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Acinetobacter is the most common pathogen associated with late-onset and recurrent ventilator-associated pneumonia in an adult intensive care unit in Saudi Arabia

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SUMMARY

Background: The guidelines for initial empiric antimicrobial therapy for ventilator-associated pneumonia (VAP) are highly dependent on the type of causative pathogen and the time of diagnosis. The objective of this study was to examine the microbial causes of VAP and describe any variability by the timing of VAP onset and over time.

Methods: A prospective surveillance study was conducted in the adult general intensive care unit of a tertiary care hospital in Riyadh, Saudi Arabia. Microbial isolates obtained from blood and different respiratory specimens of patients diagnosed with VAP (using the US Centers for Disease Control and Prevention definition) between August 2003 and June 2009 were included.

Results: A total of 457 pathogens were identified during the study; 380 (83.2%) were associated with primary VAP and 77 (16.8%) were associated with recurrent VAP. Of primary VAP pathogens, 159 (41.8%) were associated with early-onset (<5 days) and 221 (58.2%) were associated with late-onset (≥5 days) VAP. The most common pathogen identified was *Acinetobacter spp* (26.5%), followed by *Pseudomonas aeruginosa* (21.7%), *Staphylococcus aureus* including methicillin-resistant *S. aureus* (MRSA) (15.3%), *Klebsiella spp* (6.8%), *Haemophilus spp* (6.1%), and *Enterobacter spp* (5.0%). *Acinetobacter spp* and MRSA were significantly associated with late-onset VAP while *Haemophilus spp* and *Streptococcus pneumoniae* were significantly associated with early-onset VAP. *Acinetobacter spp* was the only pathogen associated with recurrent VAP and its incidence showed a significant increasing trend during the study period. *Acinetobacter spp* was significantly associated with prolonged ventilation, sedation, and nasogastric intubation.

Conclusions: *Acinetobacter baumannii* is the most common and increasingly important pathogen associated with VAP in our patients, especially late-onset and recurrent VAP.

1. Introduction

Ventilator-associated pneumonia (VAP) continues to complicate the course of 8–28% of patients receiving mechanical ventilation and accounts for 15–25% of all types of intensive care unit (ICU)-acquired infections.[1–3] VAP can prolong hospital stay by 2–10 extra days and consequently inflate inpatient healthcare costs.[4,5] Even higher than other device-associated healthcare-associated infections (HAI), VAP is a deadly HAI with 10–30% attributable mortality.[4–6] VAP is caused by a variety of pathogens that originate from the patient's flora or the healthcare environment.[7]

Awareness of the common microbial causes of VAP and confirmation of the specific cause at the individual level are considered the single most important piece of information to guide optimal antibiotic therapy.[8] Moreover, guidelines for initial empiric antimicrobial therapy for VAP are highly dependent on the type of causative pathogen and its resistance pattern.[9] This is further complicated by the time of diagnosis (early- vs. late-onset

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VAP) and prior hospitalization or use of antimicrobial therapy.[9] Early-onset VAP is frequently caused by aspiration of oropharyngeal secretions more likely to have community-type pathogens.[10] Late-onset VAP (5 days or more) is more likely to be caused by multidrug-resistant (MDR) pathogens, and is associated with increased patient mortality and morbidity.[9]

The microbial causes of VAP vary considerably by geographic location[8] and over time.[11] Studying geographic and temporal changes is critical in determining the correct local empirical antibiotic. Unfortunately data on microbial causes of VAP in Saudi Arabia are limited, outdated, or based on a small number of events.[12–14] Moreover, none of the previous local studies has explored the association between VAP onset and its causative pathogens or monitored changes over time. The objective of the current study was to examine the microbial causes of VAP among adult ICU patients and to describe any variability by the timing of VAP onset and over time.

2. Methods

2.1. Setting

The current study was conducted in an adult general ICU of a tertiary care hospital, King Abdulaziz Medical City (KAMC) in Riyadh, Saudi Arabia. KAMC is an approximately 900-bed tertiary care facility that provides healthcare services to about 600 000 Saudi National Guard soldiers, employees, and their families. The care provided ranges from primary and preventive care to tertiary care. The adult ICU at KAMC is a 21-bed closed medical–surgical–trauma unit covered by onsite board-certified intensivists 24 h per day, 7 days a week,[15] and admits approximately 900 patients per year. The nurse-to-patient ratio is 1:1.

2.2. VAP surveillance

The details of VAP surveillance have been described elsewhere.[16] Briefly, a prospective surveillance program was established in 2003 as a joint project between the Intensive Care Department and Infection Prevention and Control Department to provide regular reports on the VAP rate and microbiology to guide quality improvement projects. The same VAP definition was used throughout the study period,[17] and was based on that of the US Centers for Disease Control and Prevention (CDC).[18] Accordingly, VAP was defined as a pneumonia occurring more than 48 h after endotracheal intubation, with the following diagnostic criteria: new or progressive infiltrates, consolidation, or cavitation on chest X-ray, with one of the following: (a) new onset purulent bronchial secretions with leukopenia (white blood cells $<4 \times 10^9$/l) or leukocytosis ($\geq 12 \times 10^9$/l), or core temperature $\geq$38.5 or $\leq$36 °C without other cause, (b) significant positive culture from blood, or (c) endotracheal aspirate bronchoalveolar lavage (BAL), or culture from another relevant site of infection. The diagnostic workup for VAP was mostly done by obtaining endotracheal aspirates, which were processed non-quantitatively. Diagnostic bronchoscopy was rarely utilized and was mainly performed for patients with an immunocompromised status, unclear etiology of lung infiltrates, or non-resolving pneumonia. Both primary (first) and recurrent (second or third) episodes of VAP during the same hospitalization were included in the analysis. Recurrent VAP was diagnosed using the same criteria as primary VAP only after an evidence of clearance of the previous VAP.[19] Primary VAP events were further categorized as early-onset VAP (within the first 4 days of endotracheal intubation) or late-onset VAP (on the fifth and subsequent days following endotracheal intubation).[20]

2.3. Ventilator and patient care

Specialized respiratory therapists provided routine ventilator care[21] that involved closed endotracheal suctioning with the system changed every 72 h or as clinically indicated, changing ventilator circuits between patients or when they became soiled or damaged, and changing the heat and moisture exchangers every 7 days or when visibly soiled. Oral decontamination using 0.2% chlorhexidine was performed by nurses at least 4 times per day. Disinfection of surfaces and equipment was performed by bedside nurses or patient care technicians on a daily basis or as needed, as per a standard protocol. Disinfection sprays and wipes containing alcohol, chlorhexidine, and/or ammonium chloride were used.

2.4. Microbiological examination

Microbial isolates obtained from blood and different respiratory specimens from patients diagnosed with VAP between August 1, 2003 and June 30, 2009 were included in the current analysis. Specimens examined included blood, endotracheal aspirate, BAL, and pleural fluid. Endotracheal aspirates were sent for nonquantitative cultures before starting empirical antimicrobial therapy. BAL was processed in a quantitative manner with a cutoff of 104 colony-forming units/ml. Up to two isolates were allowed per episode. Only the first positive culture was included. Multiple cultures with the same results from one episode of VAP were re-coded just once. Culture results reported as 'no growth' or 'normal flora' were categorized as 'no pathogen identified'. Gram-positive and Gram-negative bacteria were identified to the species level using MicroScan Walkaway (Siemens, Frimley, Camberley, UK), a conventional automated biochemical identification system.

2.5. Data analysis

Significant differences in the frequency of a certain pathogen between early- and late-onset VAP, as well as between primary and recurrent VAP, were evaluated using the Chi-square test or Fisher's exact test, as appropriate. Similarly differences in the frequency of a certain pathogen of VAP between KAMC and those reported by the US National Healthcare Safety Network (NHSN)[22] were evaluated using the Chi-square test or Fisher's exact test, as appropriate. The prevalence trends of selected common pathogens, as well as those that showed significant differences between early- and late-onset VAP, or primary and recurrent VAP, were plotted over time. Significant increasing or decreasing prevalence trends over time were assessed using Mantel–Haenszel Chi square for linear trend. Significant trend differences between early- and late-onset VAP, or primary and recurrent VAP, were assessed using Mantel–Haenszel Chi square after stratification by year. All p-values were two-tailed. A p-value of <0.05 was considered significant. SPSS (release 17.0, SPSS Inc., Chicago, IL, USA), OpenEpi (version 2.2), and PEPI-for-Windows software[23] were used for all statistical analyses.

3. Results

During the period between August 1, 2003 and June 30, 2009, a total of 470 VAP events were diagnosed. Of these, 433 (92.1%) were primary events and 37 (7.9%) were recurrent events. About 39.0% of the primary VAP events were early-onset, while 61.0% were late-onset. About a third (33.3%) of the VAP events were diagnosed mainly based on clinical signs and symptoms with no pathogen identified. About two-thirds of diagnosed VAP events had at least one pathogen identified (46.7% single pathogen and 20.1% polymicrobial). A total of 457 pathogens were identified during the study; 380 (83.2%) were

Table 1
Distribution of pathogens isolated from ventilator-associated pneumonia (VAP) by recurrence status among study patients

	Primary VAP ($n=380$)	Recurrent VAP ($n=77$)	Overall ($n=457$)	p-Value
Gram-positive	85 (22.4%)	12 (15.6%)	97 (21.2%)	NS
Staphylococcus aureus	62 (16.3%)	8 (10.4%)	70 (15.3%)	NS
MRSA	31 (8.2%)	6 (7.8%)	37 (8.1%)	NS
Streptococcus pneumoniae	9 (2.4%)	2 (2.6%)	11 (2.4%)	NS
Other Gram-positive pathogens	14 (3.7%)	2 (2.6%)	16 (3.5%)	NS
Gram-negative	280 (73.7%)	62 (80.5%)	342 (74.8%)	NS
Non-fermenter				
Acinetobacter spp	91 (23.9%)	30 (39.0%)	121 (26.5%)	0.006
Pseudomonas aeruginosa	85 (22.4%)	14 (18.2%)	99 (21.7%)	NS
Stenotrophomonas maltophilia	13 (3.4%)	2 (2.6%)	15 (3.3%)	NS
Enterobacteriaceae				
Klebsiella spp	27 (7.1%)	4 (5.2%)	31 (6.8%)	NS
Enterobacter spp	19 (5.0%)	4 (5.2%)	23 (5.0%)	NS
Escherichia coli	9 (2.4%)	3 (3.9%)	12 (2.6%)	NS
Serratia spp	3 (0.8%)	2 (2.6%)	5 (1.1%)	NS
Proteus spp	2 (0.5%)	0 (0.0%)	2 (0.4%)	NS
Haemophilus spp	25 (6.6%)	3 (3.9%)	28 (6.1%)	NS
Other Gram-negative pathogens	6 (1.6%)	0 (0.0%)	6 (1.3%)	NS
Fungi	9 (2.4%)	1 (1.3%)	10 (2.2%)	NS
Others	1 (0.3%)	1 (1.3%)	2 (0.4%)	NS
Missing	5 (1.3%)	1 (1.3%)	6 (1.3%)	NS

MRSA, methicillin-resistant *Staphylococcus aureus*.

associated with primary VAP and 77 (16.8%) were associated with recurrent VAP (Table 1). Of primary VAP events, 159 (41.8%) were associated with early-onset VAP and 221 (58.2%) were associated with late-onset VAP (Table 2). The majority of isolates were obtained from tracheal aspirates (87.1%), followed by blood (11.8%), BAL (0.9%), and pleural fluid (0.3%).

The majority (74.8%) of pathogens associated with VAP were Gram-negative, while Gram-positives represented only 21.2% (Table 1). The most common pathogen associated with VAP was *Acinetobacter spp* (26.5%), followed by *Pseudomonas aeruginosa* (21.7%), *Staphylococcus aureus* including methicillin-resistant *S. aureus* (MRSA) (15.3%), *Klebsiella spp* (6.8%), *Haemophilus spp* (6.1%), and *Enterobacter spp* (5.0%). Gram-negative pathogens were slightly more encountered in recurrent VAP (80.5%) than in primary VAP (73.7%), but the difference was not statistically significant ($p = 0.182$) (Table 1). *Acinetobacter spp* was the only pathogen significantly associated with recurrent VAP compared to primary VAP (39.0% vs. 23.9%, $p = 0.006$). Gram-negative pathogens were more encountered with late-onset VAP (76.9%) than early-onset VAP (69.2%) and the difference was statistically significant ($p < 0.001$) (Table 2). *Acinetobacter spp* (30.8% vs. 14.5%, $p < 0.001$) and MRSA (10.0% vs. 5.7%, $p = 0.023$) were significantly associated with late-onset VAP. On the other hand, *Haemophilus spp* (13.8% vs. 1.4%, $p < 0.001$) and *Streptococcus pneumoniae* (4.4% vs. 0.9%, $p = 0.015$) were significantly associated with early-onset VAP. Compared to patients with primary VAP associated with other pathogens, patients with primary VAP associated with Acinetobacter were more likely to have sedation ($p = 0.031$), nasogastric intubation ($p = 0.028$), and prolonged ventilation ($p = 0.001$); although it did not reach statistical significance ($p = 0.094$), they were also more likely to have immunocompromising conditions (Table 3).

Table 2
Distribution of pathogens isolated from primary ventilator-associated pneumonia (VAP) by the time of diagnosis among study patients

	Early VAP ($n=159$)	Late VAP ($n=221$)	Overall ($n=380$)	p-Value
Gram-positive	43 (27.0%)	42 (19.0%)	85 (22.4%)	NS
Staphylococcus aureus	31 (19.5%)	31 (14.0%)	62 (16.3%)	NS
MRSA	9 (5.7%)	22 (10.0%)	31 (8.2%)	0.023
Streptococcus pneumoniae	7 (4.4%)	2 (0.9%)	9 (2.4%)	0.015[a]
Other Gram-positive pathogens	5 (3.1%)	9 (4.1%)	14 (3.7%)	NS
Gram-negative	110 (69.2%)	170 (76.9%)	280 (73.7%)	<0.001
Non-fermenter				
Acinetobacter spp	23 (14.5%)	68 (30.8%)	91 (23.9%)	<0.001
Pseudomonas aeruginosa	30 (18.9%)	55 (24.9%)	85 (22.4%)	NS
Stenotrophomonas maltophilia	4 (2.5%)	9 (4.1%)	13 (3.4%)	NS
Enterobacteriaceae				
Klebsiella spp	14 (8.8%)	13 (5.9%)	27 (7.1%)	NS
Enterobacter spp	9 (5.7%)	10 (4.5%)	19 (5.0%)	NS
Escherichia coli	2 (1.3%)	7 (3.2%)	9 (2.4%)	NS
Serratia spp	2 (1.3%)	1 (0.5%)	3 (0.8%)	NS
Proteus spp	1 (0.6%)	1 (0.5%)	2 (0.5%)	NS
Haemophilus spp	22 (13.8%)	3 (1.4%)	25 (6.6%)	<0.001
Other Gram-negative pathogens	3 (1.9%)	3 (1.4%)	6 (1.6%)	NS
Fungi	3 (1.9%)	6 (2.7%)	9 (2.4%)	NS
Others	0 (0.0%)	1 (0.5%)	1 (0.3%)	NS
Missing	3 (1.9%)	2 (0.9%)	5 (1.3%)	NS

MRSA, methicillin-resistant *Staphylococcus aureus*.
[a] Fisher exact test, otherwise Chi-square test.

Table 3
Comparison of demographic and clinical characteristics of patients with primary ventilator-associated pneumonia by type of pathogen

	Acinetobacter	Other pathogens	Total	*p*-Value
Age, years				
Mean ± SD	49.0 ± 21.0	47.6 ± 21.2	48.0 ± 21.1	0.600
18–39	38 (41.8%)	82 (41.6%)	120 (41.7%)	0.892
40–59	16 (17.6%)	39 (19.8%)	55 (19.1%)	
≥60	37 (40.7%)	76 (38.6%)	113 (39.2%)	
Gender				
Male	63 (69.2%)	149 (75.6%)	212 (73.6%)	0.252
Female	28 (30.8%)	48 (24.4%)	76 (26.4%)	
Admission category				
Medical	48 (52.7%)	95 (48.2%)	143 (49.7%)	0.247
Surgical	13 (14.3%)	19 (9.6%)	32 (11.1%)	
Trauma	30 (33.0%)	83 (42.1%)	113 (39.2%)	
Scores				
APACHE II	25.2 ± 9.0	23.3 ± 8.5	23.9 ± 8.7	0.125
ISS	24.9 ± 12.4	28.5 ± 12.3	27.5 ± 12.4	0.149
SAPS	44.0 ± 21.2	47.9 ± 14.4	47.3 ± 14.6	0.743
Chronic diseases				
Liver disease	11 (12.1%)	17 (8.6%)	28 (9.7%)	0.357
Cardiovascular diseases	18 (19.8%)	28 (14.2%)	46 (16.0%)	0.231
Respiratory diseases	19 (20.9%)	32 (16.2%)	51 (17.7%)	0.338
Renal diseases	13 (14.3%)	27 (13.7%)	40 (13.9%)	0.895
Immunocompromising condition[a]	12 (13.2%)	14 (7.1%)	26 (9.0%)	0.094
Interventional factors				
Sedation	36 (39.6%)	53 (26.9%)	89 (30.9%)	0.031
Nasogastric intubation	70 (76.9%)	126 (64.0%)	196 (68.1%)	0.028
Prolonged antibiotic therapy	10 (11.0%)	27 (13.7%)	37 (12.8%)	0.522
Ventilator days				
Mean ± SD	23.3 ± 16.7	19.6 ± 21.5	20.7 ± 20.1	0.141
≤median (≤15)	33 (36.3%)	113 (57.4%)	146 (50.7%)	0.001
>median (>15)	58 (63.7%)	84 (42.6%)	142 (49.3%)	
ICU length of stay (days)	26.2 ± 17.4	22.6 ± 23.0	23.7 ± 21.4	0.177

SD, standard deviation; APACHE, Acute Physiology and Chronic Health Evaluation; ISS; Injury Severity Score; SAPS, Simplified Acute Physiology Score.
[a] Immunocompromising conditions were defined as per APACHE II as follows: use of immunosuppressive agents or high-dose steroids (e.g., methylprednisolone ≥15 mg/kg/day for ≥5 days), active chemotherapy or radiotherapy within 1 year, Hodgkin and non-Hodgkin lymphoma requiring chemotherapy or radiotherapy, leukemia, lymphoma, diffuse metastatic cancer, or AIDS.

Comparing the VAP-associated pathogens of the current study to those of the NHSN (Table 4), KAMC had more VAP-associated *Acinetobacter spp* (26.5% vs. 8.4%, $p < 0.001$) and *P. aeruginosa* (21.7% vs. 16.3%, $p = 0.003$), but less *S. aureus* (15.3% vs. 24.4%, $p < 0.001$), *Klebsiella spp* (6.8% vs. 9.6%, $p = 0.045$), *Enterobacter spp* (5.0% vs. 8.4%, $p = 0.012$), and *Enterococcus spp* (0.2% vs. 1.3%, $p = 0.044$) compared to NHSN hospitals.

The trends in selected VAP-associated pathogens over the years were examined after excluding partial-year data. Despite the decrease in the number of VAP-associated pathogens (and VAP rate) over time, Gram-negative pathogens that represented about 76% of all isolates during the study, were relatively constant over time (*p* for trend 0.147). *Acinetobacter spp* was the only Gram-negative pathogen to show a significant increasing trend during the studied period (*p* for trend 0.033). *P. aeruginosa* had wide yearly variation but no significant trend (*p* for trend 0.363). *Klebsiella spp* and MRSA were relatively constant over time (*p* for trend 0.110 and 0.976, respectively). The incidence trends of Acinetobacter-associated primary and recurrent VAP during the studied period were different (Mantel–Haenszel $p = 0.011$), with a generally increasing trend observed in recurrent VAP (*p* for trend 0.066) but not in primary VAP (*p* for trend 0.140). *Acinetobacter spp* was more commonly associated with late-onset VAP throughout the study duration (Mantel–Haenszel $p = 0.001$).

Table 4
Comparison of selected pathogens isolated from ventilator-associated pneumonia (VAP) among study patients and the US National Healthcare Safety Network (NHSN)[a]

	KAMC (2003–2009) *n* = 462	NHSN (2006–2007) *n* = 5960	*p*-Value
Gram-positive	97 (21.2%)		
Staphylococcus aureus	70 (15.3%)	1456 (24.4%)	<0.001
Coagulase-negative staphylococci	9 (2.0%)	79 (1.3%)	0.254
Enterococcus spp	1 (0.2%)	77 (1.3%)	0.044
Gram-negative	342 (74.8%)		
Acinetobacter spp	121 (26.5%)	498 (8.4%)	<0.001
Pseudomonas aeruginosa	99 (21.7%)	972 (16.3%)	0.003
Klebsiella spp	31 (6.8%)	574 (9.6%)	0.045
Enterobacter spp	23 (5.0%)	498 (8.4%)	0.012
Escherichia coli	12 (2.6%)	271 (4.6%)	0.054
Fungi	10 (2.2%)	160 (2.7%)	0.524

KAMC, King Abdulaziz Medical City.
[a] Pathogens with no available comparable data from NHSN were not included in the table. NHSN data were derived from different types of ICUs and non-ICU locations in 463 hospitals in the USA.

4. Discussion

This study reports the bacterial causes of VAP among patients of a general adult ICU over a period of 6 years. *Acinetobacter spp* was the most common VAP pathogen (26.5%) in the current study, followed by *P. aeruginosa* (21.7%) and *S. aureus* (15.3%). The three pathogens together accounted for almost two-thirds of all VAP pathogens. The current findings are different from those reported from Western and several developing countries. In a review of 22 VAP studies between 1996 and 2007 from developing countries, *P. aeruginosa* was the most common isolated pathogen (20–52%) in 14 studies, while *Acinetobacter spp* was the most common isolated pathogen (21–36%) in only six studies.[13] Data from 55 ICUs between 2002 and 2005 in eight developing countries showed that *P. aeruginosa* and *Enterobacteriaceae* were the most common isolated pathogens (26% each), followed by *Acinetobacter spp* (20%).[24] On the other hand, reports from the USA and Europe showed that *S. aureus* (23–32%) and *P. aeruginosa* (16–22%) were

the leading causes of VAP, while *Acinetobacter spp* was responsible for only 4–8% of VAP events.[7,22,25]

Several factors may explain the high and increasing contribution of *Acinetobacter spp* to VAP. First, our VAP patients were exposed to more prolonged ventilation times (average 20.7 days) than Western patients (average 14.3)[26] and were more likely to have late-onset VAP than reported in Western patients (61% vs. 44–49%).[27,28] Similar to previous studies, Acinetobacter in the current study was associated with prolonged ventilation and late-onset VAP.[8] Second, the studied ICU experienced an outbreak of Acinetobacter in 2007. *Acinetobacter spp* is particularly known as an important cause of VAP outbreaks in ICUs from hidden sources of colonized patients and contaminated surfaces.[29,30] Third, nasogastric intubation (which was significantly associated with Acinetobacter) was extensively used (68.1%) in our patients. Nasogastric intubation is believed to increase the risk of VAP by increasing the risk of sinusitis.[9] Lastly, although the studied ICU implemented a standard disinfection protocol for surfaces and equipment, it may be insufficient to control Acinetobacter, which is particularly known for its resistance to disinfectants and long survival on dry surfaces.[30,31]

Only a few studies have evaluated VAP recurrence.[32] Moreover there has been confusion between the concepts of 'recurrence', which usually indicates prevention failure, and 'persistence', which usually indicates treatment failure.[19] The rate of VAP recurrence in the current study (16.8%) was less than reported in a recent meta-analysis (26.8%).[32] This may be partially explained by the different definitions used. In our patients, recurrent VAP was diagnosed at an average of 17.6 ± 12.0 days after the previous VAP and only after evidence of clearance of the previous VAP. *Acinetobacter spp* was the only pathogen significantly associated with recurrent VAP in our patients. Supporting this finding, a recent report showed that a high rate of VAP relapse was associated with primary infection by *Acinetobacter spp*.[33]

The difference in VAP pathogens between early- and late-onset VAP observed in the current study was identical to reports from elsewhere.[8,9,34] Several studies have shown *S. pneumoniae* and *Haemophilus influenzae* to be the predominant respiratory pathogens within the first week of intubation, and that they are subsequently replaced by multi-resistant flora, such as MRSA, *P. aeruginosa* or *Acinetobacter baumanii*.[8,9,34] This finding should have a great impact on the choice of empirical antibiotics for VAP.[9] Since the latter group of pathogens are probably more resistant and represented more than 55% of VAP pathogens in our patients, reducing the duration of ventilation (for example by accelerated weaning) may positively impact VAP treatment.

About a third of the VAP events in the current study had negative cultures. It has been shown that bacteriologic confirmation of clinically suspected VAP ranges between 22% and 55%.[35] In addition, patients might have been on antimicrobial therapy at the time that endotracheal cultures were taken.

The current study had several strengths and some limitations. The study is by far the largest epidemiologic surveillance study on ICU patients in Saudi Arabia. The data were collected prospectively and the CDC-based VAP definition used was constant during the entire study period. However, the current NHSN definition no longer allows the clinical definition. The large number of isolates included (>450) allowed us to examine the bacterial causes by time of VAP onset, by recurrence, across the years, and for less common pathogens. Since the local data is limited, the findings may help local physicians to choose the correct empirical antibiotic. However, being a single-center study may limit the generalizability of the findings. Another weakness of the study is that the majority (87.1%) of isolates were cultured in a non-quantitative manner from endotracheal aspirates. This may have limited the specificity of culture results with more false-positive results.

In conclusion, Gram-negative pathogens are responsible for about three quarters of VAP in our patients. *Acinetobacter baumannii* is the most common and increasingly important pathogen associated with VAP, especially late-onset and recurrent VAP. Our ICU should continue to actively screen for Acinetobacter in all admitted patients, shorten the duration of ventilation, minimize sedation, encourage oral gastric rather than nasogastric intubation, and improve currently implemented infection control measures, including environmental disinfection.

Ethical approval: The required approvals were obtained for this work in accordance with KAMC regulations.

Conflict of interest: Nothing to disclose.

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