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Hospital economic impact of an outbreak of *Pseudomonas aeruginosa* infections

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Summary A total of 67 patients involved in an outbreak of *Pseudomonas aeruginosa* in the intensive care unit (ICU) were retrospectively followed to determine whether case patients experienced differences in cost, length of stay and survival rates when compared with non-affected patients. The method of microcosting, a technique that involves detailed identification and measurement of all care items and services offered by the hospital, was used to identify attributable costs related to diagnostic procedures, pharmacy and ICU stay of each patient. Seventeen patients developed nosocomial *P. aeruginosa* infection. On average, these patients incurred adjusted hospital costs of €27,917, 66% higher than non-case patients ($P = 0.002$). The extra length of ICU stay attributable to *P. aeruginosa* infection was 70 days ($P = 0.0001$). In multiple linear regression analysis, we found that *P. aeruginosa* infection was an independent predictor of increased hospital costs and length of hospital stay. On the basis of these findings, a conservative estimate of the extra cost attributable to *P. aeruginosa* infection in our ICU was €312,936 (95% confidence interval: 305,676–320,196).

Introduction

From July to September 2003, an outbreak of *Pseudomonas aeruginosa* infections was detected in a 27-bed intensive care unit (ICU), resulting in 17 case patients. An ambidirectional cohort study was performed to identify risk factors for infection. The application of analytic epidemiological methods and the use of genotyping techniques contributed to identify patient-to-patient transmission and the flexible bronchoscope as significant risk factors. Eight patients died resulting in a case fatality rate of 47.0%.

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Attributable costs and length of stay (LOS) were not assessed.

The purpose of this cohort study was to evaluate the economic impact of this outbreak using direct costs incurred by the ICU of the hospital. Included are medical costs associated with the length of hospitalisation, treatment of patients and the cost of all of the required diagnostic procedures. In the interests of establishing a valid minimum estimate of the cost of this outbreak, this article concentrates on the direct costs for the ICU in our centre.

Methods

Setting

The Hospital de La Ribera is a community referral centre with 260 beds, 27 of which are located in the ICU. In 2003 there were 1486 admissions to the ICU. An infection control team formed by a hospital epidemiologist, three internal medicine specialists and a microbiologist meet daily for surveillance and evaluation of cases.

Outbreak investigation

A full description of the primary objectives and the design of this outbreak investigation has been published elsewhere.[1] A case patient was defined as any patient who developed *P. aeruginosa* pneumonia, bacteraemia or tracheobronchitis from 1 July 2003 to 30 September 2003 after having mechanical ventilation in the ICU. Cases were ascertained through review of medical records, microbiological data, and infection control databases by the epidemiologist. Patients undergoing $>$48 h of mechanical ventilation from 1 July to 30 September 2003 formed the study population. Nosocomial infections were defined using the Centers for Disease Control and Prevention criteria.[2] This study was a secondary retrospective cohort analysis of an ambidirectional cohort study of all patients who underwent $>$48 h of mechanical ventilation during the study period. Non-cases were all patients who did not develop *P. aeruginosa* infection.

The following information was registered for cases and non-cases: age, gender, underlying diseases, main diagnosis, surgical procedure, date of admission, date of discharge, duration of mechanical ventilation (MV), diagnostic procedures, treatments, onset of infection and outcome of illness. The APACHE II (Acute Physiology and Chronic Health Evaluation) and Charlson index were calculated for each patient.[3,4]

Cost estimation

Microcosting, an evaluation technique that starts with a detailed identification and measurement of all inputs, was used to identify the cost of the resources.[5] Treatments and diagnostic procedures offered by the hospital were available in the finance department and their attributable cost was obtained from the Diari Oficial de la Generalitat Valenciana.[6] This list of costs per item or procedure was then merged into the computer file of the patients' consumptions, which includes the items and services consumed by each patient. Then the actual costs for all items and services were summed over all the items and services consumed by each patient. Finally, each attributable cost related to diagnostic procedures, pharmacy and ICU stay was merged with the infection control database.

The ICU LOS was obtained for each patient, and the number of ICU bed-days was used as a proxy for fixed costs of ICU stay. Current expenditures on fixed costs were used to convert the number of ICU bed-days into euros. Defined daily doses and their associated market prices were provided by the hospital's pharmacy department. The extra cost attributable to *P. aeruginosa* infection was defined as the difference in mean total costs between case patients and non-case patients.

On the basis of these estimates, we calculated the total costs attributable to the management of the *P. aeruginosa* outbreak by using the following formula: average cost per case patient $\times$ total number of case patients. These estimates only include ICU hospital costs.

Statistical analysis

Chi-squared or Fisher's exact test was used to compare categorical variables; Wilcoxon rank-sum test and the Kruskal—Wallis test were employed for comparison of continuous variables. The risk ratio (RR) was calculated to estimate the magnitude of association between infection by *P. aeruginosa* and death. Multiple linear regression was used to predict the average ICU total cost and ICU LOS of infection by *P. aeruginosa* (case patient). A natural log-transformed dependent variable was used after checking the normality of each model's residuals. The regression coefficient of each variable was multiplied by the value of each indicator variable in the model. Antilog transformation was used to calculate the adjusted average cost and LOS attributable to infection by *P. aeruginosa* (case patient) and adjustment variables following the method suggested by Manning

Table I Outcomes and costs for patients in the medical intensive care unit (ICU) of a 260-bed secondary care centre, by *Pseudomonas aeruginosa* infection status

Variable	Cases ($N = 17$)	Non-cases ($N = 50$)	RR	95% CI	*P*
Case fatality rate (%)	47.1	18.0	2.61	1.2–5.7	0.01
Length of ICU stay (days)[a]	45 (20–66)	7 (5–17)			0.0001
Costs (€)[a]					
Diagnostic procedures	17,287.9 (6,243.5–27,459.5)	5,440.3 (3,129.9–9,207.5)			0.0007
Pharmacy	2271 (1,264.6–3,787.3)	97.6 (96.2–689.4)			0.0001
ICU stay	43,448.4 (19,310.4–63,724.3)	67,58.6 (4,827.6–16,413.8)			0.0001
Total	70,232.9 (32,821.1–82,559.3)	12,909.2 (7,666.4–27,738.2)			0.0001

ICU, intensive care unit; RR, risk ratio; CI, confidence interval.
[a] Median (interquartile range).

et al.[7] Two-tailed $P < 0.05$ was considered to be statistically significant. Statistical analysis was performed using STATA software version 9.0 (Stata, College Station, TX, USA).

Results

Outbreak characterisation

Overall, 17 case patients were identified with 25 *P. aeruginosa* infections, including infections of the respiratory tract (pneumonia in 13 cases and tracheobronchitis in eight), the bloodstream (secondary bacteraemia, one case), the urinary tract (one case), pressure ulcer (one case) and surgical site (one case). The median age of the cases was 62 (range: 40–85) years, and one was female. The median length of ICU stay was 45 (range: 4–78) days. The median time of mechanical ventilation was 30 (range: 4–72) days. Demographic, clinical and epidemiological characteristics of the outbreak have been reported elsewhere.[1]

Cost estimates

In the unadjusted analysis (Table I), estimated total ICU costs for case patients were five times as high as those for patients whose ICU stay was not complicated by *P. aeruginosa*. Higher scores on the Charlson comorbidity index, decreasing severity of disease at admission and course complicated with other infections were associated with higher unadjusted ICU costs, although these did not reach statistical significance (data not shown). All of the studied attributable costs, diagnostic procedures, treatments and ICU stay were higher among cases than non-cases. Costs for hospitalisation of the affected patients comprised the greatest direct expense to the hospital (Table I).

Emergence of antibiotic multiresistance in *P. aeruginosa* infections (76.4% of case patients) was significantly associated with a high median economic burden (€72,356.1 vs €17,090.3, $P = 0.004$).

In a multivariate linear regression model (Table II), we found that the independent predictors of increased hospital costs included course complicated by *P. aeruginosa* infection and having more than seven days of mechanical ventilation. The adjusted estimated hospital cost for an average case patient was €27,917. This was €18,408 (66%) higher than the adjusted hospital cost for a non-case patient (€9509).

The mean cost per case of *P. aeruginosa* infection was €18,408, and 17 (25.4%) of all 67 persons of the study population were case patients. On the basis of these figures, we estimated that the extra cost attributable to *P. aeruginosa* infection in the

Table II Factors leading to increased total costs on multiple linear regression analysis

Risk factor	Relative difference	95% CI	*P*
Pseudomonas aeruginosa infection	2.9	2.0–4.3	0.002
Mechanical ventilation >7 days	5.5	4.0–7.7	0.0001
APACHE II score >12	1.5	1.2–2.0	0.81

APACHE, Acute Physiology and Chronic Health Evaluation; CI, confidence interval.
Data are relative differences in estimated hospital costs (in euros) associated with the risk factor.

ICU of our hospital reached €312,936 (95% confidence interval: 305,676−320,196).

Length of ICU stay

In the unadjusted analysis, the median total length of ICU stay for patients whose course was complicated by *P. aeruginosa* infection was 38 days longer than that for patients who did not develop *P. aeruginosa* infection. The median length of ICU stay also increased proportionally with the comorbidity at admission, age and with the diagnosis of other infections but only the association between case patient and ICU LOS was statistically significant ($P = 0.0001$) (data not shown). The emergence of antibiotic multiresistance in *P. aeruginosa* infections was significantly associated with longer median ICU stay (48 vs 11.5 days, $P = 0.005$).

In the multiple linear regression analysis (Table III), the independent predictors of increased ICU LOS were infection with *P. aeruginosa* and course complicated by other nosocomial infection. Adjustment for age, sex, multiresistance, comorbidity score and APACHE II did not improve the coefficients' estimation and precision of the final model. The estimated adjusted LOS for an average case patient was 75 days. This was 70 days longer than the adjusted LOS for a typical patient whose course was not complicated by *P. aeruginosa* infection (5.1 days). The estimated adjusted LOS for a patient with other nosocomial infection was 27 days, 21 days longer than the adjusted LOS for a patient who did not suffer a nosocomial infection.

Discussion

Analysis of this outbreak involved 67 patients admitted to the ICU during a three-month interval, environmental issues and genotyping techniques towards the identification of significant risk factors for 17 case patients.

P. aeruginosa infection was associated with an average increase in total ICU costs of €18,408 per case patient and an increased length of ICU stay of 70 days. The case fatality rate was high. In the previous report of this outbreak, the authors established that the infection with *P. aeruginosa* and the APACHE II score were the only two factors independently associated with a higher case fatality rate.[1]

To our knowledge, we have reported the first outbreak of *P. aeruginosa* infections that analyses economic impact. Published reports that take into account economic outcomes of *P. aeruginosa* infections were only involved with multiresistance.[8−12] In this outbreak, multiresistance was documented in 76.4% of *P. aeruginosa* infections and the emergence of antibiotic resistance was associated with higher costs and longer ICU LOS.

Lautenbach *et al*. reported that patients infected with imipenem-resistant *P. aeruginosa* had longer subsequent hospitalisation durations (15.5 days vs 9 days; $P = 0.02$), greater hospital costs (US$81,330 vs US$48,381; $P < 0.001$) and mortality rate [RR: 1.86 (95% CI: 1.38−2.51); $P < 0.001$] compared with patients infected with imipenem-susceptible *P. aeruginosa*.[8] In a case−control study performed in 13 Brooklyn hospitals, cases with carbapenem-resistant *P. aeruginosa* experienced longer median LOS than susceptible ones. Carmeli *et al*. examined a cohort of 489 inpatients with positive clinical cultures for *P. aeruginosa* showing a trend toward increased total charges in patients demonstrating emergence of resistance.[9,10]

Ventilator-associated pneumonia (VAP) is also reported to represent higher costs.[13−15] Warren *et al*. determined that patients who acquired VAP had significantly higher hospital costs (US$70,568 vs US$21,620; $P < 0.001$).[13] They estimated the attributable cost of VAP to be US$11,897. Hugonnet *et al*. also studied the attributable cost of VAP in a retrospective matched cohort study.[14] They found that LOS and costs were greater among case patients (7.2 days and US$24,727). Dasta *et al*. studied the contribution of mechanical ventilation to increased cost in a retrospective cohort study that included 51 009 patients admitted to US hospitals.[15] Adjusting for patient and hospital characteristics, the mean incremental cost of mechanical ventilation in

Table III Factors associated with intensive care unit length of stay (LOS) using multiple linear regression analysis

Risk factor	Relative difference	95% CI	*P*
Pseudomonas aeruginosa infection	14.8	9.2−23.9	0.0001
Other nosocomial infection	5.3	3.5−8.1	0.0001

CI, confidence interval.
Data are relative differences in estimated LOS (in days) associated with the risk factor.

intensive care unit patients was US$1522 per day. The association between other nosocomial infections and healthcare consumption has been examined previously. Brun-Bruisson *et al.* studied the costs of sepsis syndromes in a medical ICU in a one-year prospective study and concluded that ICU-acquired sepsis accounted for three times the total costs of sepsis on ICU admission.[16] Chen *et al.*, using a retrospective cohort study, evaluated the impact of nosocomial infections in medical, surgical, and mixed ICUs in a tertiary care referral medical centre.[17] They reported adjusted increased total costs of US$3,306 per patient acquiring a nosocomial infection and increased LOS of 18.2 days per patient. Our report confirms that these factors are also important in the context of an outbreak although it is necessary to exercise caution when interpreting studies performed using different economic analyses.[18]

Our study contributes to previous research in this area in several ways. First, we were able to perform detailed adjustment using economic modelling. This enabled us to isolate the independent effect of *P. aeruginosa* infections on hospital costs and LOS. Second, by use of a retrospective cohort study design of an outbreak, we were able to highlight another important aspect of infection control: potential cost savings. Finally, we analysed estimated hospital costs rather than hospital charges.

This study was conducted from an ICU perspective, and we did not estimate the costs related to resources used outside the ICU, such as post-ICU hospitalisation, visits to general practitioners, emergency services, or direct costs incurred by other healthcare procedures. Indirect costs to case patients were not studied. Therefore, the overall costs related to infection from a societal perspective are higher than our estimates. Despite these limitations, this study demonstrates the substantial expense incurred by our institution as a result of a preventable outbreak.

In conclusion, we found that *P. aeruginosa* infections were associated with increased total costs and LOS. Improvement in the prevention and control of nosocomial outbreaks may thus reduce direct costs and decrease LOS of ICU patients.

Conflict of interest statement
None declared.

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