American Journal of Infection Control 47 (2019) e21–e25

Contents lists available at ScienceDirect

American Journal of Infection Control

journal homepage: www.ajicjournal.org

Major Article

Incidence and costs of ventilator-associated pneumonia in the adult intensive care unit of a tertiary referral hospital in Mexico

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Key Words:
Hospital stay
Multidrug-resistant bacteria
Health care cost
Bacterial infection

Background: Ventilator-associated pneumonia (VAP) is defined as pneumonia that occurs after 48 hours of endotracheal intubation and initiation of mechanical ventilation. The aim of this work was to use a micro-costing method to calculate the costs generated in 2017 for the care of patients with VAP at the Hospital Juárez de México.

Methods: We performed a cross-sectional, retrospective, analytical, and observational study of the databases of the registry of health care–associated infections (HAIs) in 2017, in addition to a micro-costing study.

Results: We studied 48 VAP cases in an adult intensive care unit (AICU). In this period, 1668 ventilator days were identified, with an incidence rate of 28.8 per 1000 days. All cases were caused by multidrug-resistant (MDR) bacteria and the costs of their care exceeded the average costs for the use of antimicrobials. By calculating the profit on return as an association measure, we found that VAP caused by MDR bacteria confers 9 times the risk of increasing the costs of care above the expected average.

Conclusions: The cost for a case of VAP in the AICU is high and has an impact on the institutional budget. Control measures to prevent the spread of bacteria, particularly MDR bacteria, must be put into place in order to avoid increases in hospital stay costs and mortality.

BACKGROUND

Health care–associated infections (HAIs) are acquired by patients during their treatment in a hospital or in a health care center.[1] These infections can affect patients in any type of environment in which medical attention is received. HAIs are the most frequent adverse event occurring in health care settings, and so far no institution in the world can claim to have solved this problem. Among the consequences of HAIs are increased hospital stay, long-term disability, acquisition of multidrug-resistant (MDR) bacteria, additional costs for health systems, and increased mortality.[2-4] Ventilator-associated pneumonia (VAP) is defined as pneumonia that occurs after 48 hours of endotracheal intubation and initiation of mechanical ventilation.[5,6] The real incidence of VAP is difficult to determine; however, it is estimated that between 10% and 20% of patients receive mechanical ventilation, and the mortality attributable to VAP is approximately 10%. This rate depends on a number of factors, such as age, days of mechanical ventilation, category of admission, and other chronic diseases.[7,8] According to reports issued by the Hospital Epidemiological Surveillance Network of the General Directorate of Epidemiology of the Ministry of Health of Mexico,[9] pneumonias correspond to 20.7% of HAIs, of which up to 40% can be attributed to VAP in adult intensive care units (AICUs). Of the 3040 cases of VAP reported, a rate of 18.6 per 1000 days of mechanical ventilation was observed, and the infectious agents frequently isolated were *Pseudomonas aeruginosa*, *Acinetobacter baumannii*, and *Klebsiella pneumoniae*. Other reports have also identified the same bacteria strains in VAP cases.[10-13]

Various methodologies can be used to determine the costs associated with HAIs. Among the most frequently used are traditional costing, or coarse costing, and micro-costing, or activity-based costing.[14-16] Traditional costing is a simple methodology that provides very general information about hospital costs. Unfortunately, this method of costing is not very accurate, as it expresses the average cost of all events that have common characteristics. In contrast,

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Conflicts of interest: None to report.

https://doi.org/10.1016/j.ajic.2019.02.031

micro-costing is a more exact method, and, although its execution requires greater time and more complex analysis, it provides detailed measurements of the use of economic resources and can be seen as the standard for cost analysis in health dependencies.[17] Other methods of analysis that have been developed for the cost analysis of VAP and HAIs are based on a prospective approach and are primarily aimed at generating real-time strategies to prevent their appearance.[18-21] The cost evaluation for HAIs is complex, as it requires analyzing the cases individually to evaluate the additional attention and resources necessary for the care of each patient and to later calculate the excess resources used. It has been reported that the costs arising from treating VAP range from $1728 to $10,000 per event in the United States. Moreover, in Canada it has been calculated that the annual total cost of treating VAP is $46 million.[7,22] In Mexico, information on costs associated with VAP is limited; therefore, the objective of this work was to use micro-costing methodology to determine the costs generated in 2017 by the care of patients with VAP in the AICU of the Hospital Juarez de Mexico (HJM). Implications of the impact of the costs of VAP in adult intensive care units are also discussed.

METHODS

Design of investigation

A retrospective, transversal, observational study was designed to analyze confirmed cases of VAP by the staff of the Hospital Epidemiological Surveillance Unit of the HJM in 2017.

Period analyzed, regulatory policies, and VAP case definition

We analyzed the incidence reports of VAP cases from January to December 2017. The regulatory policies in Mexico have established mandatory notification of confirmed VAP cases to the Hospital Epidemiological Surveillance Network of the General Directorate of Epidemiology of the Ministry of Health, according to the Official Mexican Standard (NOM-045-SSA2-2005), "for epidemiological surveillance, prevention and control of nosocomial infections." According to the 2016 Clinical Practice Guidelines by the Infectious Diseases Society of America and the American Thoracic Society[23] and NOM-045-SSA2-2005, a confirmed case of VAP is classified as "a pneumonia occurring >48 hours after endotracheal intubation." Additionally, the identification of new infectious pulmonary infiltrates and the appearance of fever, purulent sputum, leukocytosis, or decreased oxygenation were considered to confirm cases of VAP.

Data collection

All data for confirmed cases of VAP were processed using Microsoft Excel (Microsoft Corporation; Redmond, WA) and were sorted by such variables as gender, age, month of detection of VAP, pathogen identified in the microbiological culture of bronchial samples, length of time (days) of ventilator use before and after the appearance of VAP, antimicrobial therapy used, and duration of the antimicrobial therapy.

Statistical analysis

For the statistical analysis, simple frequencies percentages were used. The rate of VAP was calculated for 1000 days of mechanical ventilation. Risk factors were derived from calculating the prevalence odds ratios. A micro-costing methodology was used for the cost analysis of expenses generated by patients for hospital services.

Ethical considerations

No ethical approval was obtained for using the information, as the data were collected during routine activities of the Hospital Epidemiological Surveillance Unit; however, the collection and presentation of information were carried out according to the principles of confidentiality and discretion as outlined by the Federal Law of Accountability and Access to Public Government Information.

RESULTS

We studied 48 cases of VAP detected in the AICU in 2017. In this period, 1668 ventilator days were counted with an incidence rate of 28.8 per 1000 ventilator days. The highest recorded rate, 48.8 per 1000 ventilator days, was in the month of March, and the lowest rate, 7.5 per 1000 ventilator days, was recorded in the month of February (Fig 1). The average age of patients with VAP was 44 years (minimum, 17 years; maximum, 79 years). Of the 48 patients, 71% (n = 34) were male and 29% (n = 14) were female; 67% (n = 32) of the cases died during their hospital stay and 33% (n = 16) were discharged to their homes (Table 1).

Stay and hospital origin of patients with VAP

The average medical stay (from the first day of medical attention to the last day of hospital discharge) of the VAP cases was 23 days (minimum, 7 days; maximum, 54 days). The average stay of VAP patients in the AICU was 14 days (minimum, 3 days; maximum, 35 days). With regard to where the patients were intubated, 54.2% were in the AICU, 33.3% in adult emergencies, 4.2% in internal medi-

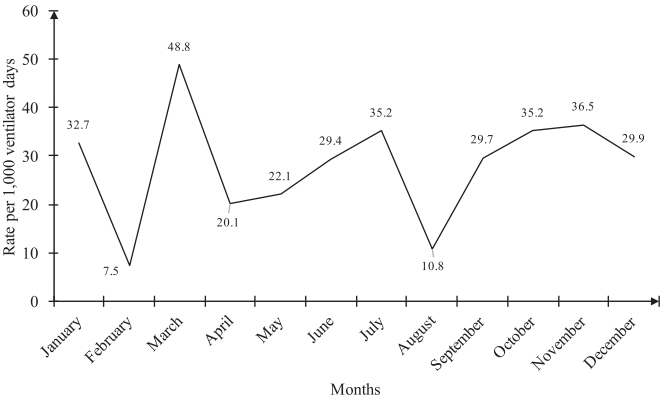

Fig 1. Incidence of ventilator-associated pneumonia in the adult intensive care unit at the Hospital Juárez de México in 2017.

Table 1
Characteristics of VAP cases in the AICU at the Hospital Juárez de México in 2017

Characteristics of patients	Value
Male, n (%)	34 (71)
Female, n (%)	14 (29)
Age (y), average ± SD	44.2 ± 14.9
Days of hospitalization in the AICU, average ± SD	14.9 ± 7.8
Ventilator days, average ± SD	13.7 ± 7.7
Patients who survived after VAP, n (%)	32 (67)
Patients who did not survive after VAP, n (%)	16 (33)

AICU, adult intensive care unit; *SD*, standard deviation; *VAP*, ventilator-associated pneumonia.

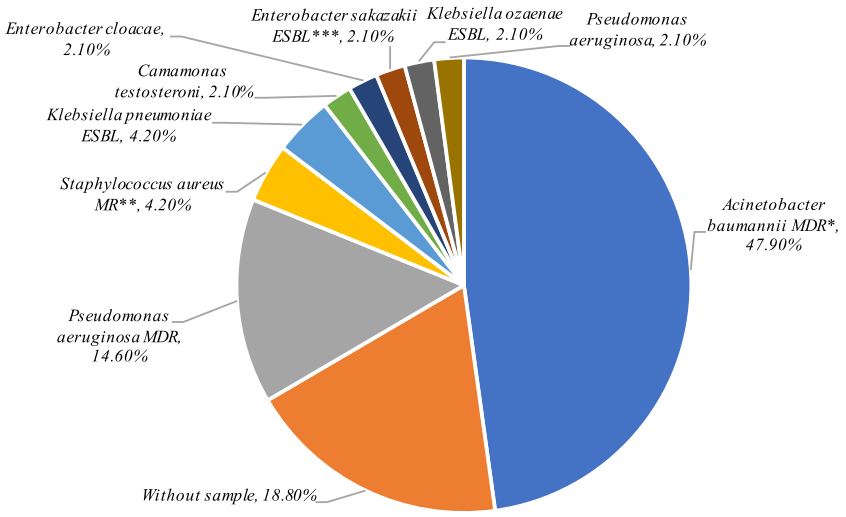

Fig 2. Distribution of infectious agents in patients with ventilator-associated pneumonia in the adult intensive care unit of the Hospital Juárez de Mexico in 2017. *ESBL*, extended-spectrum β-lactamase; *MDR*, multidrug-resistant; *MR*, methicillin-resistant.

cine, 4.2% in neurosurgery, 2.1% in general surgery, and 2.1% in infectology. For 56.2% (n = 27) of the patients, we proceeded with orotracheal intubation for mechanical ventilation, and in 43.8% (n = 21) tracheostomy was performed. The average time of mechanical ventilation was 13 days (minimum, 1 day; maximum, 36 days).

Etiological agents of VAP

In order to understand the etiological agents of the cases of VAP, in 89.6% of the cases classic microbiological cultures and automatized phenotypic identification were performed from samples of expectoration. On average, 2 microbiological cultures were carried out per case of VAP, with a maximum of 7 bacteriological analyses for a single patient. Additionally, blood cultures were performed in 50% of the cases. Chest radiography studies were performed in 97.2% of the cases, with an average of 4 radiographs per case (in 1 case, a maximum of 7 radiographs). In 35.4% of the cases, tomographic analyses were performed. With regard to results of the microbiological cultures, Gram-negative bacteria were isolated from 94.3% of the cases and Gram-positive bacteria from 5.7% of the cases. Multidrug-resistant *Acinetobacter baumannii* caused 47.9% of the VAP cases; 14.6% were caused by MDR *Pseudomonas aeruginosa*, 4.2% by methicillin-resistant *Staphylococcus aureus*, 2.1% by *Comamonas testosteroni*, 2.1% by *Enterobacter cloacae*, 2.1% by *Enterobacter zakazakii* (extended-spectrum β-lactamase), 2.1% by MDR *Klebsiella ozaenae*, 2.1% by *K. pneumoniae* (extended-spectrum β-lactamase), 2.1% by *K. pneumoniae* (carbapenemases), and 2.1% by *P. aeruginosa*; no sample was requested for microbiological analysis for 18.8% (Fig 2).

Antimicrobial treatment of patients with VAP

In all cases, antimicrobials were used. In 31.3% of the patients, 6 antimicrobials were used to treat the VAP; in 18.8%, 5 antimicrobials was used; in 14.6%, 4 antimicrobials were used; in 18.8%, 3 antimicrobials were used; and in 8%, 2 antimicrobials were used. Only in 6% of the cases was meropenem used as monotherapy. The most widely used antimicrobial was meropenem, which was administered in 85% of the cases. In the 15 cases (31.3%) in which 6 different antimicrobials were used, the MDR strains were isolated: 60%, *Acinetobacter baumannii*; 26.7%, MDR *Pseudomonas aeruginosa*; 6.7%, *Klebsiella pneumoniae* resistant to carbapenems; and 6.7%, *Enterobacter cloacae*. In all cases where the infections were associated with MDR bacteria (80%), patients died during their hospital stay.

Micro-costing analysis of VAP

The total cost of the 48 patients with VAP was $518,236.31, with an average cost per patient of $10,796.58. The analysis of unit costs revealed that the total cost of mechanical ventilation was $360,794.03, with an average cost per patient of $7561.54. With regard to the use of antimicrobials, eradication of cases of VAP cost $83,057.51, with an average cost per patient of $1730.36. For all cases of VAP caused by MDR bacteria, the cost of treatment ($2402.70 to $6571.20) exceeded the average cost of antimicrobials. The costs due to hospitalization of patients with VAP in the AICU amounted to $37,085.12, with an average cost per case of $772.60. The costs generated by hospitalization in other hospital services, before or after admission to the AICU, were $17,349.94, with an average expense of $361.45 per patient (Table 2).

Of the expenses generated for the medical care of patients with VAP in the HJM, only a percentage of the expenses is ultimately recovered, primarily by charging fees to the patient's relatives based on socioeconomic analysis of the patient's situation. These socioeconomic analyses of patients are based on criteria such as employment, monthly economic income, number of economic dependents, and housing characteristics. The socioeconomic analyses are used to classify patients into 6 categories of economic income, which determine the percentage recovery of the costs of hospital care: 10%, 18%, 33%, 55%, 75%, and 100% for categories 1, 2, 3, 4, 5, and 6, respectively. In our study, of the 48 cases of patients with VAP, 27% of them were in

Table 2
Costs of care for cases of VAP in the AICU of the Hospital Juárez de México in 2017

Category	Total cost*	Average per case*
Day bed	17,349.95	361.46
Day bed in AICU	37,085.13	772.61
Expectoration with trap	1,854.77	38.64
Blood culture	1,261.79	26.29
Thorax radiography	5,980.62	124.60
Computed tomography	3,689.74	76.87
Tracheostomy	6,016.77	125.35
Blood count	1,146.00	23.87
Mechanic ventilation	360,794.03	7,516.54
Antimicrobials	83,056.83	1,730.37
Total cost	518,236.32	10,796.59

*Costs are expressed in dollars

Table 3
Costs of medical care by socioeconomic level for cases of VAP in the AICU of the Hospital Juárez de México in 2017

Socioeconomic level	Subsidy percentage	Cases of VAP	Costs	Expenses recovered
1	10%	13	$140,355.66	$14,035.56
2	18%	21	$226,728.38	$40,811.11
3	33%	7	$755,76.12	$24,940.12
4	55%	4	$43,186.36	$23,752.49
5	75%	2	$21,593.18	$16,194.88
6	100%	1	$10,796.58	$10,796.58
Total		48	$518,236.31	$130,530.77

AICU, adult intensive care unit; *VAP*, ventilator-associated pneumonia.

Table 4
Analysis of cases of VAP in the AICU in the Hospital Juárez de México in 2017

Category	Infection by MDR bacteria	Infection by non-MDR bacteria	Prevalence odds ratio	95% confidence interval	*P* value
Above average cost	15	1	9	1.06 – 409.8	0.02
Below average cost	20	12	—	—	—

AICU, adult intensive care unit; *MDR*, multidrug-resistant; *VAP*, ventilator-associated pneumonia.

category 1, 44% in category 2, 15% in category 3, 8% in category 4, 4% in category 5, and 2% in category 6. The calculated costs of hospital care for cases of VAP were in accordance with those stipulated for category 6; therefore, the costs were equivalent to 98% of the real cost, although this calculation varied due to the different socioeconomic levels in which each patient was classified. According to the above, of the $518,236.31 directed toward the care of VAP patients, the HJM only recovered $130,530.77, so the cost to the health institution was approximately $387,705.54 (Table 3). The analyses using measures of association revealed that the costs for patients with VAP would increase 9 times above the expected average cost if the infectious agent was multidrug resistant (Table 4).

DISCUSSION

To our knowledge, this is the first study to describe and analyze the impact of costs derived from treating VAP in the AICU of a tertiary referral Mexican hospital. In this work, a seasonal association with the incidence of VAP was not identified, although previous reports have suggested a seasonal influence.[24-26] The main risk factors associated with the development of VAP in the study population were gender and age, and it was observed that adult males were the most susceptible to development of VAP. These risk factors have been previously described and evaluated in hospitalized patients in the United States.[27] VAP acquired in ICUs has been associated with significant morbidity and mortality in other hospital centers,[28] coinciding with a high percentage of cases of VAP (54.2%) identified in ICUs and in adult emergency service (33.3%). The microbiological findings in the cases of VAP we studied were consistent with those previously reported, mainly Gram-negative organisms such as *Acinetobacter*, *Klebsiella*, and *Pseudomonas* with interesting genetic markers and profiles of resistance to antibiotics, carbapenems being the most important.[30,31] The presence of MDR bacteria in HAIs represents a challenge for infection control teams and has an economic impact on health care organizations.[32]

Lemos et al[33] analyzed the costs generated by the care of HAIs caused by MDR *Acinetobacter baumannii* (including resistance to carbapenems), an important pathogen in the hospital environment. Their results showed that the costs for the MDR cases were $11,822, as compared to $4309 for cases of *A baumannii* susceptible to carbapenems, which can be interpreted as an increase in costs of 2.74 times. There is clearly a potential risk to health care facilities spending resources on treating such cases, as the cost to care for patients with VAP due to MDR bacteria is 9 times above the average to treat VAP due to non-MDR bacteria. To our knowledge, ours is the first report of isolating *Comamonas testosteroni* from a sample of expectoration of a patient with VAP. Future experiments are aimed at phenotypic and molecular characterization of this strain, as it is important to identify it in patients. This bacterium has been previously associated with several infectious processes such as acute appendicitis, bacteremias, and meningitis,[34-36] so it would not be unusual to find it in cases of pneumonia. In this work, we showed that VAP significantly increases the costs of patient care, and it considerably increases morbidity, mortality, and length of hospital stay. Earlier work that performed a cost analysis of VAP in a tertiary-level ICU in northern India revealed that the cost of VAP per patient was $5200.[37] This information contrasts with the data presented in this work, as the costs attributed to VAP in a developing country such as India are below 105.92%, even though the incidence of VAP in India, for example, is above 37%.[37] Luckraz et al[29] examined the additional costs to treat VAP as compared to pneumonias not associated with ventilation and found an increase in cost of £8829 for each VAP case, which corresponds to an increase of 140.25%.

Even when health personnel apply control measures to reduce occurrences of VAP, new cases can emerge, clearly indicating a need to implement new actions in the short or medium term, such as possible remodeling of AICUs. It has been shown that the use of single rooms for the care of patients in the ICU can reduce the prevalence of MDR bacteria.[38] It is important to note that one limitation of our study is the size of the confidence intervals for the prevalence odds ratios, which we presume is mainly due to the size of the analyzed sample (48 cases) in comparison with previous studies.[39,40] Another limitation is the absence of cost analyses by the patients' relatives, which could also have a significant impact on the total cost of care of the VAP analyzed in the study. It is necessary to update hospital strategies to prevent or reduce the occurrences of VAP, in addition to assessing whether the implementation of preventive actions is adequate. A measure that has been reported to reduce the incidence of VAP in hospitals is the use of prophylactic probiotics and subglottic endotracheal tubes, which have been demonstrated to be effective, but the decision to utilize them could require a cost-effectiveness analysis using a Markov model.[41]

Finally, the application of a checklist of clinical characteristics, laboratory studies, and epidemiological analyses is of great importance for correctly detecting VAP cases, as their incorrect classification or omission can directly impact a patient's health. The implementation

of epidemiological indicators of VAP and cost analyses can positively impact the measurement of morbidity and mortality, the economic impact of HAIs, and at some point the impact of new strategies that are implemented in health dependencies, mainly in developing countries. The development of situational diagnoses and constant evaluation of the factors that lead to VAP in hospital units must be mandatory, especially in critical areas such as the AICU. The implementation of improvement strategies could lead to significant decreases in VAP. Knowing the true costs of VAP in AICUs will further the establishment of plans, both structural and managerial, for effectively dealing with patients with VAP.

The evidence presented highlights the areas of opportunity for the application of strategies to prevent HAIs and the ability to measure the economic impact of these strategies. The cost for the diagnosis and treatment of a case of VAP in the AICU is high, and it impacts the institutional budget; therefore, control measures to prevent the spread of bacteria, particularly MDR bacteria, must be put into place to reduce the costs of hospital stays and mortality.

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