmation through Minimum Inhibitory Concentration (MIC) testing using the Vitek2 compact system (Biomerieux, France) [17, 18].

Statistical Analysis

The data was coded and entered using statistical software for the social sciences (SPSS) version 28 (IBM Corp., Armonk, NY, USA). Mean, standard deviation, median, minimum, and maximum were used to summarize the quantitative data, while frequency (count) and relative frequency (%) were used to summarize the categorical data [19]. Quantitative variables were compared using the non-parametric Kruskal-Wallis and Mann-Whitney tests, while categorical data were compared using the Chi-square (□2) test; the exact test was applied when the expected frequency was less than 5 [20] P-values less than 0.05 were considered statistically significant.

Results

Patient Demographics

The study enrolled 96 patients, with a mean age of 64.53 ± 14.73 years; 64.6% were male. The average duration of ICU admission before sampling was 8.33 ± 7.27 days. The average duration of intubation before sampling was 6.87 ± 5.43 days. Seventy-nine patients had VAP (82.3%), and 17 patients had VAT (17.7%). Fifty-three patients had diabetes (55.2%), 62 hypertensive patients (64.6%), and 41 ischemic heart patients (42.7%).

Microbiological Findings

Out of 96 endotracheal aspirate samples, 73 (76%) were culture positive. Of these positive cultures, 46.9% demonstrated monomicrobial growth, while 29.1% were polymicrobial (Figure 1): The isolated organisms were distributed as follows (Figure 2):

- *Klebsiella pneumoniae*: 26 isolates (20.6%)
- *Acinetobacter spp.*: 23 isolates (18.3%)
- *Enterobacter spp.*: 18 isolates (14.3%)
- *Pseudomonas aeruginosa*: 12 isolates (9.5%)
- *MRSA.:* 8 isolates (6.3%)
- *Candida spp.*: 8 isolates (6.3%)
- Inhibited Normal flora 8 (6.3%)
- Normal flora 15 (11.9%)

Gram-negative bacteria comprised approximately 87 (84.5%) of all isolates, whereas Gram-positive organisms constituted 8(7.8%) and fungi constituted also 8(7.8%).

Antibiotic Resistance Patterns

Antibiotic susceptibility testing revealed concerns about resistance patterns. Carbapenem resistance was observed in 45.3% of isolates, ESBL production was noticed in 3.5% of isolates, AmpC production was noticed in 27.9% of isolates and MDR was detected in 23.39%.

Resistance rates to cephalosporins (e.g., cefepime) exceeded 88%. Fluoroquinolones (ciprofloxacin and levofloxacin) demonstrated

resistance rates exceeding 80% in gram-negative and around 55% in gram-positive bacteria isolates. Tigecycline and colistin retained high susceptibility rates (above 95%) in gram-negative bacteria isolates, and vancomycin and linezolid10 mg retained high susceptibility rates (100%) in gram-positive bacteria isolates.

Relations with Clinical Parameters

Moreover, patients with polymicrobial infections had a higher resistance pattern than those with monomicrobial infections (p = 0.024). **(Chi-square test)**

Statistical analysis showed that prolonged ICU stays, and prolonged intubation periods were significantly associated with VAP than VAT (p =0.001, p < 0.001) respectively. There were statistically significant results When correlated between Days of ICU admissions, days before sample and duration of intubation before sample intubation, and VAP or VAT (p =0.001, p < 0.001) respectively. Table 1

Table 1. Correlation between Days of ICU admissions, days before sample and duration of intubation before sample intubation, and VAP or VAT (Mann-Whitney test)

	VAP or VAT						
	VAP			VAT			p-value
	Median	Minimum	Maximum	Median	Minimum	Maximum	
Duration of ICU admission before the sample	9.00	0.00	27.00	2.00	0.00	9.00	0.001
Duration of intubation before the sample	7.00	1.00	25.00	2.00	1.00	2.00	< 0.001

P-values less than 0.05 were considered statistically significant.

Also, patients with hypertension had a VAP than those with VAT (p = 0.026) (Figure 3)

Figure 1. Percentage of monomicrobial and polymicrobial growth of endobronchial aspirate samples.

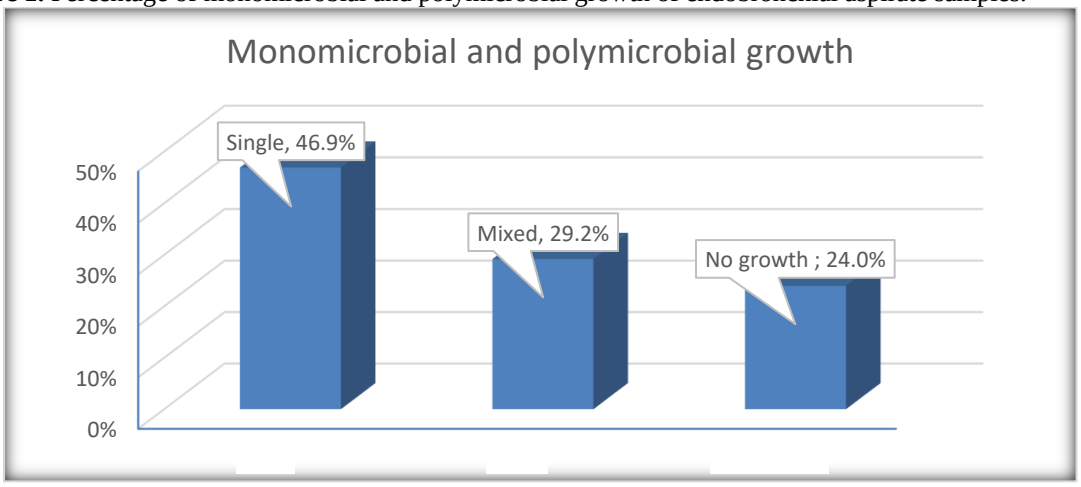


Figure 2. The distribution of isolated organisms.

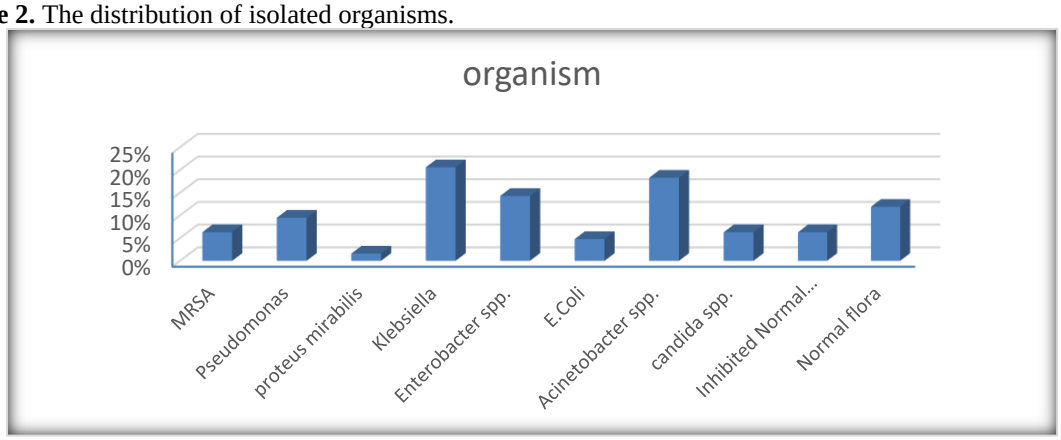
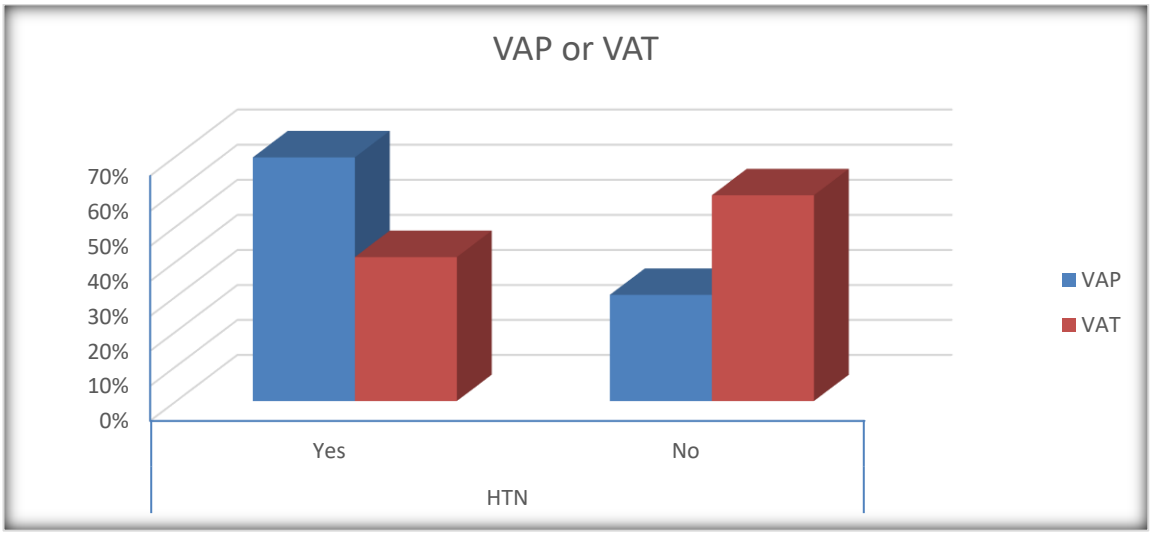


Figure 3. Relation between patients with hypertension and VAP/VAT (Chi-square test).



Discussion

Our results confirm that Gram-negative bacteria dominate the microbial etiology in ventilated patients. *Klebsiella pneumoniae*, known for its ability to acquire resistance genes *via* plasmids, was the most frequently isolated organism. This aligns with findings from Magiorakos et al. (2012)[21], who documented the emergence of multidrug-resistant *Klebsiella pneumoniae* as a global health threat. *Acinetobacter baumannii*, notorious for its survival in the hospital environment and its intrinsic resistance mechanisms, also featured prominently in our study. Similar observations have been reported by Livermore [22], who noted a disturbing trend in carbapenem resistance among *Acinetobacter spp.*

Further complicating the therapeutic situation is the detection of *Pseudomonas aeruginosa* and *Enterobacter spp*., albeit at lower frequencies; both organisms have built-in resistance mechanisms, such as efflux pumps and beta-lactamase production, which contribute to their multidrug-resistant profiles. Furthermore, the inclusion of *Candida spp*. (6.3% of isolates) in our analysis reflects the growing concern of fungal colonization in patients exposed to prolonged antibiotic therapy; while the clinical significance of *Candida* colonization in the respiratory tract is still up for debate, its presence may indicate an altered microbial ecosystem in the ICU [23].

The high rate of carbapenem resistance (45.3%) is one of the most important findings of our study. Carbapenems are used as last-resort antibiotics to treat infections caused by multidrug-resistant Gram-negative bacteria, and resistance to these agents greatly reduces therapeutic options and is linked to poor clinical outcomes[22]. The mechanisms underlying carbapenem resistance are complex and may include the production of carbapenemases (e.g., NDM-1 and OXA-48), loss of porins, and upregulation of efflux pumps. ElFeky et al. (2024)[8] have shown that carbapenem-resistant Enterobacterales (CRE) have limited sensitivity to novel β-lactam/β-lactamase inhibitor combinations, further complicating treatment regimens.

Our data also reveals an alarmingly high resistance rate to cephalosporins and fluoroquinolones. Resistance to these classes, often due to the production of ESBLs and mutations in target enzymes, leaves clinicians with few viable options. In contrast, tigecycline exhibited high susceptibility rates (>95%), suggesting that these agents remain effective for treating infections with MDR organisms. [24]. To stop the spread of MDR organisms and enhance therapeutic outcomes, it is crucial to employ quick diagnostic techniques, develop ASP, and strengthen IC measures.

Moreover, patients with polymicrobial infections had a resistance pattern than those with monomicrobial infections ($p = 0.024$). Our data also showed an alarmingly high resistance rate to cephalosporins and fluoroquinolones. Resistance to these classes, typically due to the creation of ESBLs and changes in target enzymes, leaves doctors with few effective options. The high susceptibility rates (>95%) of tigecycline, on the other hand, indicate

that these drugs are still useful in treating infections caused by MDR pathogens. In (2019), Bassetti et al.[24]

Additionally, compared to patients with monomicrobial infections, those with polymicrobial infections exhibited a resistance pattern ($p = 0.024$).

Correlation Between ICU Admission, Intubation Duration, and VAP or VAT

The results show a statistically significant link between longer ICU stays, longer intubation times, and an increased risk of VAP compared to VAT. These findings are consistent with prior research indicating that longer exposure to invasive mechanical ventilation considerably increases the risk of VAP due to reduced airway defenses and prolonged colonization by MDR microorganisms[10].

Impact of ICU Admission Duration on VAP Development

According to Papazian et al. (2020)[25], extended ICU stays are frequently linked to higher exposure to nosocomial pathogens, longer antibiotic use, and more chances of cross-contamination. According to a study on the chances of cross-contamination. According to a study by Gaudet et al. (2023)[26], critically ill patients who were admitted to the ICU for longer than seven days were at a much-increased risk of developing MDR bacterial colonization, which made them more susceptible to VAP. An essential component of VAP pathogenesis, the longer hospital stay promotes the development of bacterial biofilm in the endotracheal tube[27].

Intubation Duration and Risk of VAP

There was a significant association between the length of intubation before sample collection and the occurrence of VAP. Lower respiratory tract infections result from intubation because it interferes with normal mucociliary clearance and encourages the microaspiration of oropharyngeal secretions [28]. Studies show that the incidence of VAP rises by roughly 1% to 3% for every day of mechanical ventilation, and the presence of an endotracheal tube facilitates bacterial migration [9]. Patients with pre-existing diseases like hypertension, which may compromise immune function and increase the risk of VAP relative to VAT, should pay special attention to this [1].

Hypertension as a Risk Factor for VAP

VAP was more common in hypertensive patients than VAT, which may indicate a link between respiratory infections and cardiovascular comorbidities in critically ill individuals. Endothelial dysfunction and compromised immunological responses have been associated with chronic hypertension, perhaps making people more vulnerable to bacterial infections[29]. Additionally, hypertensive patients who needed extended ventilation had higher systemic inflammation and a higher risk of developing severe pneumonia, according to retrospective research by Rouzé et al (2021) [30].

Limitations

Despite the useful data this study offered, some limitations must be noted:

Single-center Design: The results might not be typical of other settings because they are based on data from a single tertiary hospital. Also, Limited Sample Size: Despite the inclusion of 96 patients, more extensive research is required to validate these findings, and Lack of Comprehensive Molecular Data: Although phenotypic resistance patterns were carefully evaluated, not all isolates underwent molecular analyses to pinpoint particular resistance genes (beyond those mentioned in literature).

Conclusion

According to the study, endotracheal aspirations from patients on mechanical ventilation frequently contain multidrug-resistant bacteria. Current treatment regimens are seriously challenged by the high rate of carbapenem resistance, which also highlights the necessity of updating empirical treatment procedures in the ICU. Our results confirm that Gram-negative bacteria dominate the microbial etiology in ventilated patients. *Klebsiella pneumoniae*, Moreover, patients with polymicrobial infections had a resistance pattern than those with monomicrobial infections. The results show a statistically significant link between longer ICU stays, longer intubation times, and an increased risk of VAP compared to VAT.

Conflicts of intereset:

None declared.

Financial disclosure:

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