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Pathogen Burden and Antimicrobial Resistance Patterns in Hospital Acquired Pneumonia in Saudi Arabia: A Systematic Review

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Abstract **Background:** Hospital-Acquired Pneumonia (HAP) and Ventilator-Associated Pneumonia (VAP) are major causes of morbidity, mortality and antimicrobial use in intensive care settings, particularly where Multidrug-Resistant (MDR) organisms are prevalent. Saudi Arabia has reported increasing resistance among Gram-negative pathogens; however, national evidence on pathogen distribution and resistance trends in HAP/VAP remains fragmented. This systematic review synthesizes available data on pathogen burden and Antimicrobial Resistance (AMR) patterns in HAP and VAP across Saudi hospitals. **Methods:** The review followed PRISMA guidelines. Electronic databases (PubMed, Scopus, Web of Science, Google Scholar) were searched for studies conducted in Saudi Arabia reporting microbiological profiles and/or antimicrobial susceptibility in HAP or VAP. Eligible studies included original research using defined diagnostic criteria and reporting pathogen distribution and/or resistance data. Risk of bias was assessed using the Joanna Briggs Institute checklist and the Newcastle-Ottawa Scale. **Results:** Eleven studies met inclusion criteria, spanning adult, pediatric and mixed ICU populations. Gram-negative bacilli predominated across all settings. The most frequent pathogens were *Acinetobacter baumannii*, *Pseudomonas aeruginosa* and *Klebsiella pneumoniae*, with MRSA representing the principal Gram-positive contributor. Five studies reported quantitative antimicrobial susceptibility data. Across these studies, carbapenem resistance among *Acinetobacter baumannii* isolates consistently exceeded 90%, while *Klebsiella pneumoniae* demonstrated high resistance to β-lactam antibiotics. Resistance patterns among *Pseudomonas aeruginosa* were variable across settings. Colistin generally retained activity against most isolates, although emerging resistance was reported in some centers. Overall, MDR and XDR phenotypes were common, particularly in ICU environments. **Conclusion:** Available evidence from Saudi tertiary-care hospitals suggests that HAP/VAP is predominantly caused by multidrug-resistant Gram-negative pathogens, with *A. baumannii* and *K. pneumoniae* representing the most critical therapeutic challenges. The available evidence indicates increasing carbapenem resistance and early reports of declining colistin susceptibility among selected centers highlight the urgent need for standardized national surveillance, antimicrobial stewardship and strengthened infection-prevention strategies. Coordinated molecular monitoring and optimized empirical therapy are essential to mitigate resistance escalation in Saudi critical-care settings.

Key Words Hospital-Acquired Pneumonia, Ventilator-Associated Pneumonia, Antimicrobial Resistance, Gram-Negative Bacilli, Multidrug Resistance, Saudi Arabia

INTRODUCTION

Hospital-Acquired Infections (HAIs) continue to be a significant contributor to patient morbidity, mortality and healthcare costs in Intensive Care Units (ICUs). The high prevalence, complex etiology and frequent association with Multidrug-Resistant (MDR) organisms of Hospital-Acquired Pneumonia (HAP) and Ventilator-Associated Pneumonia (VAP) are among the most significant of these. VAP develops after a minimum of 48 hours of mechanical ventilation, whereas HAP is an infection of the pulmonary parenchyma that develops at least 48 hours after hospital admission [1,2]. In critically ill patients, both conditions are acknowledged as the second most prevalent nosocomial infections and the primary causes of death from hospital-associated infections [2]. Worldwide, Hospital-Acquired Pneumonia (HAP) and Ventilator-Associated Pneumonia

(VAP) continue to be significant contributors to morbidity, mortality and healthcare expenditures. In intensive care settings, these infections are particularly difficult to treat due to the facilitation of colonization and infection by opportunistic and multidrug-resistant organisms by invasive devices like endotracheal tubing. Based on global data, it is estimated that up to 27% of mechanically ventilated patients develop VAP, which accounts for a significant portion of antibiotic prescriptions in intensive care units [3].

HAP occurs in 5 to more than 20 cases per 1000 hospital admissions, with immunocompromised, surgical and geriatric groups being at highest risk. HAP and VAP have a diverse microbial etiology, with gram-negative organisms such as *Acinetobacter baumannii*, *Pseudomonas aeruginosa*, *Klebsiella pneumoniae* and Escherichia coli predominating but gram-positive pathogens such as Methicillin-Resistant *Staphylococcus aureus* (MRSA) also play an important role [4,5]. Similarly, 54% of intensive care unit patients were infected, with gram-negative bacteria making up 67% of infections, primarily in Asia and the Middle East, according to the third international surveillance study (EPIC) [5].

Approximately 9-27% of patients on mechanical ventilation will experience Ventilator-Associated Pneumonia (VAP). Community-acquired infections such *Staphylococcus aureus*, *Haemophilus influenzae* and *Streptococcus pneumoniae* are commonly associated with early-onset VAP. On the other hand, opportunistic Gram-negative bacteria such *Klebsiella pneumoniae*, *Pseudomonas aeruginosa* and *Acinetobacter baumannii* are typically linked to late-onset VAP [2,6,7]. Cases caused by *Pseudomonas* or *Acinetobacter* species have an exceptionally high mortality rate and when the wrong empiric therapy is given, the rate can go up to 70% [2,8].

One of the most pressing challenges to global public health is antimicrobial resistance (AMR). Every year, resistant diseases kill millions of people and if nothing is done about them, the worldwide economic cost could exceed USD 100 trillion by 2050 [9]. In Saudi Arabia, the problem is made worse by a lot of people abusing antibiotics. Reports show that between 41 and 92% of prescriptions are wrong [10]. As a result, the Kingdom is experiencing a significant increase in resistance rates, with reports emphasizing the advent of extensively drug-resistant (XDR) and multidrug-resistant (MDR) strains, particularly among *Acinetobacter* and *Pseudomonas* species [11-15].

The risk of nosocomial pneumonia-related microbial resistance increases with length of stay in the Intensive Care Unit (ICU), history of exposure to broad-spectrum antibiotics and invasive medical procedures. MDR infections are closely linked to the use of mechanical ventilation for a period of seven days or more, the use of antibiotics in the past and the use of broad-spectrum medicines in the past [2]. When it comes to determining the appropriate therapy for suspected HAP or VAP, our findings underline the importance of doing an evaluation of the local microbiological epidemiology and resistance patterns.

Non-fermenting Gram-negative bacteria, including *Pseudomonas* spp., *Acinetobacter* spp. and *Stenotrophomonas maltophilia*, are acknowledged as significant contributors to healthcare-associated infections in Saudi ICUs. There has been a concerning rise in carbapenem resistance in *Acinetobacter baumannii* and *Pseudomonas aeruginosa* and there is also an emergence of resistance to tigecycline, aminoglycosides and trimethoprim/sulfamethoxazole [11,12]. *Klebsiella pneumoniae* strains that produce Extended-Spectrum β-Lactamases (ESBLs) and carbapenem-resistant isolates are increasingly documented and constitute a significant problem identified by the World Health Organization. Penicillin-non susceptible forms of *S. pneumoniae*, with resistance rates reaching 31% in Saudi Arabia, exacerbate the existing burden [16].

Given the substantial clinical burden of HAP and VAP and the growing threat of antimicrobial resistance in Saudi Arabia, a comprehensive assessment of pathogen distribution and resistance patterns is needed. This systematic review aimed to synthesize available evidence on the microbiological epidemiology of HAP and VAP in Saudi Arabia and to summarize reported antimicrobial resistance patterns among the most commonly isolated pathogens.

METHODS

Protocol and Reporting

The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines were followed to in the conduct and reporting of this systematic review [17]. Although the review protocol was developed before study initiation, this systematic review was not prospectively registered in PROSPERO or any other review registry.

Criteria for Eligibility

Inclusion: Original studies published in English that were conducted in Saudi Arabia and report the distribution of pathogens and/or antimicrobial susceptibility in patients with ventilator-acquired pneumonia and hospital-acquired pneumonia. The studies that utilized standardized or clearly defined diagnostic criteria for HAP or VAP and provided microbiological data on pathogen distribution and/or antimicrobial susceptibility and resistance patterns.

Exclusion criteria include Community-Acquired Pneumonia (CAP)-only studies, reviews, editorials, case reports, case series and studies without microbiological or antibiotic resistance data.

Search Strategy

A comprehensive literature search was conducted in PubMed, Scopus, Web of Science and Google Scholar from database inception until December 31, 2022. The final search was performed on January 15, 2023. Search terms combined controlled vocabulary and free-text keywords related to hospital-acquired pneumonia, ventilator-associated pneumonia, antimicrobial resistance, pathogen distribution and Saudi Arabia. Boolean operators (AND/OR) were used as appropriate. The complete database-specific search strategies are provided in Supplementary Table S1. For Google Scholar, the first 200 records sorted by relevance were screened. Reference lists of all eligible studies were also manually searched to identify additional relevant publications.

Study Selection

Two reviewers separately evaluated titles and abstracts according to the eligibility requirements. Complete manuscripts of potentially pertinent studies were obtained and evaluated thoroughly. Discrepancies among reviewers were reconciled through consensus or by consulting a third reviewer. In cases where an article was found in multiple databases, only the search yielding the most pertinent information was used.

Data Extraction

Data extraction was independently performed by two reviewers using a standardized extraction form. Extracted information included study characteristics (author, year, setting, study design and sample size), patient population, diagnostic criteria for HAP/VAP, microbiological findings, pathogen distribution, antimicrobial susceptibility results and reported multidrug-resistant or extensively drug-resistant phenotypes. Any discrepancies between reviewers were resolved through discussion and consensus. A third reviewer was available to adjudicate unresolved disagreements.

Risk of Bias Assessment

Two reviewers independently assessed the methodological quality of the included studies using standardized design-specific appraisal tools. Any disagreements were resolved through discussion and consensus, with a third reviewer available for adjudication when necessary.

The Joanna Briggs Institute (JBI) Critical Appraisal Checklist [18] for Prevalence Studies was used to assess cross-sectional, surveillance and prevalence-based studies [1,20-28], whereas cohort and case-control studies [11,25,27] were evaluated using the Newcastle-Ottawa Scale (NOS) [19]. The results of the quality assessment are summarized in Table 1.

Of the three studies assessed using the Newcastle-Ottawa Scale, one study [27] achieved a score of 9/9 and was considered to be of high methodological quality. The remaining two studies [11,25] scored 6/9 and were classified as fair quality, mainly due to limitations in comparability between study groups and incomplete reporting of outcome assessment procedures.

Overall, the included studies were judged to have a low to moderate risk of bias. Prospective surveillance studies generally demonstrated stronger methodological quality, whereas retrospective studies were more susceptible to confounding and reporting limitations. Although the overall quality of the available evidence was considered sufficient to support the findings of this review, the predominance of observational, single-center studies warrants cautious interpretation of the results. Future well-designed multicenter studies employing standardized methodologies and improved control of potential confounding factors are needed to strengthen the evidence base.

Due to the substantial methodological heterogeneity among the included observational studies and the narrative

Table 1: Risk of Bias

Study Setting	Study Design	Tool Applied	Individual Domain Scores	Total Score	Risk of Bias
El-Saed *et al.* [20] (Riyadh ICU Surveillance)	Prospective surveillance	JBI Prevalence Checklist	All 9 domains scored 1	9/9	Low
Al-Dorzi *et al.* [21] (Riyadh MSICU)	Prospective cohort surveillance	JBI Prevalence Checklist	All 9 domains scored 1	9/9	Low
Almuneef *et al.* [1] (Riyadh PICU)	Prospective observational	JBI Prevalence Checklist	All 9 domains scored 1	9/9	Low
Al-Obeid *et al.* [11] (Riyadh SFH)	Laboratory-based cohort (molecular study)	Newcastle-Ottawa Scale (NOS)	Selection 3/4, Comparability 1/2, Outcome 2/3	6/9	Fair
Saleem *et al.* [22] (Hail ICU)	Prospective molecular prevalence	JBI Prevalence Checklist	Representativeness 1, Sample size 1, Diagnosis 1, Criteria 1, Reliability 1, Analysis 1, Confounders 0, Bias 0, Clarity 1	7/9	Moderate
Kabrah *et al.* [23] (Makkah ICU)	Retrospective cross-sectional	JBI Prevalence Checklist	Representativeness 1, Sample size 1, Validity 1, Criteria 1, Reliability 1, Analysis 1, Confounders 0, Bias 0, Clarity 1	7/9	Moderate
Ibrahim [24] (Bisha ICUs)	Retrospective surveillance	JBI Prevalence Checklist	Representativeness 1, Sample size 1, Reliability 1, Criteria 1, Validity 1, Analysis 1, Confounders 0, Bias 0, Clarity 1	7/9	Moderate
Othman and Abdelazim [25] (Dhahran ICU)	Prospective case-control	Newcastle-Ottawa Scale (NOS)	Selection 3/4, Comparability 1/2, Outcome 2/3	6/9	Fair
Balkhy *et al.* [26] (Riyadh NGHA survey)	Point prevalence (cross-sectional)	JBI Prevalence Checklist	All 9 domains scored 1	9/9	Low
Akbar [27] (Jeddah KAUH)	Retrospective cohort	Newcastle-Ottawa Scale (NOS)	Selection 4/4, Comparability 2/2, Outcome 3/3	9/9	Good
Hakami *et al.* [28] (Jeddah MNGHA)	Retrospective cross-sectional	JBI Prevalence Checklist	Representativeness 1, Sample size 1, Diagnosis 1, Criteria 1, Reliability 1, Analysis 1, Confounders 0, Bias 0, Clarity 1	7/9	Moderate

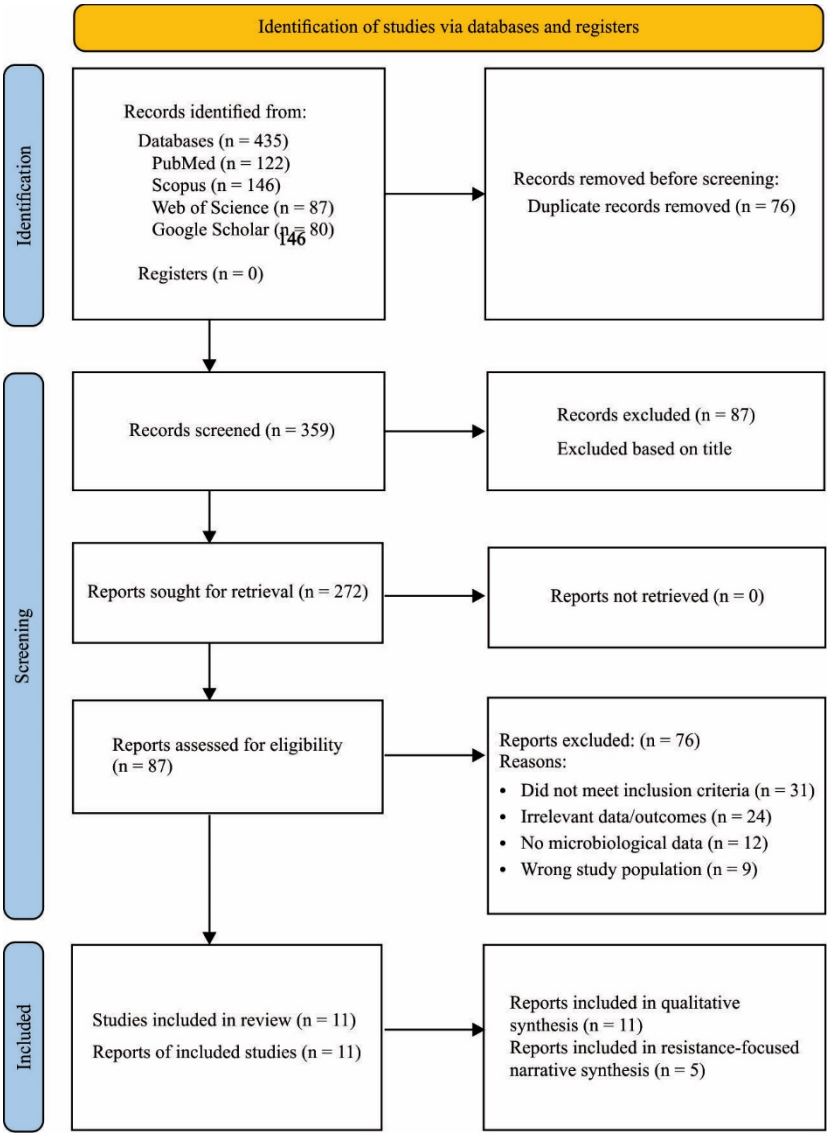

Figure 1: Flowchart for Studies Selection According to the Criteria

nature of the evidence synthesis, an overall certainty-of-evidence assessment using the GRADE approach was not performed (Figure 1).

PRISMA 2020 Study Selection Flow

A total of 435 records were identified through the database search. After removal of 76 duplicate records, 359 unique records remained for title and abstract screening. Following the initial screening, 272 records were excluded because they did not meet the inclusion criteria or were not relevant to the review question. Consequently, 87 full-text articles were assessed for eligibility. Of these, 76 articles were excluded for reasons including failure to meet the inclusion criteria, absence of microbiological data, inappropriate study population or insufficient outcome reporting. Ultimately, 11 studies fulfilled the eligibility criteria and were included in the qualitative synthesis. Among these, five studies provided detailed quantitative antimicrobial susceptibility data and were incorporated into the resistance-focused narrative synthesis.

Owing to substantial clinical, methodological and microbiological heterogeneity across the included studies, including differences in patient populations, diagnostic criteria, antimicrobial susceptibility testing methods and reported outcomes, a formal meta-analysis was considered inappropriate. Therefore, findings were synthesized narratively.

RESULTS

Riyadh, KAMC Adult ICU [20]

This is one of the first systematic VAP datasets in Saudi Arabia. It includes 2812 ventilated patients (433 with VAP) at King Abdulaziz Medical City in Riyadh and is part of a big prospective ICU surveillance. Pathogens found in

327 samples were mostly *Acinetobacter baumannii* (26.5%), *Pseudomonas aeruginosa* (21.7%), *Staphylococcus aureus* (15.3%) and *Klebsiella pneumoniae* (6.8%). The presence of mostly non-fermenting Gram-negative bacilli is due to the high antibiotic pressure in the ICU and the long length of mechanical ventilation.

Riyadh, KAMC MSICU [21]

Documenting 433 VAP cases among 2812 ventilated patients, this six-year ICU surveillance (2003-2009) was conducted at the same tertiary center but with an emphasis on infection control interventions. Polymicrobial infections were observed in 14.1% of the isolates, while Gram-negative organisms comprised 76.8% of the total. Acinetobacter, Pseudomonas and Klebsiella were the most prevalent bacteria, despite the absence of specific bacterial percentages. The study confirmed the dominance of Gram-negative bacteria and emphasized the significance of preventive bundles in the reduction of VAP incidence.

Riyadh, KAMC PICU [1]

The results of a significant pediatric prospective study that included 361 children who were ventilated showed that 37 of them (10.2%) had ventilator-associated pneumonia (VAP). In terms of the percentage of isolates, the most common was *Pseudomonas aeruginosa*, which accounted for 56.8%. *Staphylococcus aureus* came in second with 18.9%, followed by other Gram-negative bacilli with 24.3%. The results of this analysis showed that the majority of cases of ventilator-associated pneumonia in children and adolescents were Gram-negative, just like the majority of cases seen in adults, albeit with a higher prevalence of Pseudomonas.

Jeddah, KAUH [27]

A retrospective analysis that separates HAP from CAP in adult pneumonia patients with diabetes and those without (354 cultures). A significant proportion of HAP was composed of Gram-negative bacilli, including Klebsiella, Pseudomonas, Enterobacter, E. coli and Acinetobacter. On the other hand, the majority of CAP was composed of H. influenzae. The presence of *S. aureus* was responsible for at least 14-16% of HAP cases. This preliminary analysis found a correlation between diabetes and the variety of pathogens as well as differences in the outcomes of pneumonia.

Riyadh NGHA [26]

A national point-prevalence survey of 562 patients found 45 hospital-acquired illnesses, including 13 cases of VAP. Another bacterium that was found a lot was *Pseudomonas aeruginosa* (21.3%). It was followed by Enterococcus species (16.9%), *S. aureus* (13.5%) and Klebsiella species (10.1%). Forty percent of the *S. aureus* samples were MRSA. The data showed that MRSA was common early on and that Gram-negative bacteria were most common but they weren't just for respiratory infections.

King Fahd Military Complex [25]

A specific case-control study included 48 ventilated people, of whom 17 (35.4%) acquired ventilator-associated pneumonia (VAP). *Pseudomonas aeruginosa* predominated at 41%, succeeded by *Klebsiella pneumoniae*, *Staphylococcus aureus* and Escherichia coli. The occurrence of VAP was significantly correlated with an extended ICU stay and prolonged ventilation (>10 days). Despite the absence of AST data, this cohort established a direct correlation between pathogen dispersion and outcomes as well as risk factors.

Antibiotic Resistance and Susceptibility Pattern

Only five of the eleven studies reviewed provided quantitative antimicrobial susceptibility data (% resistance or susceptibility) that could be aggregated or compared. The majority of the bacteria that are covered by these datasets include *Acinetobacter baumannii*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa* and *Staphylococcus aureus*. These datasets allow for meta-estimation across carbapenems and colistin.

Riyadh Security Forces Hospital [11]

This genetic analysis examined twelve *Acinetobacter baumannii* isolates from intensive care unit patients with ventilator-associated pneumonia (VAP). A pattern of extensively drug-resistant (XDR) was identified through molecular and phenotypic characterization (Table 2-3).

All isolates were 100 percent resistant to carbapenems (imipenem, meropenem), third-generation cephalosporins (ceftazidime) and fluoroquinolones (ciprofloxacin). Tigecycline and gentamicin maintained partial susceptibility, while colistin was the sole antibiotic that remained entirely active (0% resistance). The results are among the earliest documented Saudi reports to confirm the presence of XDR *A. baumannii* in critical care settings. The authors concluded that carbapenemase-mediated resistance mechanisms were likely the cause, which underscores the imperative need for molecular surveillance and antibiotic restriction in ICU environments.

Hail Intensive Care Unit [22]

The 82 strains of *A. baumannii* that were collected from VAP patients at King Khalid Hospital in Hail were the subject of this prospective investigation, which took place between the years 2019 and 2020. The results showed that carbapenems (imipenem, meropenem) were not effective against *A. baumannii* at all during both years. This confirms that carbapenem-resistant *A. baumannii* has been widely spread. More worrying was the rise in colistin resistance, which went from 0% in 2019 to 8.6% in 2020. This was an early sign of colistin-resistant traits in northern Saudi Arabia. Molecular screening found blaIMP, blaVIM and blaNDM-1 genes in most of the isolates. This confirmed that production of metallo-β-lactamase is the main way that bacteria are

Table 2: Characteristics of Studies Included

Study	Setting	Timeframe	Population	Samples	HAP/VAP focus	Top pathogens
El-Saed *et al.* [20]	Riyadh-KAMC Adult ICU	2003-2009	Adult ICU	2812 ventilated; 433 VAP; 327 isolates	VAP	*Acinetobacter* 26.5%, *P. aeruginosa* 21.7%, *S. aureus* 15.3%, *Klebsiella* 6.8%
Al-Dorzi *et al.* [21]	Riyadh-KAMC MSICU	2003-2009	Adult ICU	2812 pts; 433 VAP	VAP	Gram-negatives 76.8%, polymicrobial 14.1%
Almuneef *et al.* [1]	Riyadh-KAMC PICU	2000-2002	Pediatric	361 ventilated; 37 VAP	VAP	*P. aeruginosa* 56.8%, *S. aureus* 18.9%, *K. pneumoniae* 10.8%, others 16.2%
Al-Obeid *et al.* [11]	Riyadh-Security Forces Hosp.	2012	Adults (ICU)	12 VAP isolates	VAP (*A. baumannii*)	*A. baumannii* (100%)
Saleem *et al.* [22]	Hail-King Khalid Hosp. ICU	2019-2020	Adults	-	VAP	*A. baumannii* (dominant)
Kabrah *et al.* [23]	Makkah-ICU	2020-2021	Adults	96 pts; 51 LRTI samples	LRTI (incl. HAP/VAP)	*K. pneumoniae* 59.4%, CoNS 11.5%, *E. coli* 8.4%, *A. baumannii* 7.3%, *S. aureus* 6.2%
Ibrahim [24]	Bisha-King Abdullah Hosp. ICUs	2016-2018	Mixed (ICUs)	3736 specimens; 358 isolates	ICU infections (incl. pulm.)	*Acinetobacter* 27.2%, *Pseudomonas* 23.8%, *Klebsiella* 18.6%, *E. coli* 12.8%
Akbar [27]	Jeddah-KAUH	1998-1999	Adults (DM vs. non-DM)	354 cultures	CAP vs HAP	HAP: GNB (Klebsiella, *Pseudomonas*, *E. coli*); CAP: *H. influenzae*
Balkhy *et al.* [26]	Riyadh-NGHA (KAMC)	2003	Mixed inpatients	562 pts; 45 HAIs; 13 VAP	HAIs (incl. VAP)	*Pseudomonas* 21.3%, *Enterococcus* 16.9%, *Staphylococcus* 13.5%, *Klebsiella* 10.1%
Hakami *et al.* [28], Cureus	Jeddah-MNGHA (≥15y)	2016-2019	Adults	1151 isolates; 568 respiratory	RTIs (incl. HAP/VAP)	*P. aeruginosa* 28.5%, *K. pneumoniae* 17.6%, *A. baumannii* 15.1%, MRSA 7.2%
Othman and Abdelazim [25]	Saudi Arabia-King Fahd Military Medical Complex (Adult ICU)	Sept 2012-Aug 2013	Adults, 48 ventilated >48h	48 patients; 17 VAP (35.4%)	VAP	*P. aeruginosa* 41%, *K. pneumoniae*, *S. aureus*, *E. coli*

Table 3: Antibiotic Resistance and Susceptibility Pattern

Study Setting	Main pathogens (quantified)	Antibiotics tested	Reported resistance (%) or findings
Al-Obeid *et al.* [11]-Riyadh SFH (VAP patients)	*Acinetobacter baumannii* (12 XDR isolates)	Imipenem, Meropenem, Ceftazidime, Ciprofloxacin, Colistin, Gentamicin, Tigecycline, Ampicillin-Sulbactam	12/12 (100%) resistant to carbapenems and cephalosporins; 0/12 (0%) R to colistin; partial susceptibility to tigecycline/ gentamicin
Saleem *et al.* [22]-Hail ICU (2019-2020)	*Acinetobacter baumannii* (82 VAP isolates)	Imipenem, Meropenem, Colistin, Aminoglycosides, Tigecycline, Teicoplanin	82/82 (100%) carbapenem-resistant both years; colistin R rose 0/41 (0%) → 4/41 (8.6%); IMP/VIM/NDM-1 detected
Ibrahim [24]- Bisha ICUs (2016-2018)	*Acinetobacter* 27.2%, *Pseudomonas* 23.8%, *Klebsiella* 18.6%, *E. coli* 12.8%	Cefuroxime, Cefotaxime, Aztreonam, Ciprofloxacin, Piperacillin, Trimethoprim-Sulfamethoxazole, Colistin	*A. baumannii* 93-97% R to nearly all; colistin ~4% R; MDR GNB ~68% overall
Kabrah *et al.* [23]- Makkah ICU (2020-2021)	*Klebsiella* 59.4%, *A. baumannii* 7.3%, *S. aureus* 6.2%, *E. coli* 8.4%	Aztreonam, Ampicillin, Co-amoxiclav, Cefotaxime, Cotrimoxazole, Meropenem, Vancomycin, Teicoplanin	Klebsiella 80-96% R to β-lactams/TMP-SMX; *A. baumannii* ~90% R to β-lactams; *S. aureus* 100% S to vancomycin/ teicoplanin
Hakami *et al.* [28]-Jeddah MNGHA (2016-2019)	*P. aeruginosa* 28.5%, *K. pneumoniae* 17.6%, *A. baumannii* 15.1%, MRSA 7.2%	Piperacillin-Tazobactam, Ampicillin, Ceftriaxone, Ciprofloxacin, Meropenem, Colistin	*P. aeruginosa* 52% R to pip-tazo; *K. pneumoniae* 83% R to ampicillin; *A. baumannii* 53% R to pip-tazo; MRSA 100% S to vancomycin

resistant. The study showed that even the last-line of defense was starting to fail. This shows how important care programs and infection control are to stop the spread of resistant clones.

Bisha King Abdullah Hospital ICUs [24]

This extensive retrospective surveillance investigation (2016-2018) examined 3736 ICU specimens, detecting 358 culture-positive isolates, primarily Gram-negative bacilli. The predominant pathogens were *Acinetobacter* spp. (27.2%), *Pseudomonas* (23.8%), *Klebsiella* (18.6%) and *E. coli* (12.8%). Resistance rates were exceedingly elevated: *A. baumannii* exhibited 93-97% resistance to nearly all evaluated antibiotics, including β-lactams and fluoroquinolones, while demonstrating approximately 4% resistance to colistin, so affirming its preserved efficacy. *Klebsiella* and *Pseudomonas* isolates exhibited extensive multidrug resistance, with numerous bacteria co-resistant to cephalosporins and aminoglycosides. In all, 68% of all Gram-negative isolates were designated as multidrug-resistant (MDR). This research provides one of the most exhaustive multicenter quantitative datasets from southern Saudi Arabia and substantiates the classification of ICU environments as high-risk reservoirs of MDR organisms.

Makkah Intensive Care Unit [23]

A mixed ICU surveillance from Makkah hospitals during 2020 and 2021 found 51 lower respiratory isolates in 96 critically sick patients. Of the pathogens that were found, 59.4% were *Klebsiella pneumoniae*, 7.3% were *A. baumannii*, 6.2% were *S. aureus* and 8.4% were *E. coli*. It was found that Gram-negative samples were very resistant to trimethoprim-sulfamethoxazole, aztreonam and β-lactams when tested for antimicrobial activity. *A. baumannii* exhibited resistance to β-lactams and intermediate resistance to aminoglycosides, with a prevalence of approximately 90%, while *Klebsiella pneumoniae* demonstrated resistance to 80-96% of the β-lactams and TMP-SMX that were tested. In contrast, glycopeptides, such as vancomycin and teicoplanin, were found to be entirely effective against all *S. aureus* isolates, including MRSA. The study emphasized the coexistence of MDR Gram-negative and Gram-positive organisms and reaffirmed the necessity of empirical regimens that are specific to the ICU and account for dual pathogen coverages.

Jeddah MNGHA Hospital [28]

This extensive retrospective investigation conducted at a tertiary care facility from 2016 to 2019 examined 1151 bacterial isolates, including 568 respiratory samples. In the subgroup of hospital-acquired pneumonia, *Pseudomonas aeruginosa* was the most prevalent at 28.5%, followed by *Klebsiella pneumoniae* at 17.6%, *Acinetobacter baumannii* at 15.1% and Methicillin-resistant *Staphylococcus aureus* at 7.2%. Resistance testing disclosed the subsequent findings: *P. aeruginosa* exhibits 52% resistance to piperacillin-tazobactam; *K. pneumoniae* shows 83% resistance to ampicillin; *A. baumannii* demonstrates 53% resistance to piperacillin-tazobactam and significant resistance to other β-lactams. *Staphylococcus aureus* (MRSA) exhibited complete susceptibility to vancomycin. These findings provide important regional data regarding antimicrobial susceptibility patterns among respiratory pathogens in Saudi Arabia.

In all of the Saudi research that were looked at, Gram-negative bacilli were found to be the main cause of HAP and VAP. In spite of the fact that *Staphylococcus aureus* and more specifically MRSA, remained to be a substantial Gram-positive contributor, the most prevalent infections were caused by *Acinetobacter baumannii*, *Pseudomonas aeruginosa* and *Klebsiella pneumoniae* among the Gram-positive bacteria. The prevalence of Pseudomonas was higher in pediatric settings; however, the trends in intensive care units for both children and adults were comparable. Antimicrobial resistance was prevalent, with carbapenem and β-lactam resistance standing out in particular. Even though there were reports of developing resistance in the north, colistin and tigecycline still worked against most MDR and XDR isolates. Carbapenem resistance in *A. baumannii* was almost universal (≥95%) in all five quantitative studies, indicating that it is a critical-priority infection in Saudi intensive care units.

The susceptibility to colistin remained high (90-100%), although Hail and Bisha studies experienced early decline (up to 9% resistance). *Pseudomonas aeruginosa* had approximately 50% resistance to piperacillin-tazobactam but *Klebsiella pneumoniae* exhibited the highest β-lactam resistance (80-96%). Vancomycin and teicoplanin remained completely effective against *S. aureus* and MRSA across all datasets. Collectively, these findings show a shift from MDR to XDR phenotypes and provide a solid quantitative foundation for future pooled or meta-analytical resistance models in Saudi hospitals. Overall, these studies show an increasing trend in resistance over the last two decades, emphasizing the critical need for national antimicrobial stewardship and infection control strategies.

DISCUSSION

This systematic review brings together data from the last 20 years on Ventilator-Associated Pneumonia (VAP) and Hospital-Acquired Pneumonia (HAP) in Saudi Arabia. The studies that were looked at all show that Gram-negative bacilli are the most common diseases. *Acinetobacter baumannii*, *Pseudomonas aeruginosa* and *Klebsiella pneumoniae* are the most common. This is in line with what's happening around the world in intensive care units, where Gram-negative organisms like HAP/VAP are more common. However, compared to many Western studies, the relative burden of *A. baumannii* in Saudi cohorts seems to be particularly high, which shows how antimicrobial resistance (AMR) works in that area.

Studies from Saudi Arabia and other parts of the region show that hospital- and ventilator-associated pneumonias (HAP/VAP) are mostly caused by Gram-negative bacteria

that are becoming more resistant to antibiotics. It was found that *Pseudomonas aeruginosa* was the most prevalent respiratory infection in Jeddah, accounting for 28.5% of all cases and it shown resistance to piperacillin-tazobactam that was greater than fifty percent [28]. The growth of β-lactam resistance across several Saudi locations is confirmed by the presence of comparable resistance levels among *Klebsiella pneumoniae* in Madina, as reported by Al-Zalabani *et al.* [10] in 2020 according to their research [29]. These results are similar to ICU reports from Bisha and Riyadh, which also talked about how common multidrug-resistant (MDR) Gram-negative organisms were, especially *Acinetobacter baumannii*, *P. aeruginosa* and *K. pneumoniae* (24). These reports showed a problem across the country, which is in line with what has been seen around the world in ICUs, where Gram-negative bacilli cause most severe infections [4,30].

A landmark study in Riyadh revealed that 8% of hospitalized patients had at least one Healthcare-Associated Infection (HAI), predominantly ventilator-associated pneumonias, line-related bloodstream infections and catheter-associated urinary tract infections, with Pseudomonas and Enterococcus identified as primary pathogens and MRSA constituting 40% of *S. aureus* cases. [26]. Similar frequency in Lebanon [31] and multicenter surveillance of device-associated infections across Saudi Ministry of Health hospitals [32] illustrates that device-related infections continue to be a significant challenge in Middle-Eastern hospitals. These results are similar to those of the EPIC III global research, which found that device-associated infections are the most common HAIs in the globe and are mostly caused by Gram-negative organisms [4,30].

Earlier data from Jeddah also showed differences between community- and hospital-acquired pneumonia: *H. influenzae* was most common in Community-Acquired Pneumonia (CAP), while Pseudomonas was most common in Hospital-Acquired Pneumonia (HAP) isolates and diabetic patients were more likely to get *S. aureus* pneumonia [27]. Shah and Hux [33] and Lipsky *et al.* [34] both support the link between diabetes and pneumonia severity. This is especially important in Saudi Arabia, where a high prevalence of diabetes makes people more likely to get serious bacterial infections and worsens outcomes. The high death rate in that group, which was close to 50%, was similar to early European ICU studies where *Pseudomonas*, *Klebsiella* and *S. aureus* were the most common bacteria [35], showing that comorbidity burden, not location, is the main factor that determines mortality severity.

In the Bisha study, *A. baumannii* was responsible for approximately 27% of ICU isolates, with carbapenem resistance that was nearly universal and MDR rates of 97.5% [24]. The organism's endemicity in critical-care settings was confirmed by the observation of comparable resistance levels in Riyadh ICUs [20,36]. The same pattern was observed in Makkah, where *K. pneumoniae* accounted for nearly 60% of ICU isolates. These isolates exhibited over 80% resistance to the majority of β-lactams and cotrimoxazole, leaving carbapenems as the sole partially effective treatment option [23]. The pervasive selective pressure from broad-spectrum antibiotic use and cross-hospital transmission of resistant clones is suggested by the multidrug resistance observed in disparate cities.

In northern Saudi Arabia, the prevalence of *A. baumannii* among VAP cases in Hail ICUs increased from 21-31% between 2019 and 2020, with carbapenem resistance attributed to the various genes-similar patterns have been documented in Gulf Cooperation Council hospitals [37,38]. Colistin is a last resort treatment, therefore the fact that these isolates have reduced their sensitivity to it from 100 to 91% is very worrisome. This discovery is in line with what was seen in the intensive care unit in Tunisia, where cases of VAP with high death rates were caused by *A. baumannii* that had developed significant drug resistance [39]. A shift from sporadic to endemic dissemination of carbapenem resistance was noted in Riyadh, with OXA-23 carbapenemase being identified as the main catalyst [36]. This enzyme, widely acknowledged as the principal mechanism in *A. baumannii* [40], underscores the necessity for molecular surveillance and stringent management to curtail further gene dissemination.

The multicenter INICC report by Rosenthal *et al.* [41] confirms these patterns, demonstrating that VAP rates in developing-country ICUs are several times greater than NHSN standards. This disparity is primarily due to resource and compliance disparities.

Despite successes in infection control, resistance challenges are being driven by *A. baumannii* and other Gram-negatives, according to local Saudi data [36]. While there has been some improvement after using ventilator bundles, the persistence of MDR still makes it difficult to get the desired results [42].

Analogous tendencies are observed in pediatric intensive care units. Elward *et al.* [43] found that previous antibiotic usage, reintubation and enteral feeding were independent risk factors for Ventilator-Associated Pneumonia (VAP) and Citak *et al.* [44] found that Gram-negative predominance and high proportions of VAP among infections in the Pediatric Intensive Care Unit (PICU) were confirmed by Turkish cohorts. The need for pediatric-specific preventative bundles and enhanced airway-care compliance is highlighted by the fact that VAP rates in Saudi pediatric settings are still significantly higher than National nosocomial infections surveillance system (NNIS) benchmarks [38].

According to Othman and Abdelazim [25] ventilated apnea (VAP) occurred in twenty-five percent of ventilated patients at King Fahd Military Medical Complex (36 per one thousand vent-days), with Pseudomonas being the most common isolate. The infection considerably lengthened the duration of ventilation and the length of stay in the intensive care unit, which is in line with the findings of European researchers [45]. However, mortality differences were not statistically significant, which may be a result of timely empiric therapy. In Tunisia, comparable reports indicated a significant prevalence of VAP with a predominance of

Gram-negative bacteria but there was a higher fatality rate linked with the infection [39]. These inter-regional discrepancies highlight how changes in intensive care unit resources, antibiotic availability and infection-control rigor can modulate outcomes even when microbial demands are comparable.

Putting together data from several Saudi centers shows a clear picture: organized prevention programs may be slowly lowering the number of VAP cases but antimicrobial resistance is still strong, especially among Gram-negative bacilli. Because of strains of *Acinetobacter* and *Klebsiella* that generate carbapenemase, decreasing colistin susceptibility and Pseudomonas' continued dominance, there is an urgent need for coordinated treatment, molecular monitoring and constant adherence to preventative bundles. This is because of the fact that these strains increase the likelihood of disease. The Saudi experience, together with the results of the regional GCC and the worldwide INICC, demonstrates both progress and gaps: surveillance has improved but resistance control is still not up to par. In order to reduce the burden of VAP and antimicrobial resistance in the healthcare system of the Kingdom in a manner that is sustainable, it is essential to make use of genomic tracking, intelligent antibiotic policies and integrated infection-prevention networks in order to correct this imbalance.

CONCLUSIONS

Multidrug-resistant (MDR) Gram-negative bacilli, particularly *Acinetobacter baumannii* and *Klebsiella pneumoniae*, continue to dominate hospital- and ventilator-associated pneumonia in Saudi Arabia. The emergent decline in colistin susceptibility, the increasing prevalence of MDR and extensively drug-resistant (XDR) strains and the rising resistance to carbapenems collectively present a significant therapeutic challenge. These pathogens have maintained a strong footing in intensive-care settings, despite localized improvements in infection-control practices, which is indicative of both environmental resilience and antibiotic selection pressures.

The evidence from Saudi centers demonstrates the pressing need for integrated national surveillance systems with uniform antimicrobial susceptibility testing to enable reliable trend monitoring. Robust antimicrobial stewardship programs targeting high-risk ICU pathogens, as well as increasing adherence to infection-prevention bundles, have been shown to reduce ventilator-associated infection rates in Riyadh and other centers. Nevertheless, resistance evolution cannot be halted solely through prevention. In order to address the increasing threat of XDR Acinetobacter and ESBL- or carbapenemase-producing Enterobacterales, it is imperative that we make strategic investments in research on novel antimicrobial drugs and alternative methods of antibiotic treatment.

HAP/VAP is a persistent clinical and public health issue in Saudi Arabia that is caused by multidrug-resistant Gram-negative pathogens, as described in the literature. Despite the fact that preventative remedies can decrease the incidence, their impact on resistance dynamics is negligible. To stop the spread of antibiotic resistance and keep current and future therapies effective in Saudi intensive care units, the country needs a comprehensive plan that includes monitoring, stewardship, infection control and innovation.

Implications for Practice

The findings of this analysis have significant repercussions for clinical practice and the policy that governs infection control in facilities that provide acute care in Saudi Arabia. *Acinetobacter baumannii*, *Pseudomonas aeruginosa* and Extended-Spectrum β-Lactamase (ESBL) or carbapenemase-producing *Klebsiella pneumoniae* should be treated early and correctly as they are still the main pathogens that cause illness and death in ventilated patients. It is important to strengthen antimicrobial management programs so that last-resort drugs like colistin keep working and so that carbapenems and β-lactam/β-lactamase inhibitor combinations like piperacillin-tazobactam are used in the right way.

Scaling infection-prevention bundles that have proven effective in lowering VAP rates in Riyadh to a nationwide scale could help to standardize best practices and maintain incidence reductions across tertiary and rural hospitals. In order to inform empirical prescribing and detect emergent resistance patterns in a timely manner, continuous, region-specific surveillance is also necessary, utilizing harmonized susceptibility testing standards. Lastly, research should concentrate on the clinical efficacy of innovative antimicrobials, including cefiderocol and ceftazidime-avibactam, in Saudi intensive care units. At the same time, strategies should be devised to prevent the transmission of carbapenemase-producing organisms. Collectively, these measures have the potential to transform existing evidence into actionable, system-wide enhancements in patient outcomes and antimicrobial resistance control.

Limitations

There are some problems with this study that should be brought up. First, the synthesis is mostly based on public data from different Saudi institutions. These institutions have different study designs, sample sizes and microbiological methods. Variations in diagnostic criteria for HAP and VAP, along with variations in Antimicrobial Susceptibility Testing (AST) methodologies, may have led to variability and diminished direct comparison among datasets. Still, a lot of the proof we have comes from big hospitals and is from the past. Some facilities, like community hospitals and smaller facilities, may not be fully reflected because their surveillance systems are not as well set up. The third limitation is that the molecular characterisation of resistance mechanisms, such as carbapenemase and ESBL genes, was inconsistent among investigations.

In addition, it is hard to judge how resistance trends change over time because some studies only look at a small amount of time. Finally, the real number of MDR pathogens in the country might be higher than what is recorded. This is

because studies that focus on secondary care or outbreaks may be more likely to be accurate. Even with these flaws, the results give us a good picture of how HAP and VAP are spreading and how resistant they are in Saudi Arabia right now. They also show us some important gaps that need to be filled in future standardized, multicenter, prospective studies.

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