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REVIEW

Narrative Review of the Epidemiology of Hospital-Acquired Pneumonia and Ventilator-Associated Pneumonia in Gulf Cooperation Council Countries

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ABSTRACT

Hospital-acquired pneumonia (HAP) and ventilator-associated pneumonia (VAP) are the most common healthcare-associated infections, with rates varying between countries. Antimicrobial resistance (AMR) among common HAP/VAP pathogens has been reported, and multidrug resistance (MDR) is of further concern across Middle Eastern countries. This narrative review summarizes the incidence and pathogens associated with HAP/VAP in hospitals across Gulf Cooperation Council (GCC) countries. A PubMed literature search was limited to available data on HAP or VAP in patients of any age published within the past 10 years. Reviews, non-English language articles, and studies not reporting HAP/VAP data specific to a GCC country were excluded. Overall, 41 articles, a majority of which focused on VAP, were selected for inclusion after full-text screening. Studies conducted over multiple years showed a general reduction in VAP rates over time, with Gram-negative bacteria the most commonly reported pathogens. Gram-negative isolates reported across GCC countries included *Acinetobacter baumannii*, *Pseudomonas aeruginosa*, and *Klebsiella pneumoniae*. Rates of AMR varied widely among studies, and MDR among *A. baumannii*, *K. pneumoniae*, *Escherichia coli*, *P. aeruginosa*, and *Staphylococcus aureus* isolates was commonly reported. In Saudi Arabia, between 2015 and 2019, rates of carbapenem resistance among Gram-negative bacteria were 19–25%; another study (2004–2009) reported antimicrobial resistance rates in *Acinetobacter* species (60–89%), *P. aeruginosa* (13–31%), and *Klebsiella* species (100% ampicillin, 0–13% other antimicrobials). Although limited genotype data were reported, OXA-48 was found in ≥ 68% of patients in Saudi Arabia with

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carbapenem-resistant *Enterobacteriaceae* infections. Ventilator utilization ratios varied across studies, with rates up to 0.9 reported in patients admitted to adult medical/surgical intensive care units in both Kuwait and Saudi Arabia. VAP remains a burden across GCC countries albeit with decreases in rates over time. Evaluation of prevention and treatment measures and implementation of a surveillance program could be useful for the management of HAP and VAP.

Keywords: Antimicrobial resistance; Critical care; Hospital-acquired pneumonia; Limited-resource countries; Mechanical ventilation; Surveillance; Ventilator-associated pneumonia

Key Summary Points

Hospital-acquired and ventilator-associated pneumonia (HAP/VAP) infections represent potentially costly comorbidities, with rates of acquisition that vary widely between nations.

Articles described VAP rates in Gulf Cooperation Council member states that varied widely by nation and time, with multi-year studies suggesting a trend of decreasing VAP rates over the last 10–15 years.

The most commonly reported organisms associated with HAP/VAP infections were multidrug-resistant species in the genera *Acinetobacter*, *Pseudomonas*, and *Klebsiella*, although methicillin (meticillin)-resistant *Staphylococcus aureus* and *Streptococcus pneumonia* were also commonly identified.

The high frequency of treatment-resistant bacterial pathogens represents a challenge to further improvement in managing these infections.

INTRODUCTION

Hospital-acquired infections (HAIs), also referred to by the broader term of healthcare-associated infections, are typically defined as infections that occur during care in a hospital facility that were not present or incubating at the time of admission [1]. HAIs usually manifest ≥ 48 h after hospital admission and include infections that present after hospital discharge. Hospital-acquired pneumonia (HAP; pneumonia occurring ≥ 48 h after hospital admission) and ventilator-associated pneumonia (VAP; pneumonia occurring ≥ 48 h after endotracheal intubation) are among the most frequent types of HAI both in high-income and low-/middle-income countries [1, 2]. Use of the term HAP varies across guidelines and studies [2]; in this review, HAP encompasses any pneumonia occurring ≥ 48 h after hospital admission and therefore includes VAP as a subset.

In general, there is wide variation in VAP rates reported across studies due to a combination of factors, including country, intensive care unit (ICU) type, patient case-mix, and differing definitions of VAP [3, 4]. Surveillance of device-associated HAIs during 2012–2017 in ICUs across 45 countries of the International Nosocomial Infection Control Consortium [INICC; predominantly countries with developing economies, including Bahrain, Kuwait, Saudi Arabia, and the United Arab Emirates (UAE)] determined pooled mean VAP rates for 11 ICU types [5]. VAP rates ranged from 7.4 (surgical cardiothoracic ICUs) up to 17.7 per 1000 ventilator-days (medical cardiac ICUs), which were considerably higher than those reported in the USA.

The pathogens most frequently associated with VAP include *Pseudomonas aeruginosa*, *Acinetobacter baumannii*, Gram-negative bacilli of the *Enterobacterales* family (particularly *Escherichia coli* and *Klebsiella pneumoniae*), and

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Staphylococcus aureus [2, 3]. Antimicrobial resistance rates, including multidrug resistance among common HAP/VAP pathogens, are substantial. International surveillance data report methicillin (meticillin) resistance in approximately one half of *S. aureus* isolates, high rates of cefepime and piperacillin-tazobactam resistance in *P. aeruginosa* (up to 30%), and carbapenem resistance in > 50% of *A. baumannii* isolates [2]. Of further concern, multidrug resistant (MDR) pathogens pose a serious problem in Middle Eastern countries due to multiple predisposing factors, including antibiotic misuse and overuse, continuous population movement, and inadequate infection prevention and control strategies [6]. Other inherently MDR organisms as a result of extensive carbapenem use (namely *Stenotrophomonas maltophilia*) are also encountered in critical care units. Furthermore, apart from bacteria, certain fungi (in particular *Candida auris*) can be challenging for hospitals and clinicians in view of MDR and their propensity to spread, persist in the hospital environment, and cause outbreaks in ICUs that are difficult to treat [7, 8].

Infection control and surveillance in Gulf Cooperation Council (GCC) countries is coordinated by the GCC Centre for Infection Control (GCC-CIC) [9]. In addition to providing evidence-based guidelines for infection control practices, the GCC-CIC conducts educational and training activities for personnel working in infection prevention and control [9]. Current standards for respiratory therapy procedures are contained in the GCC Infection Prevention and Control Manual, including detailed protocols for the setup and maintenance of mechanical ventilation circuits and artificial airways, specimen collection, personal protective equipment, and hand hygiene [10]. However, further initiatives and more extensive participation in training activities for infection surveillance and data management are needed, and there is not yet a comprehensive and integrated system in place for collecting and compiling data from hospitals throughout the region [9].

Although all GCC countries are classified as high-income, their economies are still developing, and their healthcare systems face many of the challenges common to other developing nations [9, 11]. Subsequently, this narrative review was undertaken to summarize available data related to the incidence and associated organisms of HAP and VAP in hospitals throughout GCC countries, with a view to identifying unmet medical needs and future challenges for the management of HAP/VAP in the region.

METHODS

A PubMed database search was carried out on 13 November 2021 using the search terms: "pneumonia, ventilator associated"[MeSH Terms] OR (pneumonia AND "ventilator associated") OR "ventilator-associated pneumonia" OR (ventilat* AND associated AND pneumonia) OR ((device OR catheter) AND associated AND pneumonia) OR "healthcare-associated pneumonia"[MeSH Terms] OR ("healthcare associated" AND pneumonia) OR "healthcare-associated pneumonia" OR (healthcare AND associated AND pneumonia) OR "hospital-acquired pneumonia" OR ("hospital acquired" AND pneumonia) OR (nosocom* AND pneumonia) AND (Gulf OR Bahrain OR Kuwait OR Oman OR Qatar OR "Saudi Arabia" OR "United Arab Emirates" OR UAE) NOT Review[publication type]. The search was additionally limited to English-language articles published in the preceding 10 years.

Search results were reviewed by the authors to identify articles reporting original data related to HAP or VAP in patients of any age; articles that did not report HAP or VAP data specific to a GCC country were excluded. Search results were initially screened for relevance on the basis of the title and abstract, then full copies of each identified article were further reviewed for relevance.

This article is based on previously conducted studies and does not contain any new studies with human participants performed by any of the authors.

RESULTS

Based on title and abstract, 57 articles were identified for full-text review. Among the full-text articles assessed, 41 were ultimately

selected for potential inclusion in the review (Fig. 1), including studies conducted in Saudi Arabia (n = 32), Kuwait (n = 4), Qatar (n = 2), Oman (n = 1), UAE (n = 1), and Bahrain, Oman, and Saudi Arabia (n = 1). The majority of identified studies focused on VAP, either exclusively or in the context of HAIs, with only 2 publications [12, 13] focusing on HAP; thus, the majority of the discussion in the current review focuses on VAP.

VAP Rates

Annual VAP rates varied widely between studies and over time (Fig. 2). In the studies that reported data for multiple years, there was a general trend for reduced VAP rates over time. In support of this observation, a longitudinal study (2008–2013) conducted in Bahrain, Oman, and Saudi Arabia showed a general trend for reduced ICU-associated VAP rates over time (Fig. 3A) [9]. A number of time-series analyses reported reduced VAP rates with VAP prevention bundles [9, 14–19]. Studies identified a need for further study of prevention and intervention programs, evidence-based treatment guidelines, and increased VAP-related education activities for staff to ensure that protocols are properly implemented [20–22].

One study from Qatar from 2010 to 2012 that analyzed data by ICU type demonstrated higher VAP rates within trauma ICUs than within medical or surgical ICUs (Fig. 2, inset) [23]. In contrast, a study from Bahrain, Oman, and Saudi Arabia from 2008 to 2013 reported higher VAP rates within medical/surgical ICUs than trauma ICUs, although data from trauma ICUs were collected only from 2010 to 2013 (Fig. 3B) [9].

Infective Agents and Antimicrobial Resistance

Table 1 summarizes the reported associated organisms of HAP/VAP and antimicrobial resistance data. It is noteworthy that isolation of organisms from respiratory samples is not evidence that they are causative of the HAP/VAP unless they are isolated from both the blood culture and respiratory samples at the same time, which is uncommon. Thus, for the purposes of this review, we refer to organisms as being associated with VAP.

Gram-negative bacteria were the most commonly reported organisms overall, including *Acinetobacter* species (particularly *A. baumannii*), *Pseudomonas* species (particularly *P. aeruginosa*), and *Klebsiella* species (particularly *K. pneumoniae*). Gram-positive bacteria included methicillin-resistant *S. aureus* and *Streptococcus pneumoniae*. Other pathogens of note were *S. maltophilia*, which is an important nosocomial pathogen in children in Saudi Arabia [24], and carbapenem-resistant *Providencia stuartii* [12] (Table 1).

Among studies that reported antimicrobial resistance, rates of resistance varied widely. Multidrug resistance (i.e., resistance to ≥ 1 agent in ≥ 3 antimicrobial classes) was frequently reported among *A. baumannii*, *K. pneumoniae*, *E. coli*, *P. aeruginosa*, and *S. aureus* isolates [23, 25–30]; vancomycin-resistant

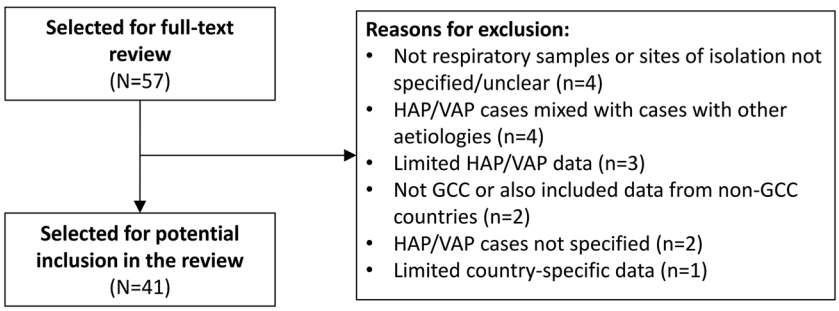

Fig. 1 Selection process. *GCC* Gulf Cooperation Council, *HAP* hospital-associated pneumonia, *VAP* ventilator-associated pneumonia

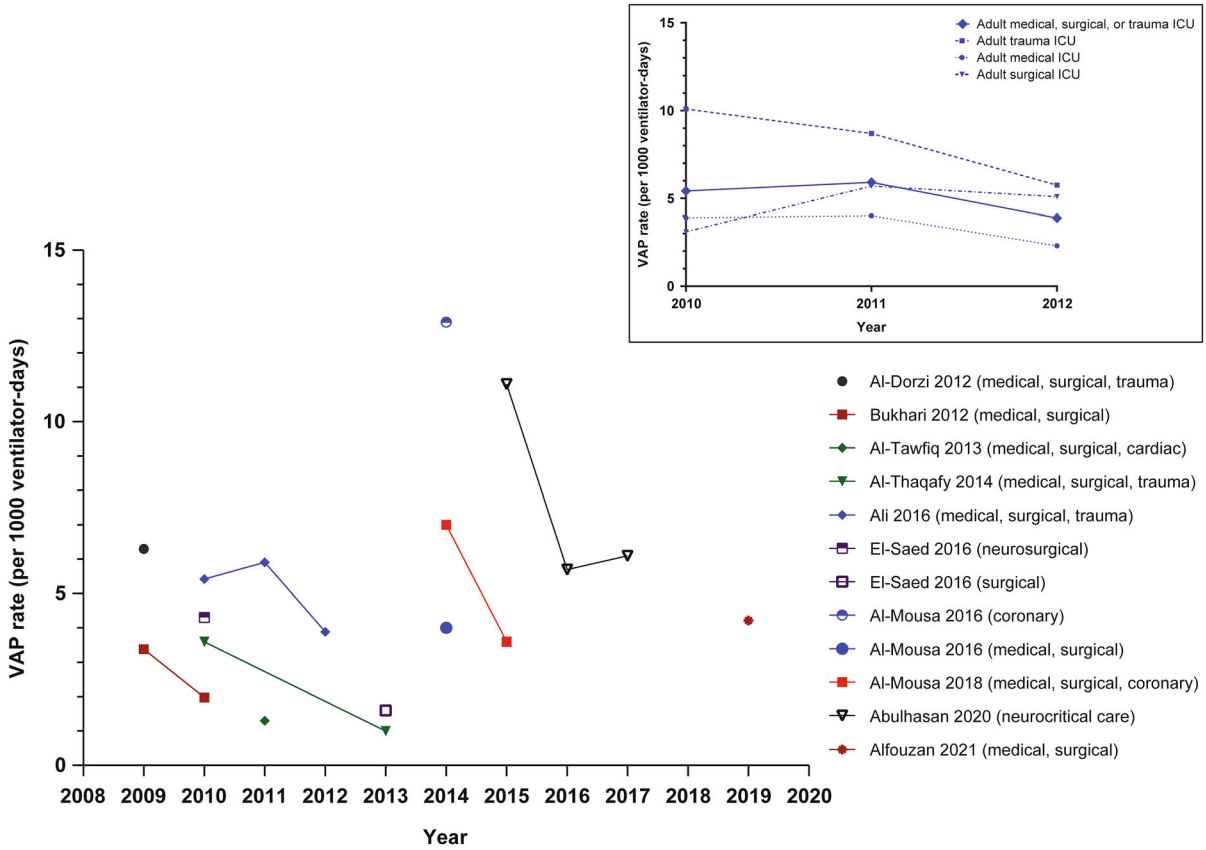

Fig. 2 VAP rates in adult ICUs across GCC countries as reported by various studies included in this review [9, 14, 17–19, 23, 29, 32, 34]. The inset shows ICU type for data from work by Ali et al. (2016), which was the only included study describing rates in a single GCC nation, Qatar [23]. *GCC* Gulf Cooperation Council, *ICU* intensive care unit, *VAP* ventilator-associated pneumonia

Enterococcus [26] and MDR *Enterococcus* species [26, 30] were rarely reported. A study in Saudi Arabia conducted from 2015 to 2018 reported carbapenem-resistant Gram-negative organisms in 25% of all VAP cases [31], while another study from Saudi Arabia from 2016 to 2019 reported 19% [25]. Two studies in Kuwait, one in Qatar, and one in Oman reported extended-spectrum beta-lactamase *K. pneumoniae* (17–32%), *E. coli* (75%), or *Enterobacterales* isolates (24%) [23, 29, 30, 32]. From 2004 to 2009, a tertiary care hospital in Riyadh reported 60–89% resistance to all tested antimicrobials for *Acinetobacter* species and 13–31% for *P. aeruginosa*; *Klebsiella* species were fully resistant to ampicillin and 0–13% were resistant to other tested antimicrobials [27].

Genotype data were sparse in the reviewed studies. One Saudi Arabian study that analyzed 12 extensively drug-resistant (XDR; defined as resistant to at least four classes of antimicrobials, including carbapenems) *A. baumannii* isolates from patients with VAP reported that none of the 12 isolates harbored a class B carbapenemase gene; class A carbapenemase bla_{GES} was detected in 2 out of 12 isolates. Insertion sequence *ISAba1* was detected in 5 out of 12 isolates, all isolates harbored *Acinetobacter*-derived cephalosporinases, and all isolates were carbapenem resistance–associated OM protein negative (i.e., had no evidence of efflux-mediated carbapenemase resistance) [33]. In another study in Saudi Arabia in patients with carbapenem-resistant infections, OXA-48 was the

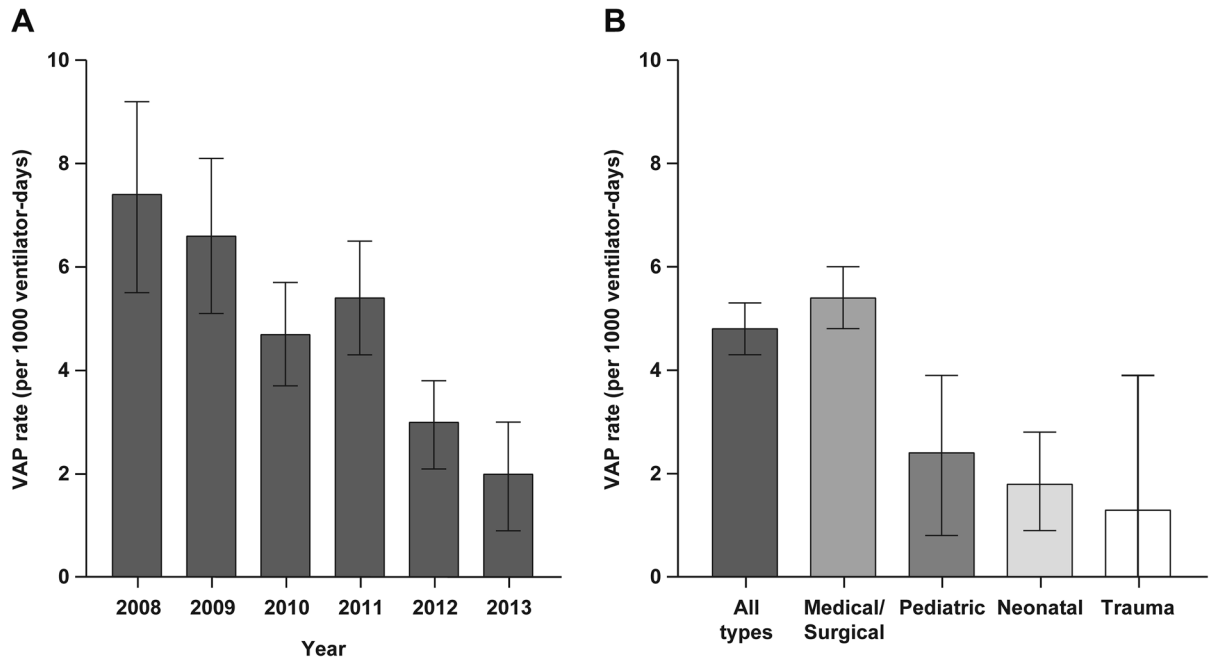

Fig. 3 VAP rates across ICUs in Bahrain, Oman, and Saudi Arabia, 2008–2013, as reported by El-Saed 2016 [9] **A** by year and **B** by ICU type. Note that, for panel **B**, the VAP rate for trauma ICUs is reported for the time period 2010–2013 (not 2008–2013). *ICU* intensive care unit, *VAP* ventilator-associated pneumonia

predominant carbapenemase in ≥ 68% of patients [13].

Ventilator Utilization Ratios

Table 2 shows reported VAP rates and ventilator utilization ratios, which varied widely over time between ICU type and between studies. A study in Kuwaiti patients from 2013 to 2015 reported a utilization rate of 0.9 for adult medical/surgical ICUs and 0.1 for adult coronary ICUs [34]. Another study in Saudi Arabia reported utilization rates of 0.7, 0.6, and 0.2 for adult medical, surgical, and cardiac ICUs, respectively [17], while a study from 2008 to 2013 conducted in Bahrain, Oman, and Saudi Arabia reported rates of 0.5–0.6 across adult ICUs [9]. There was no discernable trend over time in that study, with reported utilization ratios of 0.5 in 2008, 0.6 in 2012, and 0.5 in 2013 [9]. Another study in Saudi Arabia reported a decrease in utilization rates from 0.7 in 2003 to 0.5 in 2009 [14], while a study in Kuwait reported a rate increase from 0.7 to 0.8 in 2014 to 2015 [16].

DISCUSSION

This narrative review was undertaken to summarize available data related to the incidence and causative organisms of HAP and VAP in hospitals throughout GCC countries. Data from multi-year studies suggest that VAP rates have generally decreased over time in GCC countries [16, 18, 19, 23, 32]. Although time-series analyses suggest that VAP prevention bundles reduce VAP rates [9, 14–19], the contribution of individual components is somewhat unclear. A recent review found no high-level evidence to support an association between ventilator bundle implementation and reduced ventilator-associated event (VAE) risk [3]. Indeed, findings suggest that chlorhexidine and stress ulcer prophylaxis may actually increase VAE risk, while reduced mechanical ventilation duration will likely reduce VAE risk [3]. In controlled studies, a significant impact of probiotics on VAP rate has not been observed. These studies include a randomized controlled study carried out in ICUs across North America

Table 1 HAP-/VAP-associated organisms and antimicrobial resistance

Article	Study period	Study population and setting	ICU type	Isolated organisms	Antimicrobial resistance
Saudi Arabia					
Almangour et al., 2021 [45]	May 2015–May 2019	Adults ≥ 18 years treated at two hospitals in Riyadh who developed VAP due to MDR Gram-negative pathogens and who were treated with aerosolized plus IV colistin (n = 65) or IV colistin alone (n = 70)	NOS	MDR Gram-negative MDR *P. aeruginosa* (51%) MDR *A. baumannii* (35%) MDR *K. pneumoniae* (12%)	No colistin-resistant isolates were identified
Mahmoud et al., 2021 [25]	Jul 2016–Sep 2019	Adults > 18 years classified as "comfort care" or "support care" patients and required an infection-related admission to KAMC hospital (Riyadh) during their first year	NA	Gram-negative *Pseudomonas* spp., n = 58 (17%) *Acinetobacter* spp., n = 28 (8%) Gram-positive *S. aureus*, n = 45 (13%)	MDR, 92 of 342 (27%); Carbapenem resistance, 65 of 342 (19%)

Table 1 continued

Article	Study period	Study population and setting	ICU type	Isolated organisms	Antimicrobial resistance
Osman et al., 2020 [31]	Jan 2015–Mar 2018 (pre-bundle, Jan 2015–Feb 2017; post-bundle, Mar 2017–Mar 2018)	Patients aged 1 month to 14 years admitted to pediatric ICU of KAMC hospital, Jeddah, and requiring MV for > 48 h (n = 131)	Pediatric	Gram-negative (pre-bundle; post-bundle) *P. aeruginosa* (36%; 27%) *K. pneumoniae* (12%; 36%) *S. maltophilia* (15%; 9%) *A. baumannii* (12%; 9%) *E. cloacae* (9%; 9%) *E. coli* (6%; 9%) *H. influenzae* (6%; 0%) *Moraxella catarrhalis* (3%; 0%) *Serratia marcescens* (3%; 0%) Gram-positive *S. aureus* (9%; 0%) *S. pneumoniae* (6%; 0%)	Carbapenem-resistant Gram-negative, 11 of 44 (25%) Pre-bundle group (26%) Post-bundle group (18%)
Alsulami et al., 2020 [46]	Nov 2014–Jun 2019	Patients aged 14–84 years who underwent open heart surgery with cardiopulmonary bypass in the surgery department of a single hospital, Jeddah (n = 200)	Surgical	Gram-negative *H. influenzae*, n = 3	NR

Table 1 continued

Article	Study period	Study population and setting	ICU type	Isolated organisms	Antimicrobial resistance
Alraddadi et al., 2019 [13]	Jan–Nov 2017; Dec 2017–Aug 2018 (date ranges were compared since CAZ-AVI was not available until Dec 2017)	Patients > 18 years at a single hospital in Jeddah who had CRE infections: Treated with CAZ-AVI for ≥ 24 h (total *n* = 10; HAP *n* = 5) Treated with other agents (total *n* = 28; HAP *n* = 14)	NA	Gram-negative, CAZ-AVI; comparator *K. pneumoniae*, 7 of 10 (70%); 23 of 28 (82%) *E. coli*, 3 of 10 (30%); 5 of 28 (18%)	Carbapenem resistance (100%)
Alshamrani et al., 2019 [47]	May 2017	All inpatients of all ages at six hospitals in five cities	NA	Gram-negative *Pseudomonas* spp. (19%) *Klebsiella* spp. (19%) *E. coli* (13%) *Acinetobacter* spp. (7%) Gram-positive *S. aureus* (7%)	NR
Alyami et al., 2020 [48]	Jun 2013–May 2019	Patients of all ages infected or colonized by *Chryseobacterium/Elizabethkingia* spp. at Prince Sultan Military Medical City, Riyadh	NOS	Gram-negative *E. meningoseptica,* 22 of 27 (81%) *C. indologenes,* 4 of 27 (15%) Other *Chryseobacterium/Elizabethkingia* spp., 1 of 27 (4%)	NR

Table 1 continued

Article	Study period	Study population and setting	ICU type	Isolated organisms	Antimicrobial resistance
Balkhy et al., 2020 [26]	2008–2016	Patients of all ages diagnosed with DA-HAIs in ICUs of Ministry of National Guard Health Affairs (MNGHA) hospitals in Riyadh, Jeddah, Alhassa, and Dammam	NOS	Gram-negative *Pseudomonas* spp., 20 of 76 (26%) *Acinetobacter* spp., 18 of 76 (24%) *Klebsiella* spp., 10 of 76 (13%) *E. coli,* 6 of 76 (8%) *S. maltophilia,* 4 of 76 (5%) *Enterobacter* spp., 3 of 76 (4%) *Serratia* spp., 2 of 76 (3%) Other, 6 of 76 (8%) Gram-positive *S. aureus,* 2 of 76 (3%) Fungi *Candida* spp., 4 of 76 (5%) Non-candidal yeast, 1 of 76 (1%)	MRSA (50%) MDR *Acinetobacter* spp. (89%) *Pseudomonas* spp. (25%) *Klebsiella* spp. (11%) *Enterobacter* spp. (33%) *E. coli* (17%) *Serratia* spp. (0%) *Stenotrophomonas* spp. (0%)

Table 1 continued

Article	Study period	Study population and setting	ICU type	Isolated organisms	Antimicrobial resistance
Bosaeed et al., 2020 [28]	Jan 2017–Dec 2018	Patients ≥ 18 years diagnosed with MDR *P. aeruginosa* infection and treated with ceftolozane-tazobactam for ≥ 72 h at the KAMC, Riyadh	NOS	MDR Gram-negative *P. aeruginosa, n* = 19	MDR *P. aeruginosa* (HAP/VAP cases): Ceftazidime and ciprofloxacin resistant, 1 of 3 (33%) Amikacin resistant, 1 of 3 (33%)
Hala et al., 2019 [49]	Nov 2017	Adult male patient (mid-60s) admitted with trauma-associated airway obstruction who underwent a percutaneous tracheostomy and developed infection 1 week after surgery	NA	Gram-negative *Klebsiella quasipneumoniae* subspecies *similipneumoniae*	CRE
Abdallah et al., 2018 [12]	Feb–Mar 2017	Male aged 31 years admitted to ICU post-exploratory laparotomy/ thoracotomy with associated chest and laparotomy infections (and further complications of septic shock, acute kidney injury, and internal fixation of broken elbow)	NA	Gram-negative *P. stuartii* *K. pneumoniae* *A. baumannii*	CRE *P. stuartii* *K. pneumoniae* MDR *A. baumannii*

Table 1 continued

Article	Study period	Study population and setting	ICU type	Isolated organisms	Antimicrobial resistance
Al-Abdely et al., 2018 [15]	Sep 2013–Feb 2017	37 adult ICUs in 22 hospitals across 14 cities in Saudi Arabia	NOS	Gram-negative, baseline; intervention *A. baumannii*, 46 of 110 (42%); 169 of 405 (42%) *K. pneumoniae*, 14 of 110 (13%); 51 of 405 (13%) *P. aeruginosa*, 13 of 110 (12%); 61 of 405 (15%) *Acinetobacter* spp., 8 of 110 (7%); 21 of 405 (5%) *E. coli*, 3 of 110 (3%); 14 of 405 (3%) *S. maltophilia*, 0 of 110 (0%); 9 of 405 (2%) Gram-positive, baseline; intervention *S. aureus*, 11 of 110 (10%); 28 of 405 (7%) Fungi, baseline; intervention *C. albicans*, 6 of 110 (5%); 4 of 405 (1%) *Candida* spp., 1 of 110 (1%); 7 of 405 (2%)	NR

Table 1 continued

Article	Study period	Study population and setting	ICU type	Isolated organisms	Antimicrobial resistance
Alessa et al., 2018 [50]	NR	Male African-American nursing home resident aged 79 years (with multiple comorbidities, including end-stage renal disease, receiving intermittent hemodialysis and with history of *P. aeruginosa* airway colonization) who presented to hospital with shortness of breath and potential nasogastric tube misplacement/suspected aspiration pneumonia	NA	Gram-negative *P. aeruginosa*	MDR *P. aeruginosa*
Khan et al., 2016 [51]	Aug 2003–Dec 2010	All patients on MV for > 48 h in the KAMC tertiary care hospital adult ICU, Riyadh (patients with burns, brain death, do-not-resuscitate orders, or transferred from other hospitals were excluded)	Adult	Gram-negative (EO-VAP; LO-VAP) *H. influenzae* (25%; 2%) *P. aeruginosa* (5%; 16%) *A. baumannii* (13%; 18%) *K. pneumoniae* (10%; 5%) *Enterobacter* spp. (6%; 6%) Gram-positive (EO-VAP; LO-VAP) MSSA (11%; 7%) MRSA (5%; 4%) *S. pneumoniae* (8%; 2%)	NR

Table 1 continued

Article	Study period	Study population and setting	ICU type	Isolated organisms	Antimicrobial resistance
Al-Obeid et al., 2015 [33]	Jan–Dec 2012	*A. baumannii* isolates collected from patients at the Security Forces Hospital During 2012, 12 XDR- *A. baumannii* strains were isolated from tracheal samples of ICU patients with serious VAP (mean age 59.2 years)	NOS	Gram-negative *A. baumannii* (100%)	XDR- *A. baumannii* (> 90%)
Shaath et al., 2014 [52]	Mar–Sep 2010	Postoperative cardiac patients aged < 14 years in the pediatric cardiac ICU of KAMC hospital, Riyadh	Pediatric	Gram-negative (33%)	NR
Balkhy et al., 2014 [27]	Oct 2004–Jun 2009	Adult ICU of KAMC tertiary care hospital, Riyadh	Adult	Gram-negative *Acinetobacter* (35%) *P. aeruginosa* (25%) *Klebsiella* spp. (6%) *Enterobacter* spp. (4%) *Haemophilus* spp. (4%) *S. maltophilia* (3%) *E. coli* (2%) Gram-positive *S. aureus* (including MRSA; 17%) Coagulase-neg staphylococci (3%)	MDR *Acinetobacter* spp. (60–89%) 3-class (86%) 4-class (69%) *P. aeruginosa* (13–31%) 3-class (13%) 4-class (10%) *S. aureus* (oxacillin 42%) Coagulase-neg staphylococci (VRE 17%; oxacillin 100%)

Table 1 continued

Article	Study period	Study population and setting	ICU type	Isolated organisms	Antimicrobial resistance
El-Saed et al., 2013 [53]	Aug 2003–Jun 2009	Adult general ICU of KAMC tertiary care hospital, Riyadh	Adult/general	Gram-negative *Acinetobacter* spp. (27%) *P. aeruginosa* (22%) *Klebsiella* spp. (7%) *Haemophilus* spp. (6%) *Enterobacter* spp. (5%) Gram-positive *S. aureus* (15%; 37 of 70 were MRSA)	NR
Bukhari et al., 2012 [19]	Jan–Dec 2010	Patients admitted to the adult medical/surgical ICU at Hera General Hospital, Makkah	Adult	Gram-negative *P. aeruginosa* (31%) *A. baumannii* (28%) *K. pneumoniae* (14%) *E. coli* (8%) Gram-positive MRSA (15%) *S. aureus* (2%)	MDR *A. baumannii* (100%) *P. aeruginosa* (93%) *K. pneumoniae* (83%) MRSA (15%)
Al-Dorzi et al., 2012 [14]	Aug 2003–Jun 2009	Patients admitted to the adult ICU of KAMC hospital in Riyadh who required MV (burn patients and brain death patients were excluded)	General	Gram-negative, 251 of 327 (77%) Gram-positive, 60 of 327 (20%)	NR

Table 1 continued

Article	Study period	Study population and setting	ICU type	Isolated organisms	Antimicrobial resistance
Kuwait					
Alfouzan et al., 2021 [29]	2018, 2019	Patients ≥ 18 years admitted to a surgical/medical ICU at Farwania Hospital, a government secondary-care hospital in Kuwait	General	Gram-negative *A. baumannii,* 9 of 30 (30%) *K. pneumoniae,* 7 of 30 (23%) *P. aeruginosa,* 3 of 30 (10%) *E. coli,* 2 of 30 (7%) *Enterobacter cloacae,* 2 of 30 (7%) *Morganella morganii,* 1 of 30 (3%) *Citrobacter koseri,* 1 of 30 (3%) Gram-positive Methicillin-susceptible *S. aureus,* 1 of 30 (3%)	NR (not specified in patients with HAP/VAP)

Table 1 continued

Article	Study period	Study population and setting	ICU type	Isolated organisms	Antimicrobial resistance
Abulhasan et al., 2020 [32]	Jan 2015–Dec 2017	Patients admitted to the Neurocritical Care Unit of Ibn Sina Hospital, a tertiary care teaching hospital in Kuwait (97% of patients included in the study were aged ≥ 18 years)	Neurocritical	Gram-negative *Klebsiella* spp., 11 of 33 (33%) *E. coli,* 4 of 33 (12%) *P. aeruginosa,* 4 of 33 (12%) *Enterobacter,* 5 of 33 (15%) *A. baumannii,* 1 of 33 (3%) *S. maltophilia,* 1 of 33 (3%) Other *Enterobacteriaceae,* 1 of 33 (3%) Gram-positive *S. aureus,* 5 of 33 (15%) MRSA, 1 of 33 (3%)	NR (not specified for HAP patients)

Table 1 continued

Article	Study period	Study population and setting	ICU type	Isolated organisms	Antimicrobial resistance
Al-Mousa et al., 2018 [16]	Jan 2014–Mar 2015 (baseline period, Jan–Mar 2014; intervention period, Apr 2014–Mar 2015)	Patients admitted to three adult ICUs in two hospitals in Kuwait City	General	Gram-negative (baseline; intervention) *A. baumannii* (58%; 59%) *P. aeruginosa* (8%; 13%) *Stenotrophomonas* spp. (8%; 6%) *K. pneumoniae* (8%; 0%) *Serratia marcescens* (8%; 0%) *Enterobacter* spp. (0%; 6%) *E. coli* (0%; 3%) *Morganella morganii* (0%; 3%) Gram-positive *S. aureus* (8%; 0%) Fungi *Candida* spp. (0%, 9%)	NR

Table 1 continued

Article	Study period	Study population and setting	ICU type	Isolated organisms	Antimicrobial resistance
Oman, Qatar, or UAE					
Sannathimmappa et al., 2021 [30]	Jan 2017–Aug 2019	All bacterial isolates from ET aspirates of ventilated patients (> 95% of sampled patients were aged ≥ 21 years) at a tertiary care ministry hospital in the North-Batinah region, Oman	NOS	Gram-negative *A. baumannii* (31%) *K. pneumoniae* (24%) *P. aeruginosa* (23%) *E. coli* (3%) Other *Enterobacteriaceae* (5%) *S. maltophilia* (2%) Gram-positive *S. aureus* (4%) MRSA (5%) *Streptococcus* spp. (2%) *Enterococcus* spp. (1%)	MDR *A. baumannii* (86%) *K. pneumoniae* (73%) *E. coli* (67%) *P. aeruginosa* (24%) *S. aureus* (53%) *Enterococcus* spp. (50%) ESBL *E. coli,* 3 of 4 (75%) *K. pneumoniae,* 6 of 35 (17%) Carbapenem resistance *K. pneumoniae,* 23 of 35 (66%)

Table 1 continued

Article	Study period	Study population and setting	ICU type	Isolated organisms	Antimicrobial resistance
Ali et al., 2016 [23]	Jan 2010–Dec 2012	All patients ≥ 15 years clinically diagnosed with VAP in three adult ICUs (medical, surgical, and trauma) of Hamad General Hospital, Qatar	General	Gram-negative *Pseudomonas* spp., 39 of 106 (37%) *Klebsiella* spp., 25 of 106 (24%) *Enterobacter* spp., 24 of 106 (23%) *Acinetobacter* spp., 23 of 106 (22%) *Haemophilus* spp., 16 of 106 (15%) *E. coli,* 5 of 106 (5%) *Stenotrophomonas* spp., 4 of 106 (4%) Gram-positive *Staphylococcus* spp., 21 of 106 (20%) *Streptococcus* spp., 5 of 106 (5%)	MDR, 43 of 106 (41%)

Table 1 continued

Article	Study period	Study population and setting	ICU type	Isolated organisms	Antimicrobial resistance
Arumugam et al., 2018 [54]	Jan 2010–Jan 2013	Adult trauma patients admitted to the Trauma Centre of Hamad General Hospital who required intubation (either before hospitalization or in the trauma room) and ventilation (patients with burns, drowning, death, or discharged or those who were transferred to other facilities < 48 h after admission were excluded)	Trauma	Gram-negative (All VAP cases; VAP in PHI; VAP in TRI) *K. pneumoniae* (36%; 22%; 38%) *H. influenzae* (30%; 30%; 29%) *E. cloacae* (12%; 9%; 15%) *P. aeruginosa* (12%; 9%; 15%) *A. baumanii* (7%; 4%; 9%) *Moraxella catarrhalis* (5%; 4%; 6%) *K. oxytoca* (4%; 4%; 3%) *K. ozonae* (5%; 13%; 0%) Gram-positive *S. aureus* (28%; 35%; 24%) *S. pneumoniae* (16%; 13%; 18%)	MDR *A. baumannii*, 1 of 23 (4%) patients intubated before hospitalization *A. baumannii* and *S. aureus,* 2 of 34 (6%) patients intubated on arrival in the trauma room

Table 1 continued

Article	Study period	Study population and setting	ICU type	Isolated organisms	Antimicrobial resistance
Sonnevend et al., 2013 [55]	2009–2011	Clinically relevant NDM-producing carbapenem-resistant *Enterobacteriaceae* isolated from major hospitals in the UAE	NA	Gram-negative *K. pneumoniae,* 3 of 5 (60%) *E. coli,* 2 of 5 (40%)	Carbapenem resistance *K. pneumoniae* (100%) *E. coli* (100%)

CAZ-AVI ceftazidime-avibactam, *CRE* carbapenem-resistant *Enterobacteriaceae*, *DA* device-associated, *ESBL* extended-spectrum β-lactamase, *EO* early onset, *ET* endotracheal, *HAI* hospital-acquired infection, *HAP* hospital-acquired pneumonia, *ICU* intensive care unit, *IV* intravenous, *KAMC* King Abdulaziz Medical City, *LO* late onset, *MDR* multidrug-resistant, *MIC* minimum inhibitory concentration, *MRSA* methicillin-resistant *S. aureus*, *MSSA* methicillin-sensitive *S. aureus*, *MV* mechanical ventilation, *NA* not applicable, *NDM* New Delhi metallo-beta-lactamase, *NOS* not otherwise specified, *NR* not reported, *PHI* prehospital intubation, *TRI* trauma room intubation, *UAE* United Arab Emirates, *VAP* ventilator-associated pneumonia, *XDR* extensively drug-resistant

Table 2 Reported VAP rates and ventilator utilization ratios—all ICU types

Source	City/country	ICU type	Year(s)	VAP definition used	VAP rate[a]	Ventilator utilization ratio[b]
Al-Dorzi et al., 2012 [14]	Riyadh, Saudi Arabia	Adult medical, surgical, trauma	2003	US CDC criteria	19.1	0.7
			2009		6.3	0.5
			2003–2009		15.9	0.6
Bukhari et al., 2012 [19]	Makkah, Saudi Arabia	Adult medical, surgical	2009	Pneumonia in a patient intubated and ventilated at the time of, or ≤ 48 h before the onset of the event	3.4	NR
			2010		2.0	NR
Al-Tawfiq et al., 2013 [17]	Dhahran, Saudi Arabia	Adult medical, surgical, cardiac	2004	MV with chest X-ray showing new or progressive infiltrate, consolidation, cavitation, or pleural effusion	9.8	NR
			2011		1.3	NR
			2004–2011		4.5	NR
		Adult medical	2004–2011		5.0 (0.4–9.4)	0.7 (0.6–0.7)
		Adult surgical	2004–2011		4.9 (2.1–8.4)	0.6 (0.5–0.7)
		Adult cardiac	2004–2011		1.9 (0–3.7)	0.2 (0.2–0.3)
Al-Thaqafy et al., 2014 [18]	Riyadh, Saudi Arabia	Adult medical, surgical, trauma	2010	US CDC/NHSN criteria	3.6	0.7
			2013		1.0	0.6
Shaath et al., 2014 [52]	Riyadh, Saudi Arabia	Pediatric cardiac (postcardiac surgery patients)	2010	US CDC criteria	29.0	0.3

Table 2 continued

Source	City/country	ICU type	Year(s)	VAP definition used	VAP rate[a]	Ventilator utilization ratio[b]
Ali et al., 2016 [23]	Doha, Qatar	Adult medical, surgical, trauma	2010	US CDC criteria	5.4	NR
			2011		5.9	NR
			2012		3.9	NR
		Adult medical	2010		3.9	NR
			2011		4.0	NR
			2012		2.3	NR
		Adult surgical	2010		3.1	NR
			2011		5.7	NR
			2012		5.1	NR
		Adult trauma	2010		10.1	NR
			2011		8.7	NR
			2012		5.8	NR
Al-Mousa et al., 2016 [34]	Kuwait City, Kuwait	Adult medical, surgical	Nov 2013–Mar 2015	US CDC/NHSN criteria	4.0 (2.9–5.3)	0.9 (0.9–0.9)
		Adult coronary	Nov 2013–Mar 2015		12.9	0.1 (0.1–0.1)
		Pediatric	Nov 2013–Mar 2015		0.3 (0.2–4.6)	0.7 (0.7–0.7)
		Neonatal	Nov 2013–Mar 2015		1.0	0.5 (0.4–0.5)

Table 2 continued

Source	City/country	ICU type	Year(s)	VAP definition used	VAP rate[a]	Ventilator utilization ratio[b]
El-Saed et al., 2016 [9]	Bahrain, Oman, and Saudi Arabia	Medical/surgical, neurosurgical, surgical, trauma, pediatric, pediatric cardiothoracic, and neonatal	2008–2013	NHSN criteria	4.8 (4.3–5.3)	0.6 (0.6–0.6)
			2008		7.4 (5.5–9.2)	0.5 (0.5–0.5)
			2009		6.6 (5.1–8.1)	0.6 (0.6–0.6)
			2010		4.7 (3.7–5.7)	0.6 (0.6–0.6)
			2011		5.4 (4.3–6.5)	0.6 (0.6–0.6)
			2012		3.0 (2.1–3.8)	0.6 (0.6–0.6)
			2013		2.0 (0.9–3.0)	0.5 (0.5–0.5)
		Medical/surgical	2008–2013		5.4 (4.8–6.0)	0.6 (0.6–0.6)
		Pediatric	2008–2013		2.4 (0.8–3.9)	0.5 (0.5–0.5)
		Neonatal	2008–2013		1.8 (0.9–2.8)	0.3 (0.3–0.3)
		Trauma	2010–2013		1.3 (0.0–3.9)	0.6 (0.6–0.6)
		Neurosurgical	2010		4.3 (0.1–8.5)	0.6 (0.6–0.6)
		Pediatric cardiothoracic	2010		3.5 (0.1–7.0)	0.6 (0.6–0.6)
		Surgical	2013		1.6 (0.0–4.8)	0.5 (0.4–0.5)

Table 2 continued

Source	City/country	ICU type	Year(s)	VAP definition used	VAP rate[a]	Ventilator utilization ratio[b]
Banjar et al., 2017 [20]	Makkah region, Saudi Arabia	Adult, surgical, coronary care, pediatric, and neonatal	2013	NR	6.9[c] (IQR, 3.6–10.3)	NR
	Makkah, Makkah, Saudi Arabia	Not specified	2013		6.4[c] (IQR, 3.2–8.2)	NR
	Jeddah, Makkah, Saudi Arabia	Not specified	2013		8.8[c] (IQR, 4.6–20.2)	NR
	Taif, Makkah, Saudi Arabia	Not specified	2013		6.1[c] (IQR, 3.6–11.6)	NR
	Qunfudah, Makkah, Saudi Arabia	Not specified	2013		4.4[c] (IQR, 0.6–6.3)	NR
Al–Mousa et al., 2018 [16]	Kuwait City, Kuwait	Adult medical/surgical, coronary	Jan–Mar 2014	US CDC/NHSN criteria	7.0 (3.8–11.8)	0.7
			Apr 2014–Mar 2015		3.6 (2.5–5.0)	0.8

Table 2 continued

Source	City/country	ICU type	Year(s)	VAP definition used	VAP rate[a]	Ventilator utilization ratio[b]
Gaid et al., 2018 [56]	Provinces of Asser, Jeddah, Riyadh, and Qassim, Saudi Arabia	Adult medical/surgical	May 2015–Feb 2016	NR	18.1–26.6	0.5 (0.5–0.6)
	Provinces of Asser and Taif, Saudi Arabia	Adult medical/surgical	Sep 2013–Mar 2015		9.3–20.7	0.3 (0.3–0.3)
	Provinces of Najran and Tabuk, Saudi Arabia	Adult medical/surgical	Sep 2013–Feb 2016		0.9–16.4	0.7 (0.6–0.7)
	Provinces of Taif, Hail, and Madina, Saudi Arabia	Adult medical/surgical	Sep 2015–Mar 2016		10.1–51.6	0.9 (0.9–1.0)
	Province of Riyadh, Saudi Arabia	Adult medical/surgical	Jan 2015–Feb 2016		186.5	0.1 (0.04–0.1)
Abulhasan et al., 2020 [32]	Kuwait	Neurocritical care (97% adult patients)	2015	US CDC/NHSN criteria	11.1	0.4
			2016		5.7	0.2
			2017		6.1	0.4
Ahmed et al., 2021 [57]	Riyadh, Saudi Arabia	Not specified (60-bed hospital)	2019	US CDC criteria	2.1	NR

Table 2 continued

Source	City/country	ICU type	Year(s)	VAP definition used	VAP rate[a]	Ventilator utilization ratio[b]
Alfouzan et al., 2021 [29]	Kuwait	Adult medical/surgical	2018, 2019	Pneumonia in a patient on MV for > 2 days on the date of event	4.2	0.7

CI confidence interval, *ICU* intensive care unit, *IQR* interquartile range, *MV* mechanical ventilation, *NHSN* National Healthcare Safety Network, *NR* not reported, *US CDC* US Centers of Disease Control and Prevention, *VAP* ventilator-associated pneumonia

[a]Per 1000 ventilator-days (where provided, error is 95% CI, unless otherwise indicated)

[b]Ventilator utilization ratio is the number of ventilator days/number of patient days (where provided, error is 95% CI)

[c]Median value

and Saudi Arabia to assess the effect of the probiotic *Lactobacillus rhamnosus* GG on VAP development in critically ill patients. Results of the study showed no significant difference in VAP incidence between the probiotic and placebo groups, or for any of the other prespecified outcomes [35].

Additionally, our literature review suggests that the most common organisms associated with VAP in GCC countries were Gram-negative bacteria, particularly *Acinetobacter* species, *Pseudomonas* species, and *Klebsiella* species, as well as *Enterococcus* species, with MDR reported in many studies. The types of organisms associated with HAP/VAP and the proportions of positive isolates were similar between the countries studied (Saudi Arabia, Kuwait, and Oman; Qatar; or UAE). *E. coli* and *P. aeruginosa* were present in up to approximately 40% of isolates, and *A. baumannii* and *K. pneumoniae* were isolated from > 50% of isolates in at least one of the included studies.

Our analysis also found a wide range of ventilator utilization ratios, with higher ratios increasing the likelihood of developing VAP. Thus, ventilator utilization ratio may be a useful outcome measure in VAP prevention studies [18]. However, ventilator utilization ratios are necessarily higher in certain patient populations (e.g., very-low-birth-weight infants, patients with chronic obstructive pulmonary disease); therefore, it may be misleading to compare ratios across different hospitals/facilities due to differences in patient populations [36].

Infection prevention programs commonly incorporate multimodal horizontal strategies that aim to reduce risk from all nosocomial pathogens, such as hand hygiene protocols, environmental disinfection, and prevention bundles [37, 38]. Internationally, many organizations have developed VAP prevention guidelines and tools, and VAP bundles have been widely implemented in hospitals [39–41]. While infection control and surveillance in GCC countries is coordinated by the GCC-CIC and evidence-based guidelines for infection control practices have been provided by the organization [9], local differences in antimicrobial policies and antimicrobial stewardship programs may exist [42]. Substantial variability has been noted among the VAP bundles adopted by different hospitals in other countries, although utilized components frequently include head-of-bed elevation by 30–45°, daily interruption of sedation and assessment of readiness to extubate, use of endotracheal tubes with subglottic secretion drainage ports, and avoidance of

ventilator circuit changes unless visible soiling is present [40, 41]. The INICC Multidimensional Approach for VAP rate reduction incorporates multiple strategies: a VAP prevention bundle; education; outcome and process surveillance; and provision of feedback related to VAP rates, VAP consequences, and performance [34]. VAP data also constitute part of the performance dashboard of hospital infection prevention and control committees.

A limitation of this analysis is that the data were compiled from different and diverse healthcare organizations and laboratories, which have variations in definitions and diagnostic limitations, as well as differing methodologies and technologies used in the detection, speciation, and susceptibility testing of isolated organisms from patients with VAP [3]. An illustration of this variation is the implementation of the VAE model by the US National Healthcare Safety Network (NHSN) in 2013 [43], which resulted in a large difference in reported VAP incidences between the USA and Europe [3]. Further evidence of these variations and the limitations they place on these data analyses was found in the surveillance of device-associated HAIs in ICUs across the INICC, which showed that pooled mean VAP rates ranged from 7.4 to 17.7 per 1000 ventilator-days depending on ICU type. These were considerably higher than 2012/2013 US NHSN pooled means (0.7–3.6 per 1000 ventilator-days) [5]. Accordingly, comparison of national VAP rates with the USA has been cautioned against due to varying classifications. Also, studies evaluating the effect of prevention bundles on VAP rates may be difficult to generalize to the overall population. This paper is a review of different retrospective studies, and thus, generalization of the impact of prevention bundles is difficult due to missing data since, generally, most papers were not studying prevention bundles and a few studies correlated bundle implementation with VAP rates. Another limitation of the current review is that all of the included studies were conducted before the onset of the coronavirus disease 2019 (COVID-19) pandemic and, therefore, do not take into consideration the likely increases in VAP rates [44].

CONCLUSIONS

Although VAP rates have generally decreased over time in GCC countries, VAP and associated MDR organisms remain a burden. Overall, there is a need for further research, including prospective, randomized, multicenter studies carried out in the Gulf Region, to assess the diagnosis, prevention, and treatment of VAP. Research should also include details of bundles used to reduce VAP incidence, protocols of care, and toolkits used to carry out root-cause analysis on VAP infections. Furthermore, it would be useful to have an overarching multi-Gulf center surveillance program to continually monitor the incidence and prevalence of VAP and HAP and, indeed, other HAIs across the GCC countries.

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