Iran J Burn Wound Res
ISSN: 3060-8414
2025, Volume 1, Number 2
Research Paper

Bacterial etiology and antibiotic susceptibility pattern of ventilator-associated pneumonia (VAP) in burn patients

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Article info:
Received: 3 Jun 2025
Accepted: 18 Jun 2025

Keywords:
Nosocomial infection
Bacteria
Antibiotic resistance
Ventilator-associated pneumonia

ABSTRACT

This research aimed to identify the spectrum of microbial pathogens associated with VAP and the drug resistance patterns at an intensive care unit (ICU) burn center in Iran. We conducted this single-center, retrospective, cross-sectional descriptive study on all burn patients with VAP who were treated in the ICU at Velayat Burn Injuries Hospital in Rasht, northern Iran. In this study, 29 samples were obtained from burn patients, of which *P. aeruginosa* accounted for 48.3%, *Klebsiella* for 17.2%, *E. coli* for 10.3%, coagulase-negative Staphylococci for 6.9%, and unknown pathogens for 17.2% of the bacterial cultures. All the *E. coli* isolates and most of the *Klebsiella* isolates (80%) were obtained in the first two days of hospitalization. *P. aeruginosa* was mainly isolated during the first 2 days of hospitalization (71.4%). The mortality rate was 75.9%, while 24.1% of the patients were discharged. Antibiotic susceptibility patterns of Gram-negative bacteria revealed that *Enterobacter* and *P. aeruginosa* were predominantly susceptible to aminoglycosides, with Amikacin exhibiting the highest effective rates of 40% and 66.7%, respectively. A guideline-based approach using the local ICU antibiogram can decrease the likelihood of Multidrug-resistant (MDR) strain occurrence.

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https://iranjburns.com/
https://doi.org/10.61882/ijbwr.1.2.18

1. Introduction

Nosocomial infections (NIs) remain a significant issue among patients [1]. Nosocomial infection is defined as an infection in patients who have been in the healthcare system for over 48 hours and have no evidence of infection at the time of admission [2]. In a study of selected hospitals in Tehran, 14.9% of ICU patients tested positive for NIs [3]. VAP is among frequent healthcare-associated infections, and its prevalence among all ICU intubated patients is 9–27%. [4]. VAP is divided into two subtypes: early-onset VAP, which begins within four days of mechanical ventilation, and late-onset VAP, which occurs after four days. Antibiotic-resistant hospital-acquired organisms cause late-onset VAP, while antibiotic-susceptible community-acquired bacteria primarily cause early-onset VAP [5]. Old age, male gender, nursing home residency, alcohol consumption, smoking, and oral hygiene are among the most predisposing factors for VAP [6]. Various pathogens, including viral, bacterial, fungal agents, and parasites, may cause NIs [7,8]. The most common pathogens causing NIs are *Clostridium difficile* (12.1%), followed by *Staphylococcus aureus* (10.7%), *Klebsiella pneumoniae* (9.9%), *Escherichia coli* (9.3%), and *Enterococcus* species (8.7%) [8]. The changing spectrum of VAP in third-world countries and the development of multi-drug-resistant strains are linked to the disproportionate application of broad-spectrum antibiotics early in ICUs [9]. Therefore, the present research sought to identify the spectrum of infectious agents associated with VAP and the drug resistance pattern in an ICU of a burn center in Iran.

2. Materials and Methods

2.1 Study design

This retrospective cross-sectional investigation was conducted using recorded data on all burn patients with VAP admitted to the ICU at Velayat Burn Injuries Hospital in Rasht, Iran. We monitored the patients until they were discharged from the ICU or expired. The inclusion criteria for the study were confirmed VAP in burn patients, defined as an infection occurring within the first 48-72 hours of admission. Exclusion criteria included any other type of pneumonia with different etiologies.

2.2 Microbiological analysis

The attending nurses obtained samples from patients using aseptic conditions and inoculated them into the transfer culture media. All samples were incubated aerobically at 37°C for 24-72 h consecutive days in Eosin Methylene Blue (EMB) and Blood agar media (Merck, Germany). Any culture detected as positive growth was removed during the incubation periods and considered for further investigation. Standard microbiological methods were used to isolate and identify the bacteria from subcultured samples.

2.3 Antimicrobial susceptibility testing

Antimicrobial susceptibility tests were conducted using locally available antibiotics and the disk diffusion method, as recommended by the Clinical & Laboratory Standards Institute (CLSI) [13]. The selection of antimicrobial disks (HiMedia, India) and control strains for Gram-positive and Gram-negative isolates was also based on CLSI recommendations.

2.4 Data sets and data analysis

Demographic variables, medical history, cause of the burn, duration of admission, outcome, and inhalation of burn injury were collected from files. The patients underwent routine care provided by healthcare staff, and all data were collected from files without direct patient contact. Laboratory measures evaluated results for antibiotic resistance patterns associated with VAP. Data were analyzed using SPSS v22 by Chi-square tests. P-values of less than 0.05 were considered meaningful.

3. Results

During the study period, 594 patients were evaluated for VAP, and 29 samples were obtained from burn patients with confirmed VAP, of which *Pseudomonas aeruginosa* accounted for 48.3% (14/29), *Klebsiella* for 17.2% (5/29), *E. coli* for 10.3% (3/29), Non-fermenting bacteria (except *Pseudomonas*) for 17,2% (5/29), and Coagulase-negative *Staphylococci* for 6.9% (2/29) of the bacterial cultures (Table 1). The patient's median age was 41.2 years (±15.96 years), with a range of 21 to 84 years. 75.9% of the patients (22 out of 29) were men, and 24.1% (7 out of 29) were women. All the strains were obtained from patients admitted to ICU.

Table 1. Bacterial distribution in patients

Microbe	Count	Percent (%)
Coagulase-negative *Staphylococci*	2	6.9
E. coli	3	10.3
Klebsiella	5	17.2
Pseudomonas Aeruginosa	14	48.3
Non-fermenting bacteria (except pseudomonas)	5	17.2
Total	29	100

All *E. coli* and most *Klebsiella* isolates (80%) were obtained within the first two days of hospitalization. *P. aeruginosa* was primarily obtained from patients hospitalized for over two days (71.4%). We identified a statistically significant association between the length of hospitalization and the organism causing the infection ($P < 0.05$). The mortality rate was 75.9%, while 24.1% of the patients were discharged. However, among patients who died, the interquartile range (IQR) of total body surface area (TBSA) as a cofounder was 56.25%-77.5% compared to 22.5%-50.5% among surviving patients.

The median TBSA burn was 60%, with a range of 7% to 100%. Most patients had a TBSA burn between 50-70% (48.3%), with 20.7% suffering from burn extent over 74% TBSA. Burn patients with 24% TBSA or less accounted for 3.4%, and those with TBSA between 25% and 49% comprised about 27.6%. The average hospitalization duration was 21.82 ± 67.51 days, and the mean distance between hospitalization and infection occurrence was approximately 4.37 ± 5.01 days. 72.4% of the patients suffered from an inhalation injury, whereas 27.6% of the patients positive for VAP had no history of inhalation injury. Nine out of 14 patients had positive *Pseudomonas aeruginosa* culture, and all patients with *Klebsiella*-positive culture expired. However, we did not detect a statistically significant relationship between organisms and outcomes based on our chi-squared tests ($P > 0.05$).

The antibiotic resistance patterns of Gram-negative bacteria indicated the highest resistance rate against gentamicin (GEN) (98.7%), followed by ciprofloxacin (CIP) (90%) and imipenem (IMI) (83.3%). *Enterobacteriaceae*, including *E. coli* and *Klebsiella*, showed high rates of resistance to CFP (Cefepime) (66.7%), GEN (62.5%), and CIP (62.5%). *P. aeruginosa* and *Enterobacteriaceae* were most susceptible to AMK (Amikacin), with 40% and 66.7% sensitivity, respectively. Among the antibiotics tested in this study, Amikacin (AMK) demonstrated the highest effectiveness against both Gram-negative bacteria and *Enterobacteriaceae* causing VAP infections, with sensitivity rates of 40% and 66.7%, respectively (Table 2).

4. Discussion

Nosocomial pneumonia is a frequent complication among ICU burn patients, particularly those who require endotracheal intubation and mechanical ventilation [10]. Early diagnosis and appropriate antibiotic therapy are critical in VAP patients, as delayed suitable antibiotic treatment leads to increased mortality [11]. Moreover, patients with burn injuries are at an increased risk of immune system dysfunction and a decreased ability to eliminate bacteria and infection [12]. Therefore, accurately identifying microbial pathogens in burn hospitals and determining their susceptibility to commonly administered antimicrobial agents has a significant impact on patient outcomes [13]. The initial antibiotic choice for the empirical treatment of VAP must be sufficiently broad to protect against all possible microorganisms, including antimicrobial-resistant pathogens, especially in patients who have been previously treated with antibiotics [14]. In this study, conducted on 594 patients admitted to the ICU, 4.9% were diagnosed with VAP. Several contributing factors, including the use of enteral nutrition via nasogastric tubes, endotracheal colonization, improper body positioning, impaired consciousness, and suboptimal hygiene practices, may influence the relatively low incidence of VAP in our study. Our study reports a lower incidence of VAP compared to a review by Cook et al. in 16 intensive care units in Canada, involving 1014 mechanically ventilated patients [15].

They noted that out of 1014 patients, 177 (17.5%) were diagnosed with VAP 9.0 ± 5.9 days after admission to the ICU. Regarding data from Polish Intensive Care Units between 2013 and 2015, the incidence of VAP was 8% among 2547 ICU patients [16], which is slightly higher than the figures reported in our study. Sen et al. reported an 18% occurrence of VAP among 314 adult burn patients who underwent mechanical ventilation in a retrospective study [16]. Slightly higher than the figures reported in our study. Sen et al. reported an 18% occurrence of VAP among 314 adult burn patients who underwent mechanical ventilation in a retrospective study [17]. This higher incidence of mortality could be because our study only included critically ill burn patients who had to be mechanically ventilated in the ICU and not the entire population of burn patients with pneumonia, lack of medical healthcare, and concurrent antibiotic guidelines. In the analysis of Yesilbag et al. on 183 VAP patients between 2016 and 2019, the mortality rate accounted for 46.4% [18], which differs from our result. As in another retrospective study on 145 VAP patients, the mortality rate was 42.8% [19].

Table 2. Antibiotic resistance pattern in *P. aeruginosa*, *E. coli,* and *Klebsiella* isolates

Antibiotic	*P. aeruginosa*			*E. coli / Klebsiella*		
	S	I	R	S	I	R
AMK [1]	40	30	30	66.7	-	33.3
IMI [2]	16.7	25	58.3	40	-	60
TOB [3]	28.6	28.6	42.8	50	-	50
GEN [4]	15.4	15.4	83.3	37.5	12.5	50
CFP [5]	33.3	11.1	55.6	33.3	16.7	50
CIP [6]	10	10	80	37.5	-	62.5

1:Amikacin/2:Imipenem/3:Tobramycin/4:Gentamicin/5:Cefepim/6:Ciprorofloxacin

The findings of Sen et al., reporting a 34% mortality rate in mechanically ventilated burn patients with VAP, are inconsistent with our results. In our study, the mortality rate was remarkably higher in VAP burn patients compared to non-VAP burn patients who underwent mechanical ventilation (34% vs. 19%) [16]. Pathogenic agents commonly associated with VAP are Gram-negative bacteria (GNB), including *P. aeruginosa, A. baumannii, K. pneumoniae, and E. coli* [20].

Our findings align with these reports, but the specific distribution of pathogens differs. This distribution contrasts with findings from an analysis conducted in Turkey [18], where Acinetobacter baumannii was identified as the most common cause of VAP (49.2%), followed by *Pseudomonas aeruginosa* (19.7%) and *Klebsiella pneumoniae* (13.7%), which reported *Acinetobacter baumannii* as the most common cause of VAP (49.2%), followed by *P. aeruginosa* (19.7%) and *K. pneumoniae* (13.7%). In Shanghai tertiary teaching hospitals, the top four pathogens were *A. baumannii* (33.96%), *K. pneumoniae* (23.58%), *P. aeruginosa* (19.81%), and *S. aureus* (7.08%) [21].

In our study, the proportion of *P. aeruginosa* was much higher than in the mentioned article. Our article's microbiology pattern data align with those of Russo et al., indicating that *P. aeruginosa* is the most commonly detected pathogen in VAP [22]. A limitation of our study is that it was conducted with a small sample size of ICU patients in a single center, and as such, our results may not be generalizable to all ICU patients with VAP. Nevertheless, this article represents our community's first study on burn patients with VAP. Unfortunately, we lack detailed information on comorbidities due to the loss of recorded information. The retrospective nature of the data collection limits the ability to recapitulate our findings. Therefore, there is a need for additional prospective studies explicitly focusing on burn patients to validate and further explore our results.

VAP plays a crucial role in the mortality and morbidity of burn patients undergoing mechanical ventilation. While our study has limitations due to its retrospective nature, it remains significant for comprehending the bacterial patterns and their susceptibility to antibiotics used in the ICU setting. This understanding is crucial in preventing prolonged mechanical ventilation, extended hospitalization, and the associated complications. To mitigate these complications, we recommend ongoing monitoring of microbial flora and the prevalence of antibiotic resistance in every hospital.

Acknowledgment

We want to thank the Ethics Committee of Guilan University of Medical Sciences and all the individuals who contributed to the completion of this study.

Authors' contributions

SR, and HS: contributed to the study design. MS, and ACh: collection of the data. AJ: performed the data analysis. MM: interpreted the data. DR, and SHR: contributed to the manuscript writing. All authors read and approved the final version of the manuscript.

Conflict of interest

No potential conflict of interest was reported by the authors.

Ethical declarations

The present research was conducted with the approval of the Medical Research Ethics Committee of Guilan University of Medical Sciences (ethical code: IR.GUMS.REC.1400.289).

Financial support

Self-funded.

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